EVALUATION OF SERUM LIPID PROFILE IN PATIENTS WITH ORAL POTENTIALLY MALIGNANT DISORDERS AND ORAL SQUAMOUS CELL CARCINOMA -A CASE CONTROL STUDY

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ORAL MEDICINE AND RADIOLOGY

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CERTIFICATE

This is to certify that this dissertation titled "**Evaluation of Serum Lipid Profile in Patients with Oral Potentially Malignant Disorders and Oral Squamous Cell Carcinoma -A Case Control Study**" is a bonafide record of work done by **Dr.S.Srividhya** under my guidance during her postgraduate study period **2009-2012.**

This dissertation is submitted to **THE TAMILNADU Dr. M.G.R. MEDICAL UNIVERSITY,** in partial fulfillment for the degree of **MASTER OF DENTAL SURGERY, BRANCH IX – Oral Medicine and Radiology.**

It has not been submitted (partial or full) for the award of any other degree or diploma.

Guided By:

Dr.Capt .S. Manoj Kumar, M.D.S,
Professor
Department of Oral Medicine & Radiology
Ragas Dental College & Hospital
Chennai – 600 119.

Dr. (CAPT.) S. MANOJ KUMAR, M.D.S.,
Prof. Oral Medicine & Radiology
RAGAS DENTAL COLLEGE & HOSPITAL
2/102, East Coast Road, Uthandi
Chennai - 600 119.

Dr. S. Shanmugam, M.D.S,
Professor and Head
Department of Oral Medicine & Radiology
Ragas Dental College & Hospital
Chennai – 600 119.

Dr. S. SHANMUGAM, M.D.S.,
Prof. & H.O.D. Oral Medicine & Radiology
RAGAS DENTAL COLLEGE & HOSPITAL
2/102, East Coast Road Uthandi
Chennai - 600 119

Dr. S. Ramachandran, M.D.S,
Principal,
Ragas Dental College & Hospital
Chennai - 600 119.

PRINCIPAL
RAGAS DENTAL COLLEGE AND HOSPITAL
UTHANDI, CHENNAI-600 119

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Place : Chennai - 600 119

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LIST OF ABBREVIATIONS

S.NO	ABBREVIATION	EXPANSION
1.	PMD	Potentially Malignant Disorders
2.	OSCC	Oral Squamous Cell Carcinoma
3.	OL	Oral Leukoplakia
4.	OSMF	Oral Submucous Fibrosis
5.	TC	Total Cholesterol
6.	LDL	Low Density Lipoprotein
7.	HDL	High Density Lipoprotein
8.	VLDL	Very Low Density Lipoprotein
9.	TGI	Triglycerides
10.	WHO	World Health Organisation
11.	ST	Smokeless Tobacco
12.	BCC	Basal Cell Carcinoma
13.	AK	Actinic Keratosis
14.	EDTA	Ethylene Diamine Tetra Acetic Acid
15.	UV	Ultra Violet
16.	TNM	Tumor Node Metastasis
17.	AJCC	American Joint Cancer Committee

Hippocrates, the father of medicine coined the term "Karkinos" for the non healing neoplastic ulcers and "Karkinoma'' for the solid malignant tumours. Both the terms derived from Greek. "Karkinos" means "Crab''. The reason behind the terminology is the malignant tumors adhere to any part,which it seizes upon in an obstinate manner like crab.[1]

The term "Oral cancer'' is used to describe any malignancy that arises from the oral tissues. Oral cancer is the most life threatening disease of oral tissues, causing a major health problem in India[1].Oral cancer is the sixth most common cancer worldwide and continues to be the most prevalent cancer related to the consumption of tobacco, arecanut, alcohol and other carcinogenic products.

Several studies have shown clearly that oral cancer usually preceded by Potentially malignant disorders. Some of these lesions share the same etiological factors with oral cancer, particularly the use of tobacco and areca nut exhibit the same site and habit relationship. Individuals with Potentially malignant disorders such as oral leukoplakia and oral submucous fibrosis run a risk that is 69 times higher for them to develop oral cancer compared to tobacco users who do not have pre cancer.[2]

In recent years, emphasis has been placed on detecting molecular markers from body fluids such as saliva, urine and others, for detecting, predicting prognosis, and monitoring the oral cancer progression. The idea of screening and following patients with malignancy by blood based tests is appealing from several points of view including its ease, economic advantage, non invasiveness, and possibility of repeated sampling.[3] Lipoproteins are

clusters of proteins and lipids, all tangled up together to carry lipids in our blood.

Several authors propose that hypocholesterolemia is a predisposing factor for cancer development.[4] The habit of tobacco consumption is a known etiologic factor for development of Oral Potentially malignant disorders and Oral cancer. Patients with Potentially malignant disorders have also been reported to show a significant tendency to develop cancer. In oral cancer development, tobacco plays an etiologic role. It is believed that tobacco carcinogens induce generation of free radicals and reactive oxygen species responsible for the high rate of oxidation/peroxidation of polyunsaturated fatty acids which affects the cell membrane and are thus involved in carcinogenesis. Because of the lipid peroxidation, there is a greater utilization of lipids for new membrane biogenesis.[5]

This study is conducted to understand the role of these lipids in the oral potentially malignant disorders like Oral leukoplakia, Oral submucous fibrosis and also in Oral Squamous Cell Carcinoma . It can be suggested that Serum lipid status may be considered as a useful indicator for initial changes occurring in the neoplastic cells.

AIM:

To evaluate the serum lipid profile in Potentially malignant disorders like Oral Leukoplakia, Oral Submucous fibrosis and also in Oral squamous cell carcinoma.

OBJECTIVES:

1. To determine the serum levels of Total cholesterol, Low density lipoprotein, High density lipoprotein, Very Low density lipoprotein, Triglycerides of patients with Potentially malignant disorders like Oral Leukoplakia, Oral Submucous fibrosis.
2. To determine the serum levels of Total cholesterol, Low density lipoprotein, High density lipoprotein, Very Low density lipoprotein, Triglycerides of patients with Oral squamous cell carcinoma.
3. To compare these levels with the control group, Potentially malignant disorders as well as in Oral squamous cell carcinoma.

The study is about the Evaluation of serum lipid profile in Oral Potentially Malignant disorders and Oral Squamous cell carcinoma in comparison with healthy normal controls. To obtain a meaningful study and result, a proper and detailed review of the literature is of utmost importance. The present literature reviews the various aspects of Oral leukoplakia, Oral submucous fibrosis which are Potentially malignant disorders and Oral Squamous cell carcinoma. A correlation of Serum lipid levels in the above disease condition as well as in the control groups are being presented.

POTENTIALLY MALIGNANT DISORDERS

A new terminology has been recommended for earlier lesions which were grouped under Premalignant lesions and conditions as "**Potentially malignant disorders"** which included not only the Premalignant lesions and conditions but also includes a family of morphological alterations among which few may have an increased potential for malignant transformation. The Potentially malignant disorders include Leukoplakia and Erythroplakia, Palatal lesion of reverse cigar smoking, Oral lichen planus, Oral submucous fibrosis, Discoid lupus erythematosus, hereditary disorders such as Dyskeratosis congenita and Epidermolysis bullosa. The recognition and management of these potentially malignant disorders therefore constitutes a vital oral cancer control measure. But currently they recommend not dividing them as such, but instead clubbing them together under the heading of "Potentially malignant Disorders". [2]

ORAL LEUKOPLAKIA:

Definition:

WHO collaborating centre for oral precancerous lesion[6] defined oral leukoplakia as "A white patch or plaque that cannot be characterized clinically or pathologically as any other disease."

Axell T et al [7] defined leukoplakia as "A white patch or plaque that cannot be characterized clinically or pathologically as anyother disease and is not associated with any physical or chemical causative agent except the use of tobacco".

Axell T et al [7] also defined oral leukoplakia as "A predominantly white lesion of oral mucosa that cannot be characterised as any other definable lesion;some leukoplakia will transform in to cancer.

Pindborg et al [8] defined leukoplakia as "A predominantly white lesion of the oral mucosa that cannot be characterized as any other definable lesion".

WHO [6] declared "Leukoplakia should be used to recognize white patch of questionable risk having excluded other known diseases or disorders that carry no increased risk for cancer

Historical review:

Erno Schwimmer [6],a Hungarian dermaltologist was the first person to describe Oral Leukoplakia. He originally proposed the term

"Leukoplakia" which literally means "White patch". In Greek "Leukos" means white and "Plakia" means patch. It describes a clinical entity.

Sprage [6] found that 36% of American oral pathologists used Oral leukoplakia as clinical term and 40% as histological one.

Shafer [6] suggested that histological definition of leukoplakia is however complicated by the fact that not all lesion satisfying the histological criteria for leukoplakia will appear clinically as a white patch.

W.H.O Collaborating Centre for Oral Precancerous Lesions [6] proposed that the term Leukoplakia should be used to describe a clinical entity, that is a white patch of oral mucosa which is not removed by rubbing and not classifiable as any other oral disease like oral lichen planus, leukedema, candidiasis ,white sponge nevus, lupus erythematosus. It also suggests that microscopically leukoplakic lesions should be described in internationally approved term.

Brad W. Neville [9] proposed that as such leukoplakia should be used only as a clinical term and it has no specific histopathological connation should never be used as microscopic diagnosis. Sometimes a white patch is initially believed to represent leukoplakia, but the biopsy reveals another specific diagnosis. In such cases, the lesion should no longer be categorized as leukoplakia

Epidemiology:

In a 10 year prospective study in India in large samples, carried out in several geographic areas with various kinds of tobacco usage, the annual

age- adjusted incidence rates of leukoplakia per 1000 population per year varied from 1.1 -2.4 among men and from 0.2 -1.3 among women and the prevalence varied from 0.2-4.9%. [10]

The annual incidence was 2.1 per 1000 men 1.3 per 1000 women and the highest being in people with mixed habits, that 6 per 1000.[11]

Prevalence of leukoplakia in India varies from 0.2-5.2%. Prevalence of 0.59 also has been reported. [12]

Prevalence of leukoplakia was reported to be 3.6% and that of preleukoplakia was 6.4%. Idiopathic leukoplakia was reported to be 0.7% and tobacco specific leukoplakia was 2.9%. [13]

Less than 15 of men below the age of 30 years, have leukoplakia, but the prevalence increases to an alarming 8% in men over the age of 70 years. The prevalence in women past the age 70 years is approximately 2%.[14]

Etiology:

Many causative agents have been implicated in the etiology of leukoplakia. They include Tobacco, Alcohol, Chronic friction due to sharp tooth, Electro galvanic reaction, Ultra violet radiation, Syphilis. [15]

Tobacco use is considered to be the primary cause for the occurrence of leukoplakia. Leukoplakia associated with smoking habit seems to have less malignant potential than those not related to smoking habit. In a study of 257 patients with oral leukoplakia, 183 were smokers, out of whom 12% developed carcinomas, whereas 74 were non- smokers out of whom 32% developed carcinoma. [2,15]

Sugár.L. et al [16], made a follow-up study with 324 patients and concluded that there was a relationship between smoking and the frequency of leukoplakia. He also found that alcohol, mechanical irritants and electric potential difference in the mouth were also important etiological factors, particularly in combination. Many of the cases with mild symptoms improved when the etiological agent was removed.

Dietrich T,[17] made an analytical study on Clinical risk factors of oral leukoplakia and found the results as, Tobacco smoking as the strongest independent risk factor. The Odds Ratio were 3.00 (0.77-11.8) for < for =10 cigarettes/day and up to 6.01 (2.4-15.0) for >20 cigarettes/day. Diabetes, age and socio-economic status were found as independent predictors of Oral leukoplakia. Alcohol consumption, race/ethnicity, years of education and Body Mass Index showed no independent association with Oral leukoplakia Females with a history of estrogen use were less likely to have Oral leukoplakia with an Odds ratio of 0.34 (0.11-1.07).

Thomas SJ, et al [18] conducted a cross sectional study on Betel quid not containing tobacco and oral leukoplakia .The study recruited 1,670 adults. They recorded betel quid chewing and smoking. The prevalence of leukoplakia was 11.7%. In the nested case-control study of 197 cases and 1,282 controls, current betel chewing was associated with increased risk of leukoplakia with an adjusted odds ratio for current chewers of 3.8 (95% CI 1.7, 8.4) and in the heaviest chewers of 4.1 (95% CI 1.8, 9.1) compared to non-chewers. Current smoking was associated with an increased risk of

leukoplakia with an adjusted odds ratio for current smokers of 6.4 (95% CI 4.1, 9.9) and amongst heaviest smokers of 9.8 (95% CI 5.9, 16.4) compared to non-smokers. The systematic review identified 5 studies examining risk of leukoplakia associated with betel quid chewing in populations where betel quid did not contain tobacco and that controlled for smoking. In studies that adjusted for smoking, the combined random effect odds ratio was 7.9 (95% CI 4.3, 14.6) in betel quid chewers. The results of this study and systematic review of similar studies provide evidence of the role of betel quid not containing tobacco and leukoplakia

Prakash C.Guptha [19] made an Epidemiologic study of the association between alcohol habits and oral leukoplakia. The study included 10914 individuals for their tobacco and alcohol habits and examined for the presence of oral leukoplakia. Very few females (1.6%) were found to be alcohol users and they were excluded from further analysis. Among 7604 males, 30.4% used alcohol regularly, 25.4% occasionally and 44.2% were non-users. The prevalence of leukoplakia was significantly higher among regular (5.7%) and occasional (3.9%) users than among non-users (2.9%) of alcohol.

Alcohol usage was found to be related to age as well as tobacco habits. The prevalence of leukoplakia was higher among alcohol users in each age-group as well as in each tobacco habit category. After age-adjustment the difference between alcohol users and non-users, although reduced, remained significant. For most tobacco habit categories the trend

remained similar after age-adjustment except for the mixed habits group, for which there was a reversal of the trend. The alcohol habit may, perhaps, produce discernible effects only in association with other 'weak' etiological risk factors, such as a single tobacco habit of smoking or chewing rather than a 'strong' etiologic factor such as the mixed habits of chewing and smoking.

Local factors like chronic irritation and malocclusion which constantly irritate the oral mucosa cause oral leukoplakia. Irritation by ill fitting dentures, overhanging crowns and fillings and poor restoration refers to traumatic causes. Smoking is also considered as an irritant due to drying effect on the mucosa. These exciting factors should act on a susceptible host. Heredity plays an important role in determining an individual's susceptibility or resistance to the development of leukoplakia. [11]

Systemic factors include hormonal alterations and nutritional deficiencies. Estrogen deficiency may determine the susceptibility of females to develop leukoplakia at the period of menopause.

Vitamin A deficiency may produce Hyperkeratosis in experimental animal. Continuous irritants such as spicy food may also be a factor. Irritating mouthwashes can also be a cause but the exact role is yet to be substantiated.

Syphilis may also be responsible for leukoplakic lesions on tongue secondary to atrophic glossitis of tertiary syphilis. The glossitis is

apparently more highly susceptible to the action of local irritants in the mouth. [15]

In one preliminary study Epstein Barr virus was detected in 60% of Proliferative verrucous leukoplakia cases suggesting its possibility as an etiological agent.

Yeast organism especially candida albicans can cause leukoplakia since it has the ability to form N-Nitrosomethylamines from the precursors which are abundantly available in the saliva of smokers.

To list them under a table as [15]:

Local	**Systemic**
Local irritation Sharp ,malposed teeth Ill fitting denture Poor restorations	Heredity
Occlusal disharmony	Hormonal factors
Occlusal habit	Estrogen deficiency
Thermal factors	Nutritional deficiency
Smoking	Syphilis
Irritant foods,chemicals,mouthwashes, etc.	Atrophic glossitis

Clinical types [6] :

Two main type exists:

- Homogeneous
- Non homogeneous

Distinction between these two forms is purely clinical, based on surface color and morphological characteristics like thickness which also has predilection for prognosis.

Homogeneous type:

Homogeneous leukoplakia has been defined as a predominantly white lesion of uniform flat, thin appearance that may exhibit shallow cracks and has a smooth, wrinkled or corrugated surface with a constant texture throughout. The risk of malignant transformation is relatively low. The lesion is predominantly white but can be grayish white. It constitutes for about 84% of the leukoplakia.

Non homogeneous type:

- Ulcerative: Mixed white and red in color but retaining the predominant white character.
- Nodular (Speckled): Small polypoid outgrowths, rounded red or white excrescences.
- Verrucous: wrinkled or corrugated surface appearance.

The term "Erythro leukoplakia" is applied for predominantly red and white lesion that may be irregularly flat, nodular or exophytic. The nodular lesions are characterized by white patches or nodules on a erythematous base.

Ulcerative leukoplakia:

Ulcerative leukoplakia is characterized by areas of red which at times exhibit yellowish areas of fibrin. White patches are generally present at the periphery. It constitutes to about 135 of all leukoplakia types. It could also present with ulceration with white areas in between. Sometimes they occur with minimal keratinisation

Verrucous leukoplakia;

Verrucous leukoplakia appears as an exophytic lesion with irregular sharp or blunt projections.

Clinical Features:

Age:

The onset of lesions usually starts after 30 years, resulting in peak incidence of 50 years. Leukoplakia is seen most frequently in middle aged and older men, with an increasing prevalence with age. Oral leukoplakia can occur 5 years prior to oral cancer.[14,20]

Gender:

It has a strong male preponderance. Leukoplakia is a commonly occurring lesion particularly in patients after 40 years of age. The male to female ratio is 2:1. The gender distribution in most studies varies, ranging

from a strong male predominance in different parts of India, to almost 1:1 in Western world.[11]

Site :

Oral leukoplakia accounts for 80% of all leukoplakia of upper aero digestive tract. Most of the others are vocal cord lesions and are called as laryngeal keratosis. It can occur anywhere in the oral cavity. The site of leukoplakia depends on the type of smoking habit, the quality and the quantity of the tobacco.

Most commonly involved sites are retro commissural area, buccal mucosa, edentulous alveolar ridge, hard palate, tongue, lips. The gingival, soft palate and floor of mouth are less commonly involved in an Indian population, where as it is not true for Western population.

Waldron CA, Shafer WG.[20] made a clinico pathologic study with 3256 oral leukoplakia cases. During a 13-year period, 3256 specimens clinically diagnosed as leukoplakia ("keratosis," "white patch") were analyzed as to age of occurrence, site of involvement.

It was found that leukoplakia occurs chiefly in the 5th, 6th, and 7th decades; about half of the lesions involved the mandibular mucosa, mandibular sulcus, and buccal mucosa; leukoplakia was slightly more common in men (54.2%).

Bánóczy J [21] made a follow-up study with 670 patients with oral leukoplakia during a 30-year-period showed cancer development in 40 cases. The age distribution revealed the prevalence of leukoplakia in the

age-group 51-60 years; that of carcinoma in the age-group of 61-70 years. The sex distribution showed a male-female ratio of 3.2 : 1 in the leukoplakia-group, and a 1.9 : 1 ratio in the carcinoma-group. The tongue and the lips were the site of predilection for malignant transformation and for dysplasia. Among etiological factors, Candida albicans infection and the simultaneous existence of several etiological factors seemed to play a role in malignant transformation. Erosive leukoplakia showed the highest risk, developing in 25.9% of the cases into cancer.

Leukoplakia begins as thin, gray white plaques that may appear somewhat translucent, sometimes fissured or wrinkled and are soft and flat.

They usually have sharply demarcated borders but occasionally blend gradually in to normal mucosa. This early stage is considered as Phase –I Leukoplakia.

Thin leukoplakia may continue unchanged or disappear, but with time 2/3rd of these lesions acquire a distinct white appearance from a thickened keratin layer. It becomes leathery to palpation and fissures deepen. There may be few or localized nodules or appear as surface projections. This can be categorized as Phase-II.

Most of these lesions remain unchanged and about 2/3rd regress and disappear and few become severe. Later these lesions develop surface irregularities of a nodular or granular leukoplakia. Numerous pointed projections develop on the surface and give an appearance of verruciform leukoplakia. Both these lesions are Phase-III lesions with similar progress.

Phase-III lesions may become dysplastic or invasive with no change in clinical appearance.

Over time an additional surface change occurs and multiple circular or oval patches of non blanching redness appear in scattered areas. Such areas represent site at which cells are so immature that they are unable to produce keratin. These forms Phase-IV lesions.

Leukoplakia Clinical phases [15]:

Phase	**Descriptive terms**	**Risk of malignant transformation**
I	Thin leukoplakia Preleukoplakia Homogeneous leukoplakia	+/-
II	Thick,smooth leukoplakia Fissured leukoplakia Homogeneous leukoplkia	++
III	Granular leukoplakia Verruciform leukoplakia Rough leukoplakia	+++

	Candidal epithelial hyperplasia Homogeneous leukoplakia	
IV	Erythroleukoplakia Speckled leukoplakia Candidal leukoplakia Nonhomogeneous leukoplakia	++++

Pindborg et al [8] has given the classification and staging for leukoplakia as follows,

Classification and staging of oral leukoplakia

Provisional (Clinical Diagnosis)

L : Extent of leukoplakia

L0 : No evidence of lesion

L1 : ≤ 2 cm

L2 : 2-4 cm

L3 : ≥ 4cm

S : Site of leukoplakia

S1 : all sites excluding floor of mouth & tongue

S2 : floor of mouth &/ tongue

S3 : not specified

C : Clinical aspect

C1 : homogeneous

C2 : non homogeneous

C3 : not specified

Definitive diagnosis:(Histopathological diagnosis)

P : Histopathological features

P1 : no dysplasia

P2 : Mild dysplasia

P3 : Moderate dysplasia

P4 : severe dysplasia

Px : not specified

Staging:

1. any L,S1,C1,P1 or P2
2. any L,S1or S2,C2,P1 or P2
3. any L,S2,C2,P1 or P2
4. any L,any S,any C,P3 or P4.

Natural History:

Leukoplakia can regress spontaneously without any intervention in habit or by any other means in about 40% of cases. Significantly higher rates of regression is seen who discontinue the tobacco habit. In one long term follow-up study among the Swedish population consisting 104

samples, they found that oral leukoplakia has disappeared in 43% of the people. About 70-80% of leukoplakia is associated with tobacco habits, also about 80% of the leukoplakia lesions disappear completely about 58% or regress within 12 months after smoking cessation.[22]

Malignant transformation:

It is generally accepted that dysplastic lesions carry a 5 fold greater risk than non dysplastic ones. It refers to the development of oral cancer from preexisting oral leukoplakia. So it is necessary to follow-up a case of leukoplakia for a period of 3 months to one year. [2]

In the period of follow-up, the lesion should be evaluated for development of thickened/nodular areas, ulcerations, rolled margins, growths or indurated areas. Since these changes represent early oral cancers. Lesions on the tongue, lip vermilion border, floor of the mouth accounts for 93% of the leukoplakia with dysplastic changes or carcinoma. Globally 3-6% leukoplakia change to cancer.[23]

Lee JJ, et al [24] conducted a study to find the relation between carcinoma and oral leukoplakia and demonstrated the results that some leukoplakias contain a malignant component. Lesions with certain features are more prone to carcinoma, but no clinical attributes can bring certainty in these lesions.

Sol Silverman [25] made a follow up study on Oral leukoplakia and Malignant transformation in 257 patients for average period of 7.2 years .Seventy-three percent of the patients used tobacco, with cigarette usage

being the predominant form. Forty-five patients (17.5%) subsequently developed squamous carcinomas. High risks for malignant transformation also included non-smoking patients, the clinical presence of erythroplasia (erythroleukoplakia), and a clinical verrucous-papillary hyperkeratotic pattern. Duration of the leukoplakia progressively increased the total number of malignant transformations, with the largest rate occurring in the second year. This study confirms that oral leukoplakia is a precancerous lesion and that certain characteristics indicate greater risks and warrant consideration of more aggressive management.

Non homogeneous leukoplakia accounted for the highest frequency of malignant transformation of 20%, whereas 3% of the homogeneous leukoplakia developed carcinoma. Proliferative verrucous leukoplakia has a malignant transformation rate as high as 70.3% with mean follow-up of 11.6% [2]

Differential diagnosis [5]:

The following differential diagnosis should be kept in mind whenever a clinical diagnosis of leukoplakia is made:

- Acute pseudo membranous candidiasis or Thrush: White, curd-like or cotton like patches or plaques, most frequently occurring on the buccal mucosa and tongue, but also seen on the palate, floor of mouth and gingiva. They are usually associated with a burning sensation and the white plaque can usually be wiped away with gauze, leaving a tender, red area beneath, which may bleed.

- Reactive hyperkeratosis. A benign epithelial response, usually due to trauma from a fractured tooth or dental restoration. Check for the causative agent.
- Leukedema :Usually bilateral, that disappears on stretching the mucosa
- Lichen planus : Usually bilateral with lacy white pattern.
- Lichenoid reaction: same like lichen planus; but positive history of drug intake, amalgam restoration, pan chewing habit.
- Linea alba buccalis : Usually bilateral. The white line is present along the occlusal plane.

Diagnosis :

Axell [7] suggested that diagnosis of leukoplakia can be arrived at by excluding lesions belonging to other entities, such as Lichen planus, Lupus erythematosus, Leukedema and White sponge nevus and lesions for which an etiology can be established, such as frictional keratosis, cheek/lip/tongue biting, contact lesions and smokers palate.

Pindborg [8] proposed that when there is a doubt in diagnosing leukoplakia,one can make a provisional diagnosis of leukoplakia and the definitive diagnosis can be established after the result of removal of any possible etiologic factors and a biopsy.

ORAL SUBMUCOUS FIBROSIS:

Definition:

The most widely accepted definition is by **Pindborg J.J and Sirsat SM** [26]. They have defined Oral submucous fibrosis as "An insiduous chronic disease affecting any part of oral cavity and sometimes the pharynx, although occasionally preceded by vesicle formation it is always associated with juxta –epithelial inflammatory reaction followed by a fibro elastic change of the lamina propria, with epithelial atrophy leading to stiffness of the oral mucosa and causing trismus and inability to eat."

Schwartz[26] coined the term atrophica idiopathica mucosa oris to describe an oral fibrosing disease .He discovered in 5 Indian women from Kenya.

Joshi [26] subsequently coined the term Oral sub mucous fibrosis (OSMF) for the condition.

Historical Review:

Oral submucous fibrosis has been well established in Indian medical literature since the time of Sushrutha renowned Indian Physician who lived in the era 2500-3000 B.C.[26]

Schwartz .J [26] first described Oral submucous fibrosis in modern literature among five East African women of Indian Origin under the term " Atropica idiopathica mucosa oris". Since then this condition has been described by various investigators by various terms.

Joshi S.G [26] described this condition in India when he reported 41 cases with submucous fibrosis of the palate and it was he who suggested the use of the term "Oral submucous fibrosis''.

Lal. D [26] described it as a "Diffuse oral submucous fibrosis",Joshi S.G in 1953 described it as "Sub mucous fibrosis of the palate and pillars",Sui-Pin in 1954 described it as "Idiopathic scleroderma of the mouth",Rao.A.B.N in 1962 termed it ias "Idiopathic palatal fibrosis",Behl P.N in 1962 arrtibuted the term "Sclerosing stomatitis''.

Epidemiology:

Oral submucous fibrosis is an epidemic in India, and is prevalent throughout Indian sub continent,sparing no caste or creed, affecting the young and old ,the rich and poor alike.[9]

PindbordJ.J et al [26] reported that the prevalence of Oral submucous fibrosis in India ranges from 0.2-0.5%with a higher predominance in the southern part of the Indian subcontinent.

Reports from Western India gives an incidence of 2.6 and 8.5 per 1,00,000 per year for males and females respectively. In South India it is 9 and 20 per 1,00,000 per year for males and females respectively.

He stated that South Indian state of Kerala ,one new case could be expected per 10,000 populations per year. The prevalence rate of oral submucous fibrosis in South Africa, Burma and India range from 0-1.2%.

Gupta P.C et al [10] reported the incidence of Oral submucous fibrosis in Ernakulum ,India as 8 per 10,000 per men and 19 per 10,000

women per year. In India Bhavnagar, in Western India the incidence was 2.6 per 10,000 men and 8.15 per 10,000 women per year.

About 2.5 million people are affected by this disease. There is clear cut geographical predisposition to South East Asia. Most of these cases are found in India although cases have been reported in Taiwan, Malaysia, South Africa, New Guniea, Srilanka, Burma, United kingdom and Canada.[27]

Etiology:

The prime causes suspected on the basis of cause and effect relationship are prolonged and chronic use of arecanut, chillies, tobacco with arecanut, Pan masala, Pan, Vitamin B complex deficiency.

Arecanut chewing has the strongest evidence regarding the etiology. Arecanut is the endosperm of the fruit areca catechu tree, the fruit of which is orange yellow in colour when ripe [28].

A 10 year prospective study on 10,000 subjects showed a zero incidence of oral submucous fibrosis among those who did not chew arecanut compared with an incidence of 35 per 10,000 among arecanut chewers.[29]

It has been shown that arecanut and its extract mainly arecoline can stimulate fibroblast proliferation, collagen synthesis and increasing collagen cross linking in invitro studies. The flavinoids and tannins from betel nut can stabilize collagen and render them resistant to degradation by collagenase.[30]

Maher R et al [31] conducted a case control study in Role of arecanut in the causation of Oral submucous fibrosis, Information on habits was collected by personal interview of 157 cases and 157 controls. Despite overall female preponderance, a substantial number of young men were enlisted. The male/female risks were found to be similar.

No differences between risks were found when comparing the three age categories, 0-20, 21-40, 41-60 yr. Among the cases, an increased risk was observed for areca nut chewing. This habit when practiced alone appeared to have the highest risk (Relative Risk 154), followed by pan with or without tobacco (Relative Risk 64, 32 respectively). Logistic regression and discriminant analysis showed that daily consumption rates appeared to be more important with respect to risk than lifetime duration of habit.

Tobacco habits were more prevalent amongst those 15 cases who presented with concurrent carcinoma and OSMF. They concluded that areca nut chewing has a causal relationship with OSMF. Additional tobacco insult may be necessary for subsequent carcinoma development.

Rajendran.R [30] reviewed the etiology and pathogenesis of Oral submucous fibrosis. According to him oral sub mucous fibrosis, a pre cancerous condition of the oral cavity has been studied by a number of workers in the field. The available epidemiological data showed a clear cut geographical and ethnic pre dispositions, which suggested that certain customs or habits (chewing) prevalent among the population groups in South East Asia might be possible etiological factors. However none of

these customs was shown to be casually linked. This led some workers to consider the importance of systemic pre dispositions, in addition to the effects of local factors on the oral mucosa. More research is needed to elucidate this problem.

Murti.P.R. [32] reviewed the etiology of oral submucous fibrosis, a high risk pre cancerous condition, predominantly affecting Indians. Consumption of chilly was hypothesized as an etiologic factor on the basis of ecological observations and a solitary animal experimental study. Subsequent epidemiologic studies that included case-series reports, large cross-sectional surveys, case control studies, cohort and intervention studies have identified arecanut as the major etiologic factor. Currently the role of genetic susceptibility and that of autoimmunity are receiving attention. Influence of nutritional factors if any remains unclear.

Shah N et al [33] conducted a study to identify the role of chewing and smoking habit in the etiology of oral submucous fibrosis. In this study 236 cases of oral submucous fibrosis were compared with 221 control subjects matched for age, sex and socioeconomic conditions. It was found that chewing of areca nut, quid and pan masala was directly related to oral submucous fibrosis and not a single case was found without any chewing habit.

The study showed that the pan masala chewers develop oral submucous fibrosis in half the time taken by areca nut betel quid chewers. It was also found that duration of chewing was not significantly correlated but

the frequency of chewing was directly correlated to manifestation of oral submucous fibrosis.

Chung CH, et al [34] made a study to find the relation between Oral precancerous disorders with areca quid chewing, smoking, and alcohol drinking in southern Taiwan and found of 1075 subjects,136 12.7%). Precancerous lesions and conditions were detected .The analysis of the spectrum of oral precancerous disorders detected, leukoplakia (n = 80), OSMF (n = 17) and verrucous lesions (n = 9), demonstrated an association with gender ($P < 0.001$). There were statistically significant associations among leukoplakia ($P < 0.01$), OSMF ($P < 0.0001$), and verrucous lesions

The synergistic effect of smoking and areca quid chewing habit on leukoplakia and OSMF was demonstrated. Conclusion of this study reinforced the association of current areca quid chewing without tobacco, cigarette smoking, and alcohol drinking to leukoplakia, Oral submucous fibrosis, and verrucous lesions in Taiwan.

Ranganathan K, et al [35] conducted a case control study in south India, over a 3 year period. A total of 185 consecutive patients with OSMF were matched with age- and sex-matched controls. History was recorded in a pre-determined format by qualified Dental Surgeons. The results obtained were, the male to female ratio of OSF cases was 9.9 : 1. All areca nut products were associated with OSF, with the risk being greatest for pan masala. The duration of the habit was more significant than the frequency of

the chewing habit. The present study confirms the strong association between areca nut use and OSF and the increasing use of pan masala

Punnya V. et al [36] made a a clinicopathologic study of 205 cases in Indians. The study evaluated 205 cases of oral submucous fibrosis for the age, sex, site of involvement, duration of disease at the time of diagnosis, associated habits and common presenting symptoms, presence of other mucosal lesions, malignant potential, and the histopathology.

The results revealed Oral submucous fibrosis seen in younger age (20–30 years) than that reported in literature and showed a characteristic male preponderance. A strong association with smokeless tobacco use especially arecanut in the form of gutkha was established and was related to earlier development of oral sub mucous fibrosis within a year of the habit. A total of 11.6% of cases were associated with malignancy and occurred predominantly in males.

Among systemic factors the main ones incriminated are chronic Iron, Vitamin B complex deficiency and anemia. Iron metabolism is important in maintaining the health of oral mucosa as well as the epithelium of the digestive tract and it contributes to normal enzyme activity.[37]

Clinical Features:

Age :

There is no predilection for any age group however a broad age distribution with a peak in the range of 20-40 years was observed. [10]

Gupta PC, et al [37] conducted a study in India. A total of 11,262 men and 10,590 women aged 15 years and older were interviewed for their tobacco habits. Among 5018 men who reported the use of tobacco or areca nut, 164 were diagnosed as suffering from OSF. All but four cases were diagnosed among 1786 current areca nut users (age-adjusted relative risk: 60.6). Areca nut was used mostly in mawa, a mixture of tobacco, lime and areca nut, and 10.9% of mawa users had OSF (age-adjusted relative risk: 75.6). The disease as well as areca nut use was concentrated (about 85%) in the lower (< 35 years) age group. They concluded the study by depicting an increase in the prevalence of OSF, especially in the lower age groups, directly attributable to the use of areca nut products. This could lead to an increase in the incidence of oral cancer in the future.

Ahmad et al in 2006[38] conducted an etiological and epidemiological study of oral submucous fibrosis in Patna, Bihar. Total 157 cases of OSMF and 135 control subjects were selected for study in the period of 2002-2004. It was observed that male: female ratio was 2.7: 1. The youngest case of OSMF was 11 year old and the oldest one was 54 years of age. Maximum numbers of cases were belonging to 21-40 years of age and they were belonging to low or middle socioeconomic class. Most of the OSMF cases used heavy spices and chillies, whereas control mild had spices and chillies. Gutkha was the most commonly used by the OSMF cases. Only 3 per cent did not use any gutkha or other areca nut product where as 80 per cent control did not have any chewing habit. The OSMF cases used gutkha and

other products 2-10 pouches per day and kept in the mouth for 2-10 minutes and they were using since 2-4 years. Most of the OSMF cases kept gutkha in the buccal vestibule or they chewed and swallowed it, only a small number of patients chewed and spitted it out. It was also observed that OSMF developed on one side of the buccal vestibule where they kept the chew and other side was normal.

Gender :

There is equal sex distribution, though some reports may vary indicating a female preponderance[37].

The major presenting complaint is progressive inability to open the mouth owing to the accumulation of inelastic fibrous tissue in the juxtaepithelial region of the oral mucosa. Patients may describe a sudden onset of inflammation or ulceration of the oral mucosa and burning pain while eating highly seasoned food that previously caused no distress.[11]

The fibrosis also leads to difficulty in mastication speech and swallowing, pain in the throat and ears and relative loss of auditory acuity due to stenosis of the Eustachian tube. [11]

In the early cases the fibrosis is seen arching from the anterior pillars in to the soft palate as a delicate reticulum of interlacing white strands which later become confluent. In the cheeks a mottled marble like appearance may be seen when dense pale depigmented fibrosed areas alternate with pinker normal mucosa.[39]

The floor of the mouth become pale and thickened, the tongue gets reduced in size and mobility, bands of encircling collagen distort lips.

At any stage in the disease the overlying epithelium may become the site of nonspecific ulceration, dysplastic change or malignant transformation. If fibrosis extends in to the esophagus the patient may experience progressive dysphagia and reduced esophageal mobility.[38]

Patients with Oral sub mucous fibrosis often complains of sudden onset of inflammation or ulceration of oral mucosa with vesicle formation and increased sensitivity or burning sensation when eating spicy food that are followed by trismus, increasing difficulty in mastication speech and swallowing.[39]

In advanced cases the jaws may be in separable and the total inelastic mucosa is forced against the buccal aspects of the teeth were sharp edges or restorations may cause ulcerations which become secondarily infected. The fibrosis progress in to the posterior part of the buccal mucosa, the anterior pillar of fauces and the soft palate including uvula. [38]

Rajendran.R [11], reviewed the etiology, clinical features, epidemiology, pathology and management of Oral submucous fibrosis and concluded in his study as Oral submucous fibrosis is a chronic progressive, scaring disease that predominantly affects people of South East Asian origin.

Gupta P C and Dinesh Chandra [40] suggested the Clinical Grading as follows,

The diagnosis of Oral submucous fibrosis is based on the positive history of areca nut chewing, Clinical and histopathological criteria. The severity of the disease can be graded based on the clinical grading system.

Grade I :

Presence of only blanching of oral mucosa without symptoms

Grade II :

Presence of blanching and burning sensation, dryness mouth, vesicles or ulcers in the mouth.

Grade III

Presence of blanching and burning sensation, dryness mouth, vesicles or ulcers in the mouth with restriction of mouth opening

Grade IV :

Presence of blanching and burning sensation, dryness mouth, vesicles or ulcers in the mouth with restriction of mouth opening and palpable bands all over the mouth without tongue involvement.

Grade V :

Presence of all features of Grade IV with tongue involvement.

Grade VI :

Oral sub mucous fibrosis along with histopathologically proven carcinoma.

Malignant transformation:

Paymaster [26] was the first one to mention the precancerous nature of Oral submucous fibrosis when he observed the development of slowly growing Squamous cell carcinoma in One third of his Oral submucous fibrosis patients. There is 3-19% malignant transformation in Oral sub mucous fibrosis.

Pindborg [26] reported that Oral submucous fibrosis patients in India have higher occurrence of leukoplakia and carcinomas than those without this disease.

Murthi P.R et al [32] conducted a follow-up study of 66 patients over a 17-year period, and found cancer developed in 7.6% of patients.

Pindborg [8] summarised the criteria in support of the precancerous nature of the disease as,

1. Higher prevalence of leukoplakia among Oral submucous fibrosis patients.
2. High frequency of epithelial dysplasia.
3. Concurrent finding of Oral submucous fibrosis in oral cancer patients.
4. Histological diagnosis of carcinoma without clinical suspicion of it and
5. Incidence of oralcancer patients with oral submucous fibrosis.

Differential diagnosis [41] :

1. Radiation induced fibrosis : which is confirmed by proper history taking regarding cancer history and radiation therapy.
2. Scleroderma : which is detected by the clinical features of the disease like progressive sclerosis all over the body, including skin and internal organs.
3. Fibrosis due to Actinomycosis infection : Patients history reveals period of infection and the treatment obtained.
4. Fibrosis due to Trauma : patient history reveals history of trauma, surgery.

ORAL SQUAMOUS CELL CARCINOMA

Willis[42] described neoplasm as an abnormal mass of tissue, the growth of which exceeds and is uncoordinated with that of normal tissue and persists in the same excessive manner after cessation of the stimuli which evoked the change.

The term oral cancer is used to describe any malignancy that arises from the oral tissues. Cancer is the second leading cause of death in United States. It is the sixth most common cancer in world wide. Oral cancer is more common than leukemia, lymphoma, cancer of stomach, ovary. More than 90-95%of the Oropharyngeal cancers are Squamous cell carcinoma[23].The other 10% are salivary gland tumours, lymphomas, sarcomas. Oral cancer has been reported at higher rate in India, Southeast Asia , Hungary, France. Lesions which are likely to turn into oral cancer

include Leukoplakia, Oral submucous fibrosis, Erosive lichen planus. OSCC is the most common malignant neoplasm of the oral cavity. It can occur at any intraoral site but certain areas are most commonly involved.

DEMOGRAPHICAL REVIEW

Cancer is one of the major threats to public health in the developed world and increasingly in the developing world. In developed countries cancer is the second most common cause of death. According to the World Health Report 2004, cancer accounted for 7.1 million deaths in 2003 and it is estimated the overall number of new cases will rise by 50% in the next 20 years.[43]

The prevalence of oral cancer is particularly high among men; oral cancer is the eighth most common cancer worldwide. Incidence rates for oral cancer vary in men from 1 to 10 cases per 100 000 population in many countries. In south-central Asia, cancer of the oral cavity ranks among the three most common types of cancer. In India, the age standardized incidence rate of oral cancer is 12.6 per 100 000 population.[44]

In the South Asian region over one-third of tobacco consumed is smokeless. Traditional forms like betel quid, tobacco with lime and tobacco tooth powder are, commonly used and the use of new products is increasing, not only among men but also among children, teenagers, women of reproductive age, medical and dental students. In India, where chewing tobacco is used with betel nuts and reverse smoking (placing the lit end in

the mouth) is practiced, there is a striking incidence of oral cancer- these cases account for as many as 50% of all cancers.[43]

India has the highest rate of oral cancer in the world, caused by tobacco consumption. WHO research indicates a 500 percent increase in cancer by 2025, of which 220 will be due to tobacco use. According to Women's Health in South East Asia (WHOSEA), almost one-half of all cancer cases in men and one-quarter of all cancer cases in women in India are believed to be tobacco-related.[43]

Salonen et al [45] reported on occurrence of oral mucosal lesions and the influence of tobacco habits in a randomly selected adult Swedish population. Nine hundred twenty (920, 95%) of the selected samples of 967 subjects comprising approximately 0.75% of the total adult population were examined; lesions were registered in 596 of the 920. The relationship between tobacco habits and mucosal lesions was analyzed and the time needed for treatment for the lesions was estimated. A positive correlation could be demonstrated between tobacco use and leukoplakia, frictional white lesion, coated tongue, hairy tongue and excessive melanin pigmentation, while a negative correlation was observed for geographic tongue and aphthous ulcer.

Sankaranarayanan [46] found that oral cancer ranks number one among all cancers in male patients and number three among cancers in female patients. Causal association between oral cancer and the chewing of

betel quid containing tobacco leaves or stem and other tobacco habits has been extensively established.

Chakrabarti et al [47] in a Calcutta population compared the prevalence of oral carcinoma and dysplasia in smokeless tobacco users and non-users. A total of 3205 subjects were studied. Of the smokeless tobacco users, 1.96% had oral carcinoma compared with 0.36% of non-users. The prevalence of oral dysplasia in the user's group was 14.4% as compared with 6.85% in the group of non-users.

Warnakulasurya [48] reviewed the data on smoking and chewing habits that were prevalent in the rural population of SriLanka and provided an assessment of the risk from these habits for oral pre cancer. According to one study among 1133 villagers, 54% men, and 42% woman chewed betel quid out of which 46% of men and 63% of women included tobacco. Tobacco was chewed alone by 2.6%. A community based case control study conducted on oral precancerous lesion and condition in a screening camp included 359 patients (316 men and 43 women) aged over 20 years in whom the lesion was diagnosed and equal number of age and sex matched controls were included. The relative lowest risk of 5.3 among men and 5 women were observed among chewers of betel quid without tobacco and were not significant. When the quid was chewed with tobacco the relative risk was 15 for men and 33 for women. Men who chewed betel quid with tobacco carried a higher risk than smokers (15 and 9.7 respectively). However a

higher relative risk of 24.7 was seen among men who both smoked and chewed indicating a synergistic action.

Prabhu SR et al [49] stated that oral cancer is currently the most frequent cause of cancer related death among Indian men, which is usually preceded by oral pre cancerous lesion like leukoplakia or condition like oral sub mucous fibrosis.

Crispian Scully et al [50] stated that the etiological factors of oral cancer include tobacco use 75% of people with oral cancer smoke, betel use which includes Bidi leaf, and often tobacco, plus spices, slaked lime, and areca nut, alcohol consumption, a diet poor in fresh fruit and vegetables, infective agents immune deficiency, and in the case of lip carcinoma exposure to sunlight.

Jeng et al [51] stated that betel quid chewing is widely prevalent oral habit in India, Taiwan, Papua New Guinea, South Asia, and South Africa. It has been estimated that 600 million people chew betel quid worldwide. An average of 15 to 20 quid had been chewed by the betel quid users daily. A casual link between betel quid chewing and oral diseases such as oral leukoplakia, oral submucous fibrosis and oral cancer had been strongly established.

Zain et al [52] stated about the role of tobacco smoking, chewing of tobacco, areca nut, and betel quid and drinking of alcohol are established cultural risk factors of oral pre-cancer and oral cancer worldwide. A geographic and regional variation in the prevalence of oral pre-cancer and

oral cancer indicates that the socio cultural life style plays an important role in the etiology and pathogenesis of the disease.

Mehrota et al [53] stated that oral cancer was the commonest malignancy in Allahabad and the habit of chewing was particularly high among the oral cancer patients. The buccal mucosa was the most common site of oral cancer.

Sinha [54] stated that oral use of smokeless tobacco is widely prevalent in the South East Asia Region; the different forms include chewing, sucking and applying tobacco preparations to the teeth and gums. In Southeast Asia over 250 million people use Smokeless tobacco products; about 17% of total population in Southeast Asia uses oral tobacco; of which 95% belong to India 82% and Bangladesh 13%. The global youth tobacco survey revealed high 10-20% prevalence of smokeless tobacco use among young students of age 13-15 year in Southeast Asia. Among disadvantaged youth group high 45%-71% prevalence of tobacco use was reported in Southeast Asia. Tobacco is chewed in multiple forms in Southeast Asia, betel quid, leaf alone, leaf with lime and tobacco and areca nut preparation and tobacco water. Smokeless tobacco use varied from 7.2% to 59.4% in different states of India. In J & K, Goa, Himachal Pradesh, Haryana, Punjab, Kerala, Andhra Pradesh, Tamil Nadu, Delhi, Karnataka, Meghalaya, Rajasthan and West Bengal smoking prevailed over smokeless tobacco use while in Maharashtra, Uttar Pradesh, Sikkim, Madhya Pradesh, Assam, Orissa, Bihar, and Arunachal Pradesh smokeless tobacco use prevailed over

smoking. In Gujarat, Manipur and Mizoram proportion of smoking and smokeless tobacco use, among males was almost equal 28.3 years. 29.4 while among female proportion was 5:1 12.4% years. 2.5 in rural and urban areas respectively.

Warnukulasurya [55] reviewed different types of smokeless tobacco habits all around the world and its role in occurrence of oral cancer. There are two main types of smokeless tobacco , chewing tobacco and snuff. It may be used alone or in combination with other substances. Chewing tobacco comes in various forms, loose leaf, plug or twist. Loose leaf or dry powdered tobacco is often mixed with various ingredients according to the local custom. Snuff is commercially made in many different forms from fine cut or ground tobacco and can be dry or moist. Moist snuff is marketed as loose snuff in containers or as sachets . Many forms of ST are carcinogenic to humans and in animal studies. Cancer development at the site of placement and other oral mucosal lesions caused by these products has been described from several population groups.

Durazzo et al [56] performed a study in Brazil on 374 patients with oral squamous cell carcinoma. Their ages varied from 14 to 94 years with mean = 57.4 years, with 255 men 68.2%, and 295 out of 366 Caucasian 80.6%. A majority had tumours of the tongue and or floor of mouth 55.6%, while 20.3% had lip cancer. Squamous cell carcinoma was found in 90.3%, and glandular carcinoma in 4%, T4 tumours in 39.6%, T1 lesions in 15.2% of all patients. Nearly 62% had no regional metastases, and the relative

incidence in young patients 40 years or younger reached 8.6%, and concluded that in spite of the predominance of locally advanced tumours, a majority of patients had no neck metastases. The 31.8% incidence in females indicates an increasing incidence of oral cavity cancer among women when compared to previous periods at the same institution.

Neufeild [57] and his co workers conducted a survey in India between 1995-96 constituting 4, 71,143 subjects and stated that the prevalence of alcohol consumption was present in 4.5%, smoking of tobacco was present in 16.2% and chewing of tobacco was present in 14% of the study subjects. The prevalence of these habits was found to be more common among men and among the rural population with no formal education.

Mathew et al [58] studied total of 1190 subjects who visited the department of oral medicine and radiology for diagnosis of various oral complaints over a period of 3 months were interviewed and clinically examined for oral mucosal lesions. The result showed the presence of one or more mucosal lesions in 41.2% of the population. Fordyce's granules was observed most frequently 6.55% followed by frictional keratosis 5.79%, fissured tongue 5.71%, leukoedema 3.78%, smoker's palate 2.77%, recurrent aphthae, oral submucous fibrosis 2.01%, oral malignancies 1.76%, leukoplakia 1.59%, median rhomboid glossitis 1.50%, candidiasis 1.3%, lichen planus 1.20%, varices 1.17%, traumatic ulcer and oral hairy leukoplakia 1.008%, denture stomatitis, geographic tongue, betel chewer's mucosa and irritational fibroma 0.84%, herpes labialis, angular cheilitis

0.58%, and mucocele 0.16%. Mucosal lesions like tobacco-related lesions leukoplakia, smoker's palate, oral submucous fibrosis, and oral malignancies were more prevalent among men than among women. Denture stomatitis, herpes labialis, and angular cheilitis occurred more frequently in the female population.

LIPIDS

Lipids are the heterogenous group of compounds related to the fatty acids. They are insoluble in water and soluble in other solvents such as Ether, Chloroform and Benzene. They are chemically the esters of fatty acids and some alcohol. Lipids occur widely in plants and animal kingdom. It includes fats, oils, waxes and related compounds. Oils are liquid at 20°C but fats are solid at this temperature. In the body, fat serves as an efficient source of energy when stored in an adipose tissue. The fat soluble vitamins and the essential fatty acids are found with the fat of natural foods. It serves as an insulating material in the subcutaneous tissues and around certain organs. Lipoproteins are combination of fat and protein and glycolipids are combination of fat and carbohydrates. Both are essential for maintaining cellular integrity. They provide building blocks for different molecular weight substances like acetic acid and can be used for the synthesis of cholesterol and certain hormones. They produce metabolites through oxidation in the tissues which are used in the conversion of substances.

Williams et al [59] conducted a study on 5,209 patients in Framingham for 24 years, in which 691 cases of cancer were documented with

histological confirmation and were tested for associations with occurrence of cancer in patients with low serum cholesterol. It was found that that Serum cholesterol level was inversely associated with incidence of colon cancer with p=0.01 and with other sites only in men; these inverse associations were statistically significant after adjustment for age, alcohol consumption, systolic blood pressure, and relative weight.

Kark et al [60] conducted a study on 3102 people in Evans which were followed for over 12-14 years to assess the incidence of cancer and serum cholesterol and there was an inverse association between incidence of cancer and serum retinol and serum cholesterol concentrations with p-value of 0.05 and 0.002 respectively.

Vitols et al [61] conducted a study on 59 patients with acute leukaemia were examined to see if hypocholesterolaemia, which is commonly found in acute leukaemia, was due to the high low-density-lipoprotein (LDL)-receptor activity of leukaemic cells and the results showed LDL-receptor activity was inversely correlated with plasma-cholesterol concentration.

Richmond et al [62] did a study involving 10 subjects with a history of smoking and 10 controls, they measured cholesterol and TGL, HDL-3, HDL-2. They found that there is decrease in the concentration of HDL2 cholesterol with p=0.043 and the ratio of HDL2 to HDL3 cholesterol with p=0.02 is observed in smokers when compared to non-smokers

Alexopoulos et al [4] conducted a study on 103 cancer patients (60 men and 43 women; mean age, 56 years) and 100 age-matched non cancer patients to assess the total serum cholesterol, free and esterified cholesterol, high-density lipoprotein (HDL) and low-density lipoprotein (LDL) cholesterol, serum triglycerides. The results showed Cancer patients as a group demonstrated significantly lower total cholesterol with **P <** 0.02, esterified cholesterol with **P < 0.05** and LDL cholesterol with **P < 0.05** compared with non cancer patients.

Arthur et al [63] did a cohort study for 10 years to evaluate relation of total serum cholesterol to all cancer and site-specific cancer incidence in 459 male cancer patients and 398 female cancer patients. There was an inverse association between cholesterol and all cancer; lung, colorectal, pancreatic, and bladder cancers with P = 0.02 ,P = 0.5, P = 0.02, P = 0.23 respectively. They also found that the inverse association was present between serum cholesterol for smoking-related cancers diagnosed.

Larry [64] conducted a study to determine the extent to which regular use of smokeless tobacco is associated with hypercholesterolemia among 2,840 adult males. Individuals with smokeless tobacco users were 2.5 times, heavy smokers were 2 times and mild/moderate smokers were 1.5 times more likely to have hypercholesterolemia than non-users of tobacco. There were no differences in risk of hypercholesterolemia between the smokeless tobacco and cigarette smoking groups. It was concluded that the present findings that the consequences of using smokeless tobacco may reach

beyond the oral cavity which may lead to cardiovascular disease, as well as leukoplakias and oral cancer.

Pugalendi et al [65] evaluated the blood cholesterol and HDL cholesterol in 24 cigarette smokers, who were compared with age and sex matched controls. They found that elevated total cholesterol in smokers and significant decrease of HDL cholesterol.

Whig et al [66] conducted a study which measured Serum lipids and lipoproteins of 50 active and passive smokers were compared with levels in 25 control subjects where they found active smoking resulted in an increase in total cholesterol and triglycerides as compared to control group. The passive smokers also showed relatively higher levels but the effect was not significant. Active smoking raised the low density lipoprotein cholesterol and very low density lipoprotein cholesterol levels whereas high density lipoprotein cholesterol content was lowered, thus resulting in decreased ratios of HDL/Tc and HDL/LDL. The passive smokers also showed slightly higher levels of LDL and VLDL but lower levels of HDL, and a lower HDL/LDL ratio. Their findings suggest that smoking alters the serum lipids and lipoproteins and these changes are related to the duration and amount of smoking.

Manoharan et al [67] evaluated the role of life-style on plasma and erythrocyte membrane lipid profile in 25 adult male gastric cancer patients as well as age and sex-matched controls. Total, free and LDH cholesterol were markedly elevated in plasma and erythrocyte membrane whereas HDL

cholesterol and triglycerides were significantly reduced in gastric cancer patients. These changes can be attributed to alcohol consumption and cigarette smoking-risk factors in gastric carcinogenesis, associated with low levels of ascorbic acid and vitamin E.

Neufeld et al [68] conducted a cross-sectional, pilot-scale study to examined the relationship of HDL cholesterol levels to passive smoking in children and adolescents. HDL cholesterol levels were 38.7±1.2 mg/dL (mean±SEM) in passive smokers versus 43.6±1.2 mg/dL in children without smoke exposure (*P*=.005). They found that mean HDL cholesterol levels were significantly lower in hyperlipidemic children who came from households with smokers compared with those from nonsmoking households. The results of this small-scale study suggest that interventions resulting in decreased cigarette exposure may substantially increase HDL cholesterol levels in this group of patients at higher risk for premature cardiovascular disease.

Vural et al [69] conducted a study involving 13 patients with Actinic Keratosis and 12 patients with Basal Cell Carcinoma to evaluate the serum Cholesterol, phospholipid, triglyceride, and total lipid levels. They found that the levels of all lipid fractions were increased in both Actinic chelitis and Basal cell carcinoma. A significant increase in phospholipids and total lipids with $p < 0.02$, $p < 0.01$ respectively was found in BCC. Serum cholesterol with $p < 0.001$, phospholipid with $p < 0.001$), triglyceride with $p < 0.05$, and total lipid with $p < 0.001$ concentrations of AK patients were

significantly higher than those of the control group. When BCC and controls were compared, a significant increase in phospholipids and total lipids with $p < 0.001$ was seen. Serum cholesterol in BCC patients was significantly lower with $p < 0.001$ and serum phospholipid levels were significantly higher with $p < 0.05$ than those in the AK group. They concluded that an increase in the metabolically active serum phospholipid fraction contributed to the elevated neoplastic tissue phospholipid. This produced altered proportions between lipid fractions in tumorous areas and resulted in changes in the intact nature of the cellular membrane, spread, and malignant proliferation.

Khurana et al [70] conducted a study on Serum lipid profile of 30 smokers, 30 tobacco chewers and 30 controls to evaluate lipid profile in cigarette smokers and tobacco chewers and to see whether tobacco chewing causes same degree of alteration in lipid profile as done by smoking and found that High density lipoprotein-cholesterol was lower both in smoker ($P < 0.01$) as well as in tobacco chewers ($P < 0.001$) than the controls. Both smokers and tobacco chewers had higher values of total cholesterol, low density lipoprotein cholesterol, very low density lipoprotein-cholesterol and, triglycerides as compared to non-smoker, non-tobacco chewer group whereas the differences in levels of lipids in smokers and tobacco chewers were not statistically significant.

Raste et al [71] conducted a study to examine the lipid profile in normal healthy age matched control and patients with various malignancies.

They found that total lipids, cholesterol and HDL cholesterol levels with p<.001 are inversely associated with incidence of cancer where as triglycerides levels were significantly elevated with p>.01 in cancer patients.

Neki [72] conducted a study to evaluate lipid profile in young cigarette/bidi smokers and compare it with non smokers in the fasting state on 50 healthy cigarettes smokers and compared with 50 healthy age and weight matched non-obese non-smokers who served as controls. It was revealed that mean TC,LDL , and VLDL were significantly higher in smokers with p <0.05 as compared to non-smokers. Mean serum TG levels in smokers were significantly high with (p <0.01 as compared to non-smokers. Mean serum HDLC was significantly lower with p <0.01 in chronic smokers as compared to non-smokers. He concluded that smoking produces adverse effects on lipid profile, therefore increasing the cardiovascular disease risk

Patel et al [5] conducted a case control study on 184 head and neck cancer patients, 153 patients with Oral precancerous conditions and 52 controls and their Plasma lipids including Total cholesterol, LDL ,HDL , VLDL and triglycerides were analysed and found a significant decrease in plasma total cholesterol and HDLC was observed in cancer patient P=0.008 and P=0.000 respectively as well as in patients with OPC P=0.014 and P=0.000

Manoharan et al [73] conducted a study to assess the level of oxidative stress in oral cancer patients with various clinical stages. Level of lipid peroxidation and antioxidants in oral cancer patients were studied. They found that the elevated lipid peroxidation and decline in non-enzymatic and enzymatic antioxidants status were noticed in oral cancer patients as compared to healthy subjects. They concluded that altered lipid peroxidation in plasma and erythrocytes of oral cancer patients may be related to their compensatory changes in the antioxidants defense system.

Barcin et al [74] conducted a study to the effects of non-heavy smoking < or =20 cigarettes a day on HDL-c in 1012 male students between 19 and 25 years old. They found that HDL-c with $p<0.001$ showed a stepwise decrease as the level of smoking increased. Total cholesterol, triglycerides and low-density cholesterol were not different among the smoking levels. Body mass index (BMI) and waist/hip ratio were found to be slightly decreased in smokers with $p < 0.001$.They concluded that smoking, even in relatively low levels, has a negative stepwise relationship with HDL-c in a homogeneous population of healthy young men in whom other major non-genetic factors that are known to affect HDL-c levels are identical.

Venkatesan et al [75] conducted a study to to assess the association between smoking and the alteration in plasma concentration of lipid profile and lipid peroxides in fourteen smokers and 11 age matched control group. Plasma levels of fasting cholesterol, triglycerides, lipoprotein cholesterol

and malondialdehyde were estimated. They found that in smokers the levels of total cholesterol p=0.021, LDL cholesterol p=0.006, Non-HDL cholesterol p= 0.016 and MDA p=0.001 were significantly elevated when compared with the controls.

Lim et al [76] conducted a study to investigate the relationship between prediagnostic HDL-C and non-Hodgkin lymphoma (NHL) in 27,074 healthy male smokers of ages 50 to 69 years. They found that there is an inverse association between HDL-C and NHL with P < 0.0001. They concluded that HDL-C as a preclinical indicator of NHL .

Patel et al [77] conducted a study to monitor oxidative stress and predict overall survival in oral cancer patients by estimating markers of oxidative stress such as total antioxidant status, lipid peroxidation, and total thiol levels in 140 oral cancer patients and 50 healthy controls, who were classified as with the habit of tobacco and no habit of tobacco. They found that Thiol levels were significantly lower in controls with the habit of tobacco P= .033, oral cancer patients P= .0001, and malignant tissues P= .015 as compared to controls with no habit of tobacco, controls with the habit of tobacco, and adjacent normal tissues, respectively. They concluded that lipid peroxidation and thiol could be useful for predicting the risk of oral carcinogenesis in healthy tobacco consumers and predicting overall survival of oral cancer patients.

Wakabayashi [78] conducted a study to determine whether influences of drinking alcohol on serum lipid levels are different in smokers

and non-smokers in 25,689 healthy male patients. Serum total cholesterol, HDL, triglyceride concentrations and LDL cholesterol concentrations were estimated. He found that in the smoker groups, serum total cholesterol was significantly lower in heavy drinkers than in non-drinkers, while no difference in total cholesterol was observed in non- and heavy drinkers of the non-smoker group. Both in the smoker and non-smoker groups, HDL cholesterol was higher with $P < 0.01$ and LDL cholesterol was lower in drinkers than in non-drinkers. He concluded that smoking increases the lowering effect of alcohol drinking on LDL cholesterol, but does not affect the relationship of alcohol drinking with HDL cholesterol.

Lohe et al [3] conducted a study on 210 patients with 70 in oral cancer, oral precancer and 70 control group to evaluate and correlate the decreased cholesterol levels in oral cancer, oral precancer. They found a significant decrease in TC ,HDL,VLDL and Triglyceride in Oral cancer group with $p<.001$ and significant decrease in TC,HDL with $p<.001$ in oral precancer as compared to control group. They concluded that there is an inverse relationship between serum lipid profile and oral cancer, oral precancer.

Nayak et al [79] conducted a study on 56 subjects with the study group consisting of a total of 28 patients 14 with OFS and 14 with LP to evaluate changes in plasma lipid profile in patients with oral precancerous conditions and to evaluate if any relation exists between the plasma lipid level and malignant potential. They found that TC, HDL, LDL TC, HDL, and LDL ($p < 0.05$), were reduced in Oral Precancerous patients. They concluded that

TC, HDL, LDL of lipid profile were reduced in OPC patients .Reduced lipid values in plasma may be due to greater utilization of lipids for new membrane biogenesis.

Chawda et al [80] conducted a study to investigate the alterations and clinical significance of plasma lipid profiles in untreated head and neck cancer patients in 30 subjects .They found that the levels of total lipids, cholesterol and HDL with $p<0.005$ were significantly lower in oral cancer patients as compared to controls, but LDL and VLDL values were not significant. They concluded that an inverse relationship was found between the lipid levels and the occurrence of oral cancer.

Shally et al [81]conducted a study on 25 patients of oral squamous cell Carcinoma, 15 patients each of OSMF, leukoplakia, and lichen planus and 15 healthy controls to evaluate the alterations in extended lipid profile . A significant decrease in plasma total cholesterol, HDLC, and triglycerides with $p<.001$ was observed in the patients with the precancerous lesions and conditions as compared to the controls. Thus, an inverse relationship between plasma lipid levels and patients was found Hence, the lower plasma lipid status may be a useful indicator to detect the initial changes seen in neoplastic process.

This is a cross sectional hospital based study conducted between from March 2010 to March 2011 which was designed to estimate the lipid profile in serum in patients with Potentially Malignant diseases namely Oral Leukoplakia and Oral Submucous fibrosis and Oral Squamous cell carcinoma in the Department of Oral Medicine and Radiology of Ragas Dental College and Hospital, Uthandi, Chennai.

Study design:

The present study is a Case Control Study.

Study population:

Study population includes all subjects reporting to Ragas Dental College and Hospital, Outpatient Department, Uthandi seeking dental advice and who are from a wide variety of socioeconomic background. The age group selected was between 20-60 years.

Study sample:

A total number of 75 patients were involved in the study.

a. Normal controls-Group-I : 25
b. Patients with Oral Potentially malignant disorders-Group-II : 25
c. Patients with Oral Squamous cell carcinoma–Group-III: 25

Obtaining approval from the authorities:

Permission from the ethical committee of Ragas Dental College and Hospital, Chennai was obtained before starting the study for interpretation and examining subjects, for drawing 5ml of blood .

Also an informed consent was obtained from the subjects forming the study sample, both in English and Tamil to participate in the study and to undergo blood investigation in the course of study.

Selection Criteria:

For Normal controls

This study group I consists of 25 patients. These patients were selected from the Department of Oral Medicine and Radiology.

Inclusion criteria :

Routine intra oral examination was carried out on all subjects reporting to Ragas Dental College and Hospital, Chennai and during soft tissue examination thorough examination was carried out to rule out any mucosal lesions which is in consistent with the diagnosis of leukoplakia and Oral submucous fibrosis.

Exclusion Criteria :

1. Subjects with major systemic ailments with cardiovascular, respiratory diseases were excluded.
2. Subjects with any form of immunosupression and with autoimmune disorders were excluded

Subjects with history of corticosteroid therapy were excluded

Oral Potentially malignant disorders

This study group II consists of 25 patients suffering from Oral Potentially malignant disorders like Oral Leukoplakia and Oral Submucous fibrosis diagnosed clinically. These patients were selected from the Department of Oral Medicine and Radiology.

LEUKOPLAKIA:

Inclusion Criteria:

Routine intra oral examination was carried out on all subjects reporting to Ragas Dental College and Hospital ,Chennai and subjects with positive history of smoking tobacco and during soft tissue examination, subjects with well-defined white patch, localized or extensive, that is slightly elevated and that has a fissured, wrinkled or corrugated surface or a mixed red – white lesion in which keratotic white nodules or patches are distributed over an atropic erythematous background or presence of thick white lesions with papillary surfaces in the oral cavity and on palpation which reveals leathery consistency and which is in consistant with the diagnosis of leukoplakia were taken for the study.

Exclusion Criteria :

1. Lesions belonging to other entities such as Lichen planus, lupus erythematosus, leukedema and white sponge nevus and lesions for which etiology can be established, such as frictional keratosis, cheek/lip/tongue biting, contact lesions and stomatis nicotina palatini.

2. Subjects with major systemic ailments with cardiovascular, respiratory diseases were excluded.
3. Subjects with any form of immunosupression and with autoimmune disorders were excluded
4. Subjects with history of corticosteroid therapy were excluded.

For subjects with Oral Submucous fibrosis:

Inclusion criteria:

Routine intra oral examination was carried out on all subjects reporting to Ragas Dental College and Hospital, Chennai ,subjects with positive history of arecanut chewing and during soft tissue examination clinical features like blanching of oral mucosa, burning sensation, dryness of mouth, vesicles or ulcers in the mouth ,restriction of mouth opening, palpable fibrotic bands in any area of the mouth with smooth and bald tongue with limited tongue movement and which is in consistent with the diagnosis of Oral submucous fibrosis were taken for the study.

Exclusion criteria :

1. Fibrosis due to radiation therapy, scleroderma, post Actinomycosis healing fibrosis, fibrosis due to trauma, surgery were excluded by taking proper case history and if positive history was present, they were excluded from the study.
2. Subjects with major systemic ailments with cardiovascular, respiratory diseases were excluded.

3. Subjects with any form of immunosupression and with autoimmune disorders were excluded
4. Subjects with history of corticosteroid therapy were excluded

Oral Cancer

This study group III consists of 25 patients suffering from oral cancer diagnosed clinically. These patients were selected from the Department of Oral Medicine and Radiology, Dr.Rai Memorial Medical and Cancer center and Cancer shelter. Clinical Selection Criteria:

Presence of a non – healing ulcer proliferative growth with pain, tenderness, limitation / loss of function, bleeding and indurated margins. Presence of regional lymphadenopathy

MATERIALS

Examination of the patient

- Conventional Dental chair with illumination facility with halogen lamp.
- A pair of sterile gloves.
- Disposable mouth mask.
- Stainless steel Kidney trays.
- Dental Plain mouth mirror, Dental straight probe, tweezer.
- Sterile gauze pieces and cotton.
- Glass tumbler with water.
- 0.2% chlorhexidine gluconate.

- Sterilizer, cheatel forceps.

Collection of blood sample:

- 24 gauge needle and 5ml plastic syringe
- Vacutainer coated with Ethylene diamine tetra acetic acid (EDTA)
- Torniquet
- Sterile Cotton
- 70% alcohol as surface disinfectant
- Sterile vials
- Refrigerator

Equipments:

- Centrifuge for separating plasma from blood
- Shimadzu UV spectrophotometer
- Micro pipette

The experimental subjects were made to sit comfortably on a dental chair. Relevant Demographic data and datas relevant to the habit of smoking, chewing, alcoholism were collected. Subjects were examined under halogen lamp .Sterile hand gloves were used during examination of the subjects. For subjects who showed characteristic features of Oral leukoplakia and Oral submucous fibrosis based on history and clinical features, clinical diagnosis was made by using the clinical grading system for each lesions separately.

For Oral Leukoplakia clinical diagnosis was made with the aid of classification and staging given by **Pindborg et al in 1997.** [8]

Classification and staging of oral leukoplakia:

Provisional (Clinical Diagnosis)

L : Extent of leukoplakia

L0 : No evidence of lesion

L1 : ≤ 2 cm

L2 : 2-4 cm

L3 : ≥ 4cm

S : Site of leukoplakia

S1 : all sites excluding floor of mouth & tongue

S2 : floor of mouth &/ tongue

S3 : not specified

C : Clinical aspect

C1 : homogeneous

C2 : non homogeneous

C3 : not specified.

For Oral submucous fibrosis clinical diagnosis was made with the aid of clinical grading given by **Gupta P C and Dinesh Chandra in 1992**[40]

Grade I :

Presence of only blanching of oral mucosa without symptoms,

Grade II :

Presence of blanching and burning sensation, dryness mouth, vesicles or ulcers in the mouth.

Grade III :

Presence of blanching and burning sensation, dryness mouth, vesicles or ulcers in the mouth with restriction of mouth opening

Grade IV :

Presence of blanching and burning sensation, dryness mouth, vesicles or ulcers in the mouth with restriction of mouth opening and palpable bands all over the mouth without tongue involvement.

Grade V :

Presence of all features of Grade IV with tongue involvement.

Grade VI :

Oral submucous fibrosis along with histopathologically proven carcinoma.

For Oral squamous cell carcinoma , TNM staging is given according to

AJCC

Cancer Staging 2005 [82]

T-SIZE OF THE TUMOUR

- **TX** Primary tumor cannot be assessed.
- **T0** There is no evidence of primary tumor.
- **Tis** Carcinoma is *in situ*.
- **T1** Tumor is 2 cm or less in greatest dimension.
- **T2** Tumor is more than 2 cm but not greater than 4 cm in greatest dimension.

- **T3** Tumor is more than 4 cm in greatest dimension.
- **T4** (lip) Tumor invades through cortical bone, inferior alveolar nerve, floor of mouth, or skin of face, chin or nose.
- **T4a** oral Tumor invades adjacent structures (e.g., through cavity) cortical bone, into deep [extrinsic] muscle of tongue, maxillary sinus, skin of face.
- **T4b** Tumor invades masticator space, pterygoid plates, or skull base and/or encases the internal carotid artery

N-NODE STATUS

- **NX** Regional lymph nodes cannot be assessed.
- **N0** There is no regional nodes metastasis.
- **N1** Metastasis is in a single ipsilateral lymph node, 3 cm or less in greatest dimension.
- **N2** Metastasis is in a single ipsilateral lymph node, more than 3 cm but not more than 6 cm in greatest dimension; or metastasis is in multiple ipsilateral lymph nodes, none more that 6 cm in greatest dimension; or metastasis is in bilateral or contralateral lymph nodes, none greater than 6 cm in greatest dimension.
- **N2a** Metastasis is in a single ipsilateral lymph node, more than 3 cm but not more than 6 cm in greatest dimension.
- **N2b** Metastasis is in multiple ipsilateral lymph nodes, none more that 6 cm in greatest dimension.

- **N2c** Metastasis is in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension.
- **N3** Metastasis is in a lymph node more than 6 cm in greatest dimension

M-Distant Metastasis

- **MX** Distant metastasis cannot be assessed.
- **M0** There is no distant metastasis.
- **M1** There is distant metastasis

Stage Grouping

Stage 0	Tis N0 M0
Stage I	T1 N0 M0
Stage II	T2 N0 M0
Stage III	T3 N0 M0 , T1 N1 M0
	T2 N1 M0, T3 N1 M0
Stage IVA	T4a N0 M0, T4a N1 M0
	T1 N2 M0 , T2 N2 M0
	T3 N2 M0, T4a N2 M0
Stage IVB	T4b Any N M0
	Any T N3 M0
Stage IVC	Any T Any N M1

Blood sample collection:

The patients arm was rested on the working table comfortably. The anti cubital fossa was exposed and the tourniquet was applied above 1 ½ - 2 inch above the anti cubital fossa. The area was rendered aseptic with 70% alcohol and using 24 gauge needles and vacationer 5 ml of fasting blood was drawn, then the tourniquet was relieved and the needle was removed, simultaneously, a sterile cotton was placed on the needle puncture site and instructions were given to apply finger pressure for 5 minutes and dispose the cotton. The collected blood was centrifuged, serum was separated and stored in vials. This freshly obtained serum was used immediately for biochemical analysis.

BIOCHEMICAL ANALYSIS

Estimation of serum lipid profile [83]

Total cholesterol: Serum cholesterol levels were estimated using cholesterol kits obtained from HiTech diagnostics, Chennai.

Methodology:

Principle:

The estimation of cholesterol involves the following enzyme catalysed reactions

1. Cholesterol ester is converted into cholesterol and fatty acid in the presence of cholesterol esterase.

2. Cholesterol then combines with oxygen in the presence of cholesterol oxidase and forms cholest-4-en-3-one and hydrogen peroxide
3. 2 molecules of H2O2 combines with 4 aminoantipyrine and phenol and forms 4 molecules of water and quinoeimine. absorbance of quinoeimine so fromed is directly proportional to cholesterol concentration.

Reagent composition

Reagent 1 : cholesterol reagent

cholesterol esterase	200IU/L
Cholesterol oxidase	150IU/L
Peroxidase(horseradish)	2000IU/L
Sodium phenolate	20mmol/L
4 aminoantipyrine	0.5mmol/L
Phosphate buffer	68mmol/L
Lipid clearing agent	

Reagent 2:

Cholesterol	200mg/dl 5.2mol/l

Reagent 3: Double deionized ,0.2 micron,membrane filtered ,particle free water for reconstitution of reagent 1

Procedure : Reagents 1 and 3 are allowed to attain the room temperature. Aqua 4 is added on to the contents of each vial on the reagent 1,swirled and dissolved.

A blank solution is prepared by adding 1000µl of reagent to 20µl of distilled water. A standard solution is prepared by adding 1000µl of reagent to 20µl of cholesterol standard. A test solution is prepared by adding 1000µl of reagent to 20µl of sample. Blank is aspirated followed by standard and tests. The mixture is shook well and incubated at 37^0 c. The three solutions are read using the analyser. The blank is read first followed by standard and test solution.

High density lipoprotein: Serum High Density Lipoprotein levels were estimated using HDL Cholesterol kits obtained from HiTech diagnostics,Chennai.

Reagent 1:

Phosphotungstic acid	2.4 mmol/L
Magnesium chloride	40mmol/L

Reagent 2:

HDL cholesterol standard	25mg/dl

Reagent preparation: the reagent is ready for use.

Supernatant of sample is obtained by adding 500µl of precipitating reagent to 250µl of sample. Mixture is shook well and allowed to stand for 10 minutes at room temperature. Then the mixture is centrifuged at 4000 rpm for 10 minutes and clear Supernatant fluid is obtained which is used to determine the concentration of HDL cholesterol in the sample.

A blank solution is prepared by adding 1000µl of reagent to 50µl of distilled water. A standard solution is prepared by adding 1000µl of reagent to 50µl of HDL cholesterol standard. A test solution is prepared by adding 1000µl of reagent to 50µl of supernatant. The mixture is shook well and incubated at 37^0 C. The three solutions are read using the analyser. The blank is read first followed by standard and test solution.

Triglyceride : Serum Triglyceride levels were estimated using HDL Cholesterol kits obtained from HiTech diagnostics, Chennai.

Reagent 1:

Ingredient	**Concentration**
ATP	2.5mmol/L
Mg^{2+}	2.5mmol/L
4 aminoantipyrine	0.8mmol/L
3,5 dichloro-2-hydroxybenzen sulfonate	1mmol/L
Peroxidase	2000IU/L

Glycerol kinase	550IU/L
Glycerol phosphate oxidase	8000IU/L
Lipoprotein lipase	3500IU/L
Buffer	53mmol/L

Reagent 2 :

Triglyceride standard	200mg/dl

Procedure : Reagent bottles and aqua 4 are allowed to attain the room temperature. Aqua 4 is added on to the contents of each vial , swirled and allowed to stand for 10 minutes at room temperatue.

A blank solution is prepared by adding 1000µl of reagent to 10µl of distilled water. A standard solution is prepared by adding 1000µl of reagent to 10µl of triglyceride standard. A test solution is prepared by adding 1000µl of reagent to 10µl of sample.The mixture is shook well and incubated at 37^0 c. The three solutions are read using the analyser. The blank is read first followed by standard and test solution.

Very lowdensity lipoprotein : calculated by the fomula

VLDL=Triglyceride/5

Lowdensity lipoprotein : calculated by the fomula

LDL=Total clolesterol-(VLDL-HDL)

Normal values

Parameter	Normal serum concentration (mg%)
Total cholesterol	140-250
HDL	30-80
LDL	65-130
TGL	25-160
VLDL	5-32

The study group was compared with the above normal values.

Statistical Analysis:

All the datas were entered in Microsoft excel sheets. Statistical analysis was done using SPSS software SYSTAT version 7.0.

Mean and standard deviation were estimated in the sample for each study group. Mean values were compared by using one-way ANOVA followed by multiple range tests by Tukey-HSD for multiple group comparison and students 't" test for two group comparison.

In the present study P <0.05 was considered as the level of significance.

$$\text{Mean } (X) = \frac{\sum \overline{X}i}{n}$$

$$\text{Standard Deviation} = \sqrt{\frac{\sum(Xi-X)^2}{n-1}}$$

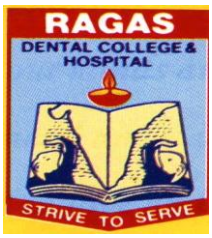
Where Xi is the individual observation and n is the sample size.

ANOVA:

$$\text{F Ratio} = \frac{\text{Variation between observed group averages}}{\text{Variation within each group}}$$

Students “t” test(unpaired)

t=difference in means/standard error of difference



RAGAS DENTAL COLLEGE & HOSPITAL

2/102, East Coast Road, Uthandi, Chennai – 600119

DEPARTMENT OF ORAL MEDICINE & RADIOLOGY

CASE SHEET PROFORMA

Date:

S.No	:	
OP.No	:	
Study group	:	Group I / Group II / Group III
Name	:	
Age/Sex	:	
Address	:	
Phone number	:	
Occupation	:	
Monthly income	:	

Past medical /surgical/dental /history

HABITS	PRESENT	ABSENT	DURATION
Smoking			
Chewing			
Alcohol			

:

Leukoplakia :

Site :

Size :

Type :

Oral submucous fibrosis :

Grade :

Oral Squamous cell carcinoma

Site :

Size :

Type:

Clinical staging:

LIPID PROFILE:

Parameters/ Lesion	Total Cholesterol (TC) (mg%/)	Lowdensity Lipoprotein (LDL) (mg%)	Highdensity Lipoprotein (HDL) (mg%)	Very Low Density Lipoprotein (VLDL) (mg%)	Triglyceride (TGL) (mg%)
Potentially malignant disorders					
Oral Squamous Cell Carcinoma					

Figure 1: Armamentarium for Clinical Examination

Figure 2: Normal Mucosa

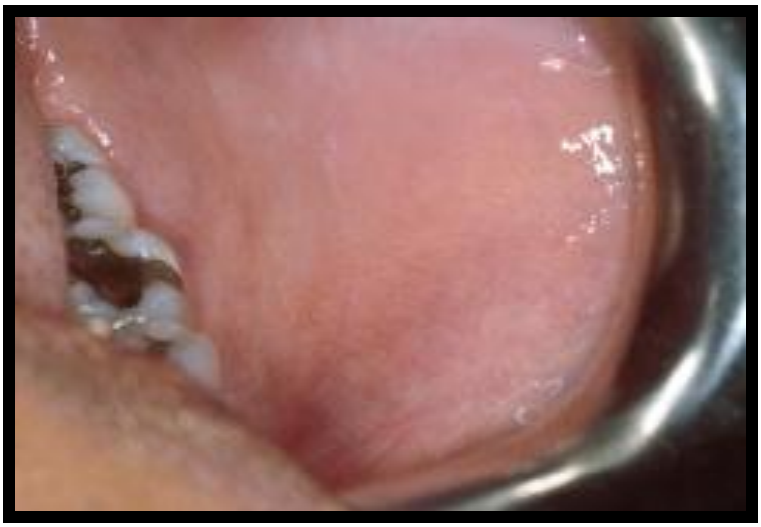


Figure 3: Clinical Lesion - Leukoplakia

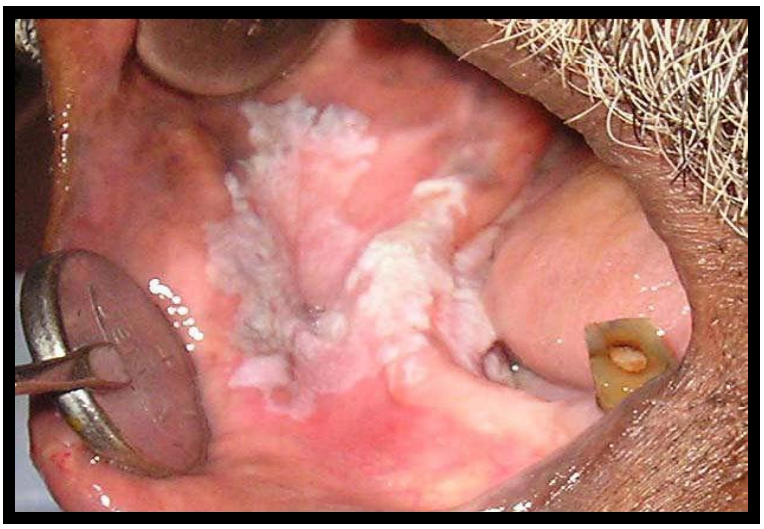


Figure 4: Clinical Lesion – Oral Submucous Fibrosis

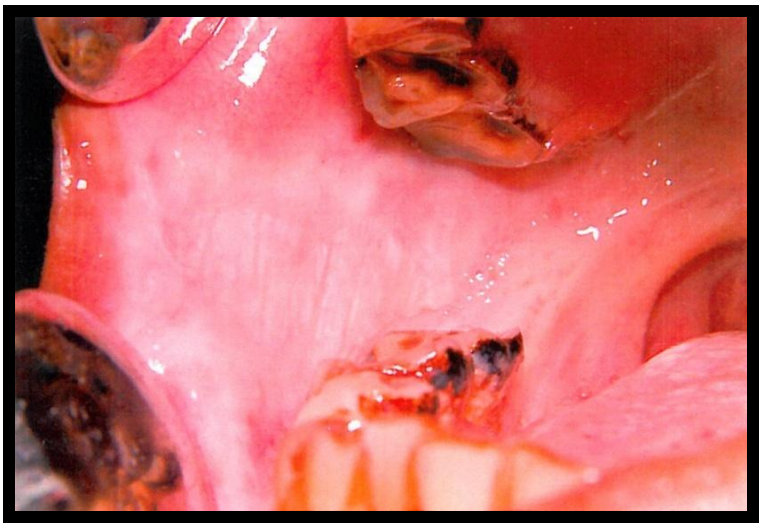


Figure 5: Clincal Lesion-Oral Cancer

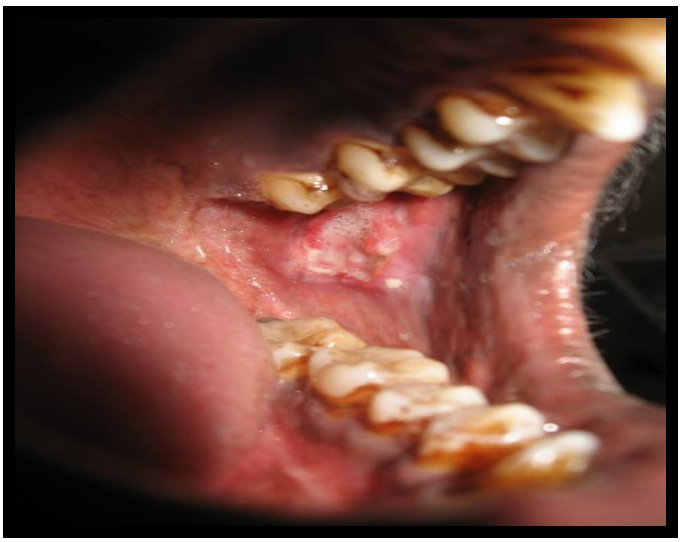


Figure 6: Clinical Lesion – Oral Cancer

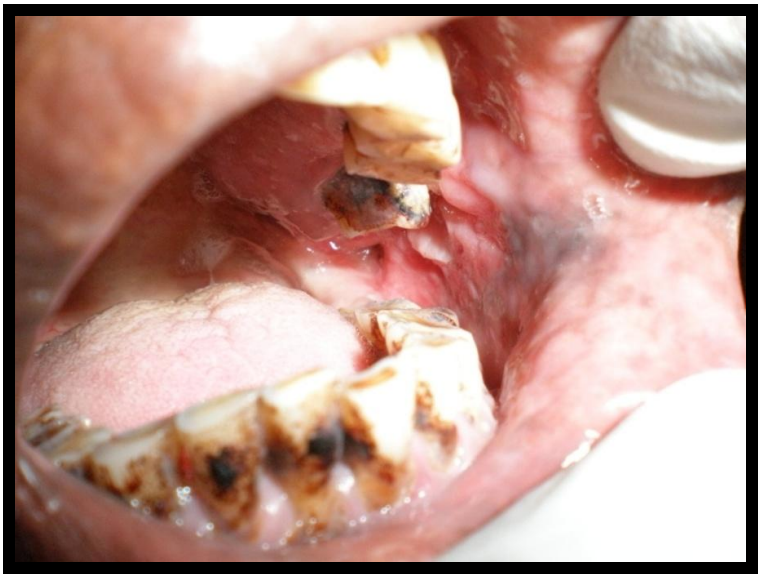


Figure 7: Materials for Sample Collection

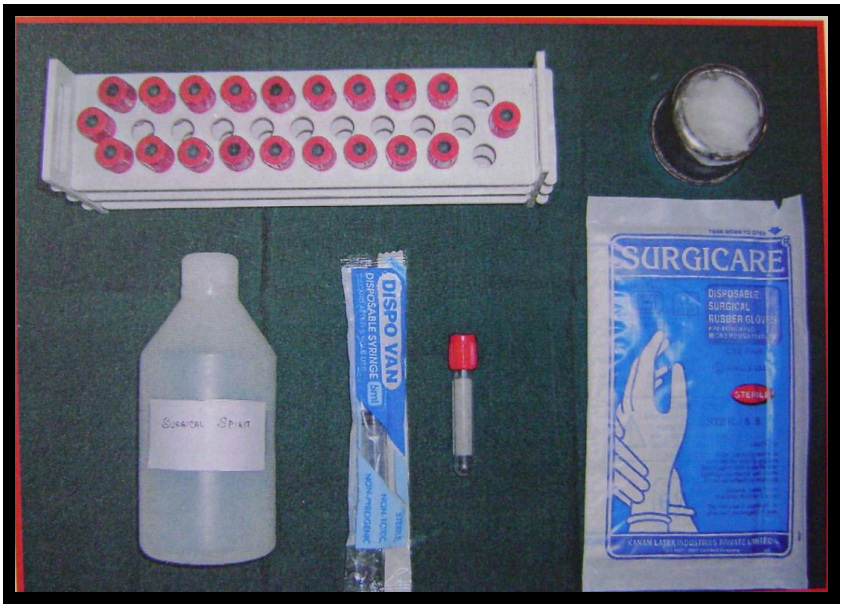


Figure 8: Materials for Biochemical Analysis

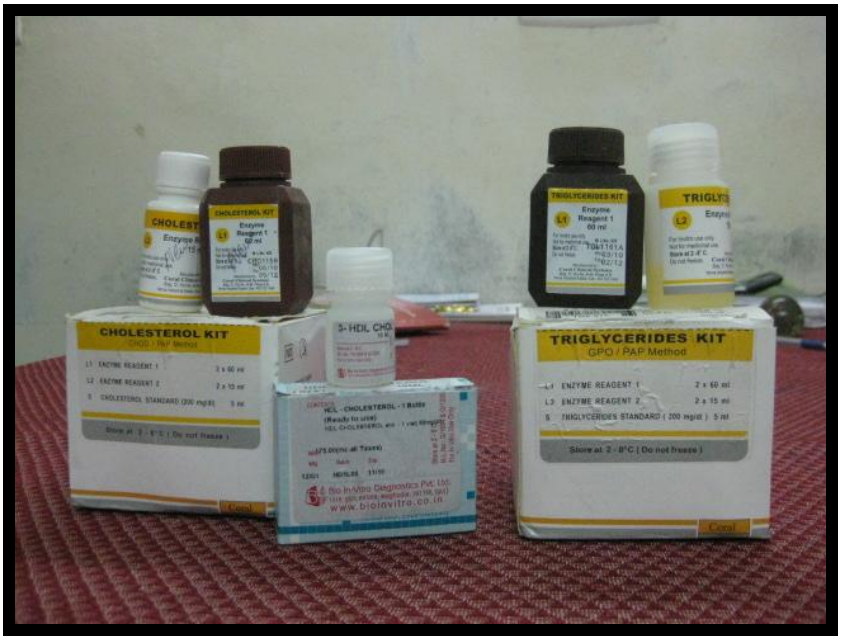
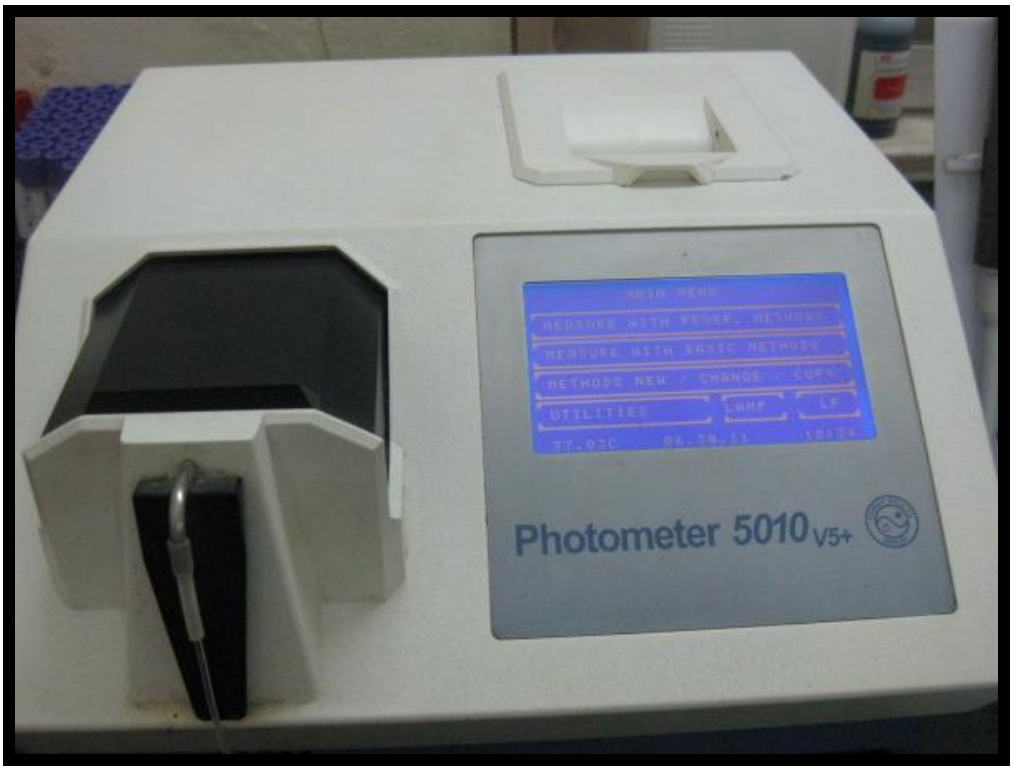


Figure 9: Spectrophotometer



The present study is a randomized case control study which was conducted in the Department of Oral Medicine and Radiology of Ragas Dental College and Hospital, Uthandi, Chennai. It was devised to estimate the Serum lipid profile in patients with Oral Potentially Malignant disorders, Oral squamous cell carcinoma and healthy controls. The study was conducted between March 2010-March 2011 on a total of 75 subjects with 25 subjects in each group. The datas obtained from the study were statistically analysed. The results extracted are compared with various variables included in the study and are presented here.

Table 1: Sex wise distribution of subjects

The study group consisted of a total number of 75 subjects. Out of the 75 patients, 25 subjects were included in normal controls (Group I) and among them 17 (68%) were males and 8 (32%) were females,25 subjects were included in Oral Potentially malignant disorders (Group II) and among them 23(92%) were males and 2 (8%) were females, 25 were included in Oral Squamous cell carcinoma (Group III) and among them 16 (64%) were males and 9 (36%) females .

The sex wise distribution of subjects were found to be **statistically insignificant**, which means that both the experimental and control subjects were similar with respect to sex in distribution with **p value 0.157.**

Table 2: Age wise distribution of subjects

The age of the subjects included in the study ranges between 20-70 years. So the subjects were divided into five age groups which are as follows: 20-30 years, 31-40 years, 41-50 years, 51-60 years and 61-70 years. Among the 25 in group I, 09(36%) were between 20-30 years, 07(28%) were between 31-40 , 02(8%) were between 41-50 years and 05(20%) were between 51-60 years and 02(8%) were between 61-70 years. Among the 25 in group II, 05(20%) were between 20-30 years, 11(44%) were between 31-40 yrs , 8(32%) were between 41-50 years , 1(4%) were between 51-60 years and no subjects were in the age group of 61-70 .Among the 25 in group III, no subjects were in the age group of 20-30 years and 31-40 years, 4(16%) were between 41-50 years , 10(40%) were between 51-60 years 11(44%) were between 61-70 years.

The age wise distribution of subjects were found to be **statistically highly significant**, which means that there exists correlation among the 3 groups with respect to age in distribution with **p value≤ 0.001**

Table 3: Age and Sex wise distribution of subjects in Group-I

Table three shows the distribution of subjects based on age and sex in the Group I. The age range was from 23 to 63 years with the mean age of 39.08 years. There is a clear male predilection of 17(68%) compared to the females who accounted for 8 (32%) in the total of 25.

Table 4: Age and Sex wise distribution of subjects in Group-II:

Table four shows the distribution of subjects based on age and sex in Group-II. The age range was from 22 to 58 years with the mean age of 37.4 years. There is a clear male predilection of 23(92%) compared to the females who accounted for 2(8%) in the total of 25.

Table 5: Age and Sex wise distribution of subjects in Group-III:

Table five shows the distribution of subjects based on age and sex in Group III. The age range was from 46 to 70 years with the mean age of 59.08 years. There is a clear male predilection of 16(64%) compared to the females who accounted for 9(36%) in the total of 25.

Table 6: Show Distribution of the subjects based on the habits:

The distributions of habits were grouped as follows, smoking, chewing, chewing and smoking, smoking and alcohol, chewing and alcohol, and chewing, smoking and alcohol.

In group I out of the 25 (100%), subjects, 14(56%) had the no habits,7(28%) of only smoking, 4(16%) had the habit of only chewing, none had the habit of smoking, smoking and chewing and alcohol consumption and all three habits together

In group II among the 25 (100%), subjects, 8(32%) had the habit of only smoking, 14(56%) had the habit of only chewing, 3(12%) had the combined habits of smoking and alcohol consumption, while none had the habit of smoking and chewing ,chewing and alcohol and all three habits together.

In group III among the 25 (100%), subjects, 14(56%) had the habit of only chewing, 7(28%) had the habit of smoking and chewing while none had the habit of only smoking, smoking and alcohol consumption and 4(16%) had all three habits together.

The distribution of subjects based on habits were found to be **statistically significant,** with the habit of chewing , smoking, alcoholism alone or in combination of habits with the p value ≤ 0.000.

Table 7: Show Distribution of the subjects according to the lesion in Group II:

The subjects in Group II were divided into two classes based on the type of Potentially malignant disorder present as follows, Leukoplakia and Oral submucous fibrosis. Among the 25 (100%), subjects in Group II, 14(56%) had Oral submucous fibrosis and 11(44%) had Leukoplakia. The group is constant and hence the p-value is not attained.

Table 8: Show Distribution of the subjects according to the grades of OSMF in Group II:

In Group II 14(56%) subjects out of the total of 25(100%) had OSMF with 4(28.6%) in Grade I, 6(42.8%) in Grade III, 4(26.6 %) in Grade IV and none in Grade II. The p-value is not attained as the group is constant. The group is constant and hence the p-value is not attained.

Table 9: Show Distribution of the subjects according to the site of Leukoplakia in Group II:

In Group II among the total of 25 (100%) subjects, 11(44%) had leukoplakia in which 5(45.5%) were present in the retro-commissure area, 5 (45.5%) in the buccal mucosa and 1(9%) in the floor of the mouth. The group is constant and hence the p-value is not attained

Table 10: Show Distribution of the subjects according to the site of carcinoma in Group III:

In Group III oral carcinoma was seen in 5 different sites: tongue, buccal mucosa, alveolar mucosa, floor of the mouth, palate

In Group III among the 25 subjects, 3(12%) had carcinoma in the tongue, 12(48%) had in the buccal mucosa, 5(20%) had in the alveolar mucosa, 1(4%) had carcinoma in the floor of the mouth and 4(16%) in the palate. The group is constant and hence the p-value is not attained.

Table 11: Show Distribution of the subjects according to the stages of OSCC in Group III:

In Group III, among the total of 25(100%) had OSCC with 5(20%) in Stage I, 4(16%) in Stage II, 8(32%) in Stage III and 8(32%) in Stage IV. The group is constant and hence the p-value is not attained.

TABLE 12: LIPID PROFILE IN GROUP I, II, III

TOTAL CHOLESTEROL IN THREE GROUPS

The total cholesterol (TC) levels is highest in controls (Group-I)which is 172.56 with a standard deviation of 29.2 followed by subjects with oral potentially malignant disorder (Group-II) which is 159.84±15.5 and the lowest value is seen with Oral Squamous Cell carcinoma (Group-III) which is157.56±12.3.The p value in relation to the variable TC with reference to Group-I,Group-II,Group-III is <0.01 and it is significant.

LDL CHOLESTEROL IN THREE GROUPS

LDL levels is highest in controls (Group-I) which is 102.60 with a standard deviation of 24.4 followed by subjects with Oral Squamous Cell carcinoma (Group-III) which is 92.44±14.6 and the lowest value is seen with oral potentially malignant disease (Group-II) which is 91.16±17.0.The p value in relation to the variable LDL with reference to Group-I,Group-II, Group-III is 0.07 and it is insignificant.

HDL CHOLESTEROL IN THREE GROUPS

HDL levels is highest in controls (Group-I)which is 42.76 with a standard deviation of 3.1 followed by subjects with oral potentially malignant disease (Group-II) which is 40.72±3.2 and the lowest value is seen with Oral Squamous Cell carcinoma (Group-III) which is 38.92±2.5.The p value in relation to the variable HDL with reference to Group-I,Group-II,Group-III is <0.001 and it is significant.

VLDL CHOLESTEROL IN THREE GROUPS

VLDL levels is highest in controls (Group-I) which is 33.32 with a standard deviation of 9.4 followed by subjects with oral potentially malignant disease (Group-II) which is 29.96±10.7 and the lowest value is seen with Oral Squamous Cell carcinoma (Group-III) which is 26±9.The p value in relation to the variable VLDL with reference to Group-I, Group-II,Group-III is <0.01 and it is significant.

TGL CHOLESTEROL IN THREE GROUPS

TGL levels is highest in controls (Group-I) which is 151.68with a standard deviation of 20.5 followed by subjects with oral potentially malignant disease (Group-II) which is 141.04±53.4 and the lowest value is seen with Oral Squamous Cell carcinoma (Group-III) which is 131.16±44.7. The p value in relation to the variable TGL with reference to Group-I, Group-II, Group-III is 0.22 and it is insignificant.

Table 13: CORRELATION OF TOTAL CHOLESTEROL BETWEEN GROUP I, II &GROUPIII.

The mean difference between Group-I and Group-II is 12.60, with p value < 0.01 which is significant. The mean difference between Group-I and Group-III is 14.88, with p value <0.01 which is significant.

The mean difference between Group-II and Group-I is -12.60, with p value <0.01 which is significant. The mean difference between Group-II and Group-III is 2.28, with p value 0.91 which is insignificant.

The mean difference between Group-III and Group-I is-14.88, with p value <0.01 which is significant. The mean difference between Group-III and Group-II is-2.28, with p value 0.91 which is insignificant.

Table 14: CORRELATION OF LDL BETWEEN GROUP I, II & GROUP III:

The mean difference between Group-I and Group-II is 11.44, with p value 0.09 which is insignificant. The mean difference between Group-I and Group-III is 10.16, with p value 0.15 which is insignificant.

The mean difference between Group-II and Group-I is -11.44, with p value 0. 09 which is insignificant. The mean difference between Group-II and Group-III is -1.28, with p value 0.97 which is insignificant.

The mean difference between Group-III and Group-I is-10.16, with p value 0.15 which is insignificant. The mean difference between Group-III and Group-II is 1.28, with p value 0.97 which is insignificant

Table 15: CORRELATION OF HDL BETWEEN GROUP I, II &GROUPIII:

The mean difference between Group-I and Group-II is 1.04, with p value <0.05 which is significant. The mean difference between Group-I and Group-III is 2.84, with p value <0.001 which is highly significant.

The mean difference between Group-II and Group-I is -1.04, with p value <0.05 which is significant. The mean difference between Group-II and Group-III is 1.80, with p value 0.09 which is insignificant.

The mean difference between Group-III and Group-I is-2.84, with p value <0.001 which is highly significant. The mean difference between Group-III and Group-II is-1.04, with p value 0.09 which is insignificant.

Table 16: CORRELATION OF VLDL BETWEEN GROUP I, II & GROUP III:

The mean difference between Group-I and Group-II is 5.36, with p value 0.13 which is insignificant. The mean difference between Group-I and Group-III is 7.32, with p value <0.05 which is significant.

The mean difference between Group-II and Group-I is -5.36, with p value 0.13 which is insignificant. The mean difference between Group-II and Group-III is 1.96, with p value 0.75 which is insignificant.

The mean difference between Group-III and Group-I is-7.32, with p value <0.05 which is significant. The mean difference between Group-III and Group-II is-1.96, with p value 0.75 which is insignificant

Table 17: CORRELATION OF TGL BETWEEN GROUP I, II & GROUP III:

The mean difference between Group-I and Group-II is 10.64, with p value 0.64 which is insignificant. The mean difference between Group-I and Group-III is 20.52, with p value 0.19 which is insignificant.

The mean difference between Group-II and Group-I is -10.64, with p value 0.64 which is insignificant. The mean difference between Group-II and Group-III is 9.88, with p value 0.68 which is insignificant.

The mean difference between Group-III and Group-I is-20.52, with p value 0.19 which is insignificant. The mean difference between Group-III and Group-II is -9.88, with p value 0.68 which is insignificant

TABLE 18: CORRELATION OF LIPID PROFILE WITH AGE IN GROUP I (CONTROL)

TC is 171.24± 32.71 in the males and 175.00±22.04 in the females. TC is more in females when compared to males, however the differences are not statistically significant with p value 0.07.LDL is 102.82±27.27 in males and 102.13± 18.77 in females.LDL is almost equal in both the groups and the difference is statistically insignificant with p value 0.09.HDL is more in females with value of 42.25± 4.2 and less in males with value of 41.53±2.70. The difference is not statistically significant with p value of 0.06.VLDL in males is 30.82±7.00 and in females is 38.63± 12.06. VLDL is more in females with difference which is statistically significant with p value of <0.05. TGL in males is 154.47±18.89 and in females is 145.75±24.03.TGL is more in males when compared to females. However the differences are not statistically significant with p value of 0.38

TABLE 19: CORRELATION OF LIPID PROFILE WITH AGE IN GROUP II (OPC)

TC is 161.13± 15.55 in the males and 145.00±1.41 in the females. TC is more in males when compared to females, however the differences are not statistically significant with p value 0.16. LDL is 92.04±17.52 in males and 81± 4.24 in females.LDL is more in males when compared to females but

the difference is statistically insignificant with p value 0.06. HDL is more in males with value of 40.83± 0.3 and less in females with value of 39.5±0.71. The difference is not statistically significant with p value of 0.16. VLDL in males is 28.26±11.17 and in females is 24.50± 2.12. VLDL is more in males with difference which is not statistically significant with p value of 0.20. TGL in males is 142.52±55.11 and in females is 124±9.90.TGL is more in males when compared to females. However the differences are not statistically significant with p value of 0.19

TABLE 20: CORRELATION OF LIPID PROFILE WITH AGE IN GROUP III (OSCC)

TC is 155.19± 11.76 in the males and 161.78±12.99 in the females. TC is more in females when compared to males, however the differences are not statistically significant with p value 0.20. LDL is 87.88±12.76 in males and 100.56± 14.89 in females.LDL is more in females when compared to males but the difference is statistically insignificant with p value 0.35. HDL is almost equal in both groups , in males with value of 39.94± 2.93 and in females with value of 39.8±2.03. The difference is not statistically significant with p value of 0.95. VLDL in males is 28.06±9.66 and in females is 22.33± 6.96. VLDL is more in males with difference which is not statistically significant with p value of 0.16. TGI in males is 140.50±48.59 and in females is 114.56±33.03.TGI is more in males when compared to females. However the differences are not statistically significant with p value of 0.12.

TABLE 21 CORRELATION OF DURATION OF HABITS AND LIPID PROFILE IN OPC

Group II (PMD) had 25 patients. They were divided on the basis of duration of habits in to two categories namely Category A –Subjects with the habit for less than 15 years and Category B –Subjects with the habit for more than 15 years. 11 subjects had habit for less than 15 years and 14 subjects had habits more than 15 years. TC is 155.91±11.37 in the habit less than 15 years group and 162.93± 17.96 in habit more than 15 years group.TC is more in Category B. The difference is not statistically significant with p value of 0.27. LDL is 86.00±17.69 in the habit less than 15 years group and 95.21± 16.03 in habit more than 15 years group. LDL is more in Category B. The difference is not statistically significant with p value of 0.18. HDL is 39.93±2.58 in the habit less than 15 years group and 41.73± 3.77 in habit more than 15 years group .HDL is more in Category B. The difference is not statistically significant with p value of 0.16. VLDL is 27.78±9.56 in the habit less than 15 years group and 28.18± 12.59 in habit more than 15 years group. VLDL is more in Category B. The difference is not statistically significant with p value of 0.9. TGL is 139.50±47.57 in the habit less than 15 years group and 143± 61.67 in habit more than 15 years group. TGL is more in Category B. The difference is not statistically significant with p value of 0.8

TABLE 22: CORRELATION OF TYPES OF LEUKOPLAKIA AND LIPID PROFILE:

The subjects in Group II were divided into two classes based on the type of Potentially malignant disorder present as follows, Leukoplakia and Oral submucous fibrosis. Among 11 subjects who had Leukoplakia, 7 subjects had homogenous type and 4 had speckled type.TC is 162.14±13.05 in homogenous type and 151± 9.83 in speckled type .TC is more in homogenous type. The difference is not statistically significant with p value of 0.17. LDL is 96.67±11.88 in homogenous type and 70.75± 14.24 in speckled type LDL is more in homogenous type .The difference is not statistically significant with p value of 0.15. HDL is 43.14±3.13 in homogenous type and 41.25± 4.64 in speckled type. HDL is more in homogenous type. The difference is statistically significant with p value of <0.05. VLDL is 24.28±5.82 in homogenous type and 37± 18.34 in speckled type. VLDL is more in speckled type. The difference is not statistically significant with p value of 0.1. TGL is 124.29 ±8.85 in homogenous type and 185±46.46 in speckled type. TGL is more in speckled type. The difference is not statistically significant with p value of 0.12.

TABLE 23: CORRELATION OF GRADES OF OSMF AND LIPID PROFILE:

The subjects in Group II were divided into two classes based on the type of potentially malignant disorder present as follows, Leukoplakia and Oral submucous fibrosis.Among 14 subjects who had OSMF, 4 subjects

were in Grade I , 6 subjects were in Grade III, 4 subjects were in Grade IV and none in Grade II.TC is 165.65±18.26 in Grade I, 148.67±4.08 in Grade III and 175.75±19.67 in Grade IV.TC is highest in Grade IV followed by Grade I and Grade III. The difference is not statistically significant with p value of 0.36. LDL is 101.75±18.96 in Grade I, 84±4.24 in Grade III and 102.00±20.51 in Grade IV.LDL is highest in Grade IV followed by Grade I and Grade III. The difference is not statistically significant with p value of 0.12. HDL is 39.25±1.25 in Grade I, 38.67±1.36 in Grade III and 42.00±3.74 in Grade IV. HDL is highest in Grade IV followed by Grade I and Grade III. The difference is not statistically significant with p value of 0.10. VLDL is 24.50±1.00 in Grade I, 26±3.57 in Grade III and 31.75±17.74 in Grade IV. VLDL is highest in Grade IV followed by Grade III and Grade I. The difference is not statistically significant with p value of 0.5. TGL is 123.50±7.32 in Grade I, 131.17±16.25 in Grade III and 158.75 ±9.61 in Grade IV. TGL is highest in Grade IV followed by Grade III and Grade I. The difference is not statistically significant with p value of 0.56.

TABLE 24: CORRELATION OF DURATION OF HABITS AND LIPID PROFILE IN OSCC:

Group III (OSCC) had 25 patients. They were divided on the basis of duration of habits into two categories namely those had the habit for less than 15 years and those had the habit for more than 15 years.1 subject had habit for less than 15 years and 24 subjects had habits more than 15 years. TC is 171 in the habit less than 15 years group and 157± 12.31 in

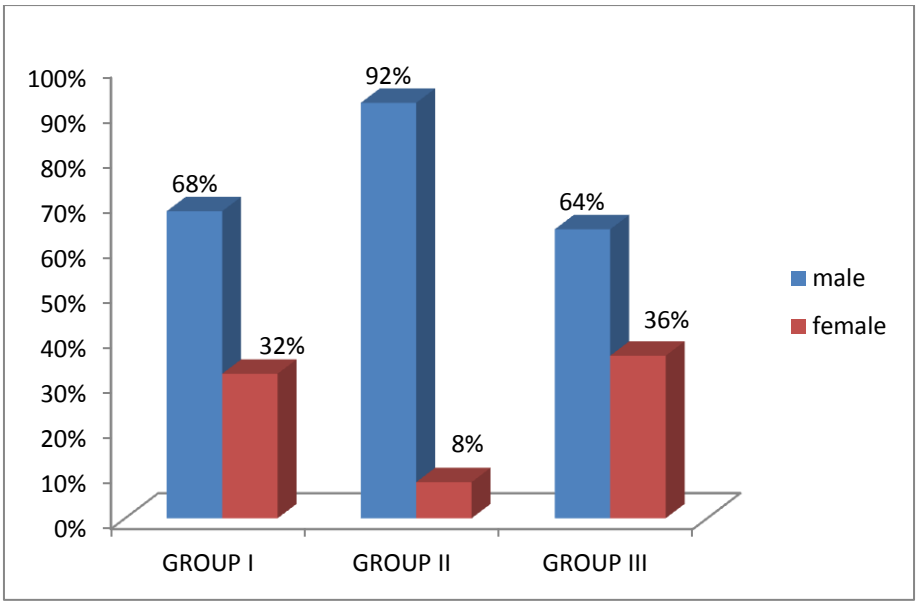
habit more than 15 years group which is more than the second category. The difference is not statistically significant with p value of 0.27. LDL is 115 in the habit less than 15 years group and 91.5± 14.16 in habit more than 15 years group which is more than the second category. The difference is not statistically significant with p value of 0.11. HDL is 40 in the habit less than 15 years group and 38.88± 2.66 in habit more than 15 years group which is more than the second category. The difference is not statistically significant with p value of 0.68. VLDL is 16 in the habit less than 15 years group and 26.14± 9.02 in habit more than 15 years group which is less than the second category. The difference is not statistically significant with p value of 0.27. TGL is 81 in the habit less than 15 years group and 133.25± 43.43 in habit more than 15 years group which is less than the second category. The difference is not statistically significant with p value of 0.26

TABLE 25: CORRELATION OF STAGES OF OSCC AND LIPID PROFILE:

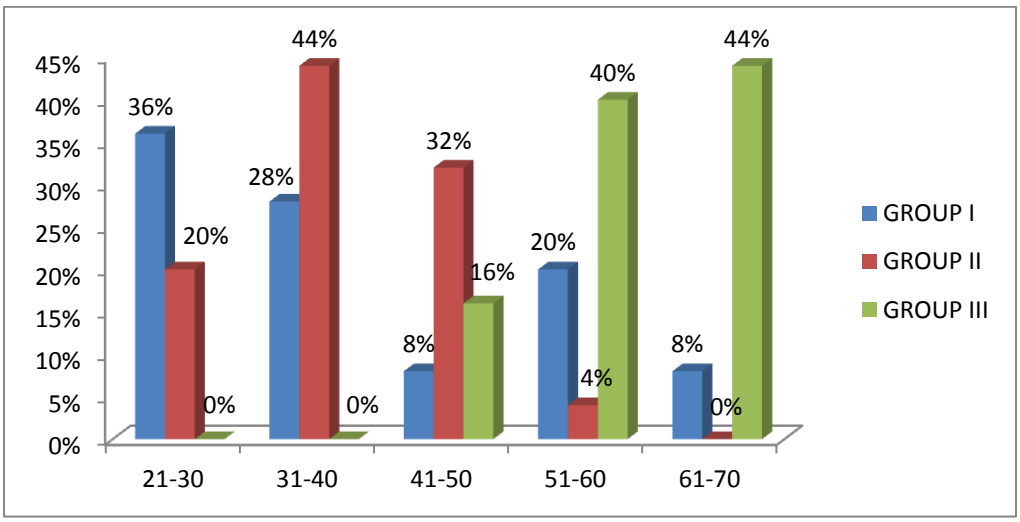
Among the 25 subjects in Group III (OSCC) 5 subjects were in Stage I , 4 subjects were in Stage II, 8 subjects were in Stage III and 8 subjects in Grade IV .TC is 165.6±7.40 in Stage I , 172.7±2.63 in Stage II, and 149.7±13.04 in Stage III and 152.7±6.79 in Stage IV. TC is highest in Stage II followed by Stage I, Stage IV and Stage III. The difference is statistically significant with p value of 0.00. LDL is 105.80±13.33 in Stage I, 109.50±4.04 in Stage II, and 83.25±12.78 in Stage III and 84.75±2.25 in Stage IV. LDL is highest in Stage II followed by Stage I, Stage IV and

Stage III. The difference is not statistically significant with p value of 0.35. HDL is 39.20±0.83 in Stage I , 40.75±1.70 in Stage II, and 37.88±2.85 in Stage III and 38.88±3.18 in Stage IV. HDL is highest in Stage II followed by Stage I, Stage IV and Stage III. The difference is statistically significant with p value of 0.00. VLDL is 19.60±4.92 in Stage I , 22.50±2.64 in Stage II, and 28.62±12.81 in Stage III and 29.12±6.79 in Stage IV. VLDL is highest in Stage IV followed by Stage III, Stage II and Stage I. The difference is not statistically significant with p value of 0.19. TGL is 98.60±25.22 in Stage I , 120.25±16.64 in Stage II, and 143.75±64.22 in Stage III and 144.38±32.37 in Stage IV. TGL is highest in Stage IV followed by Stage III, Stage II and Stage I. The difference is not statistically significant with p value of 0.24.

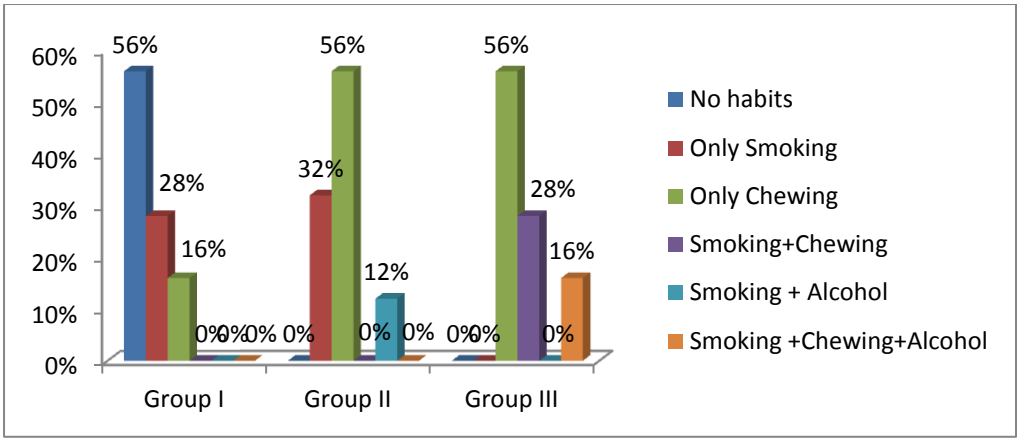
GRAPH – 1: DISTRIBUTION OF SUBJECTS BY SEX



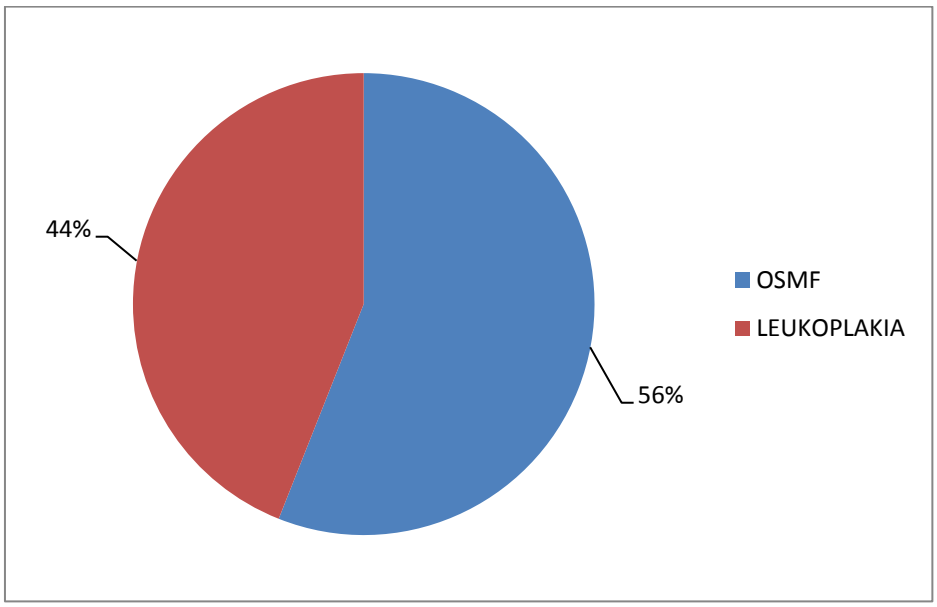
GRAPH – 2: DISTRIBUTION OF SUBJECTS BY AGE



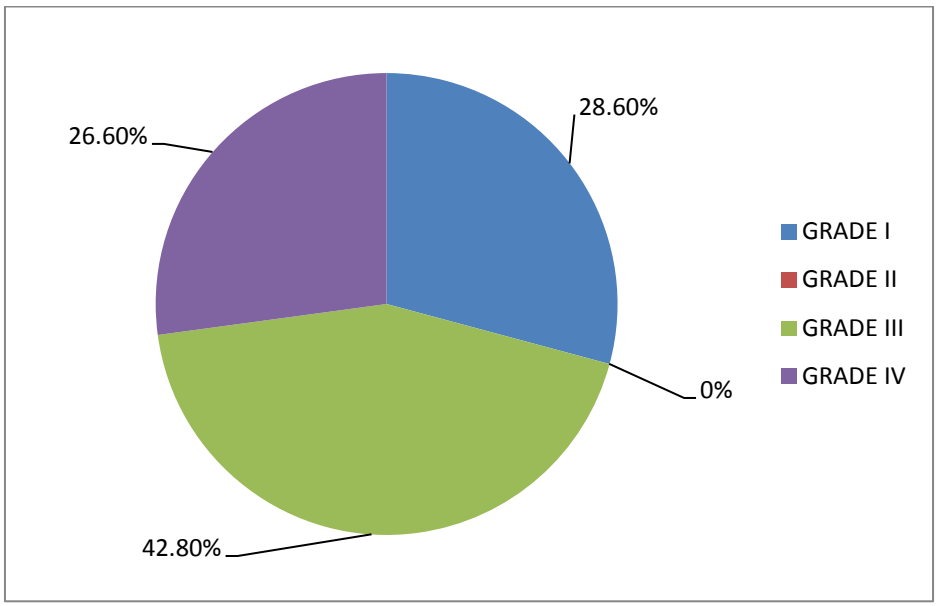
GRAPH – 3: DISTRIBUTION OF SUBJECTS BASED ON HABITS



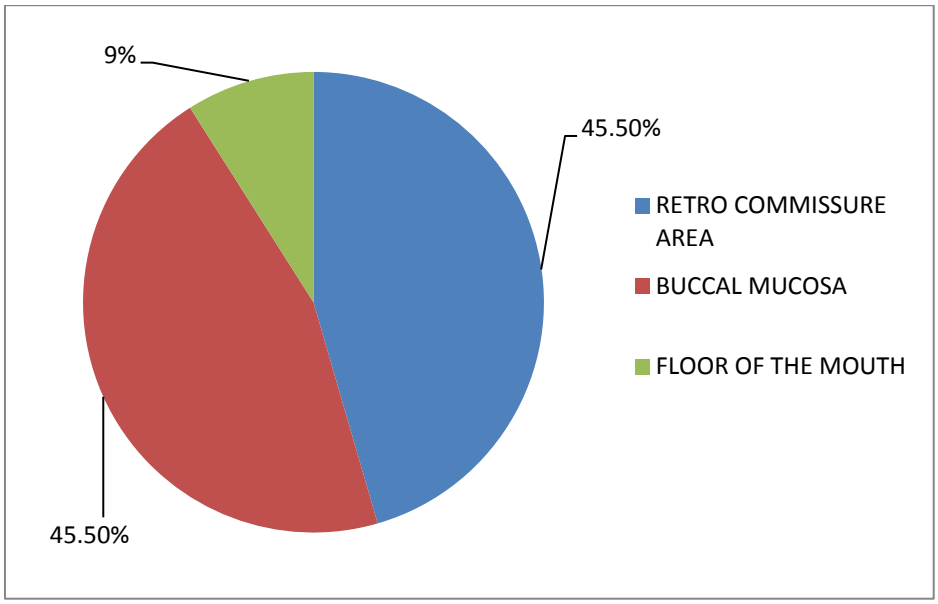
GRAPH – 4 DISTRIBUTION OF SUBJECTS ACCORDING TO LESION IN GROUP II



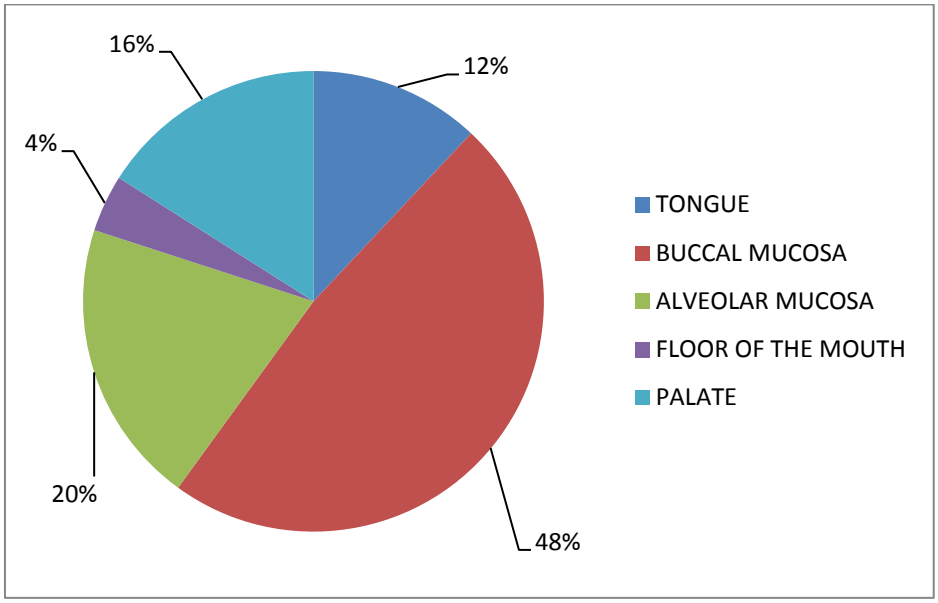
GRAPH – 5 DISTRIBUTION OF SUBJECTS ACCORDING TO THE GRADE OF ORAL SUBMUCOUS FIBROSIS



GRAPH – 6 DISTRIBUTION OF SUBJECTS ACCORDING TO THE SITE OF LEUKOPLAKIA



GRAPH – 7 DISTRIBUTION OF SUBJECTS ACCORDING TO THE SITE OF CARCINOMA IN GROUP III



GRAPH – 8 DISTRIBUTION OF SUBJECTS ACCORDING TO THE CLINICAL STAGING OF GROUP III

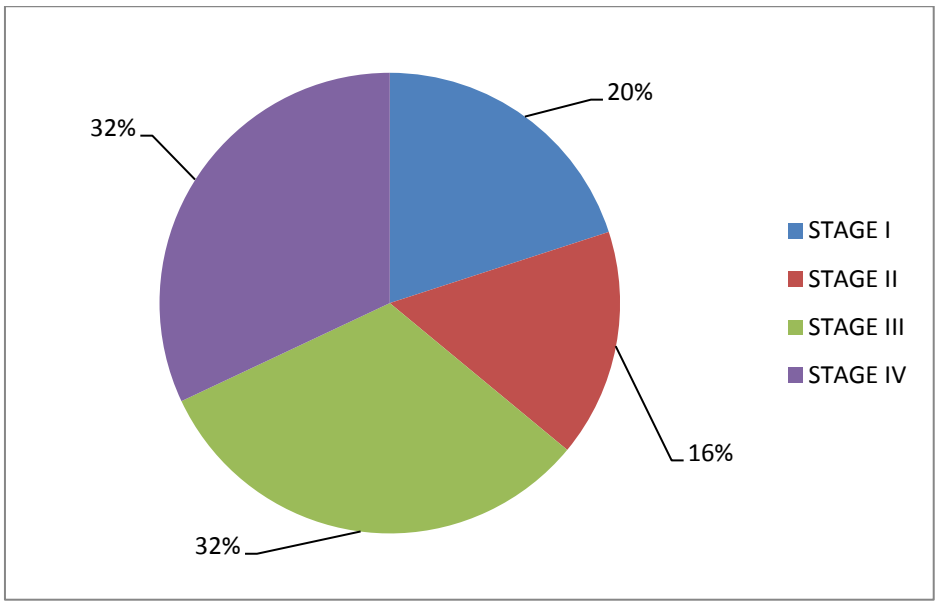
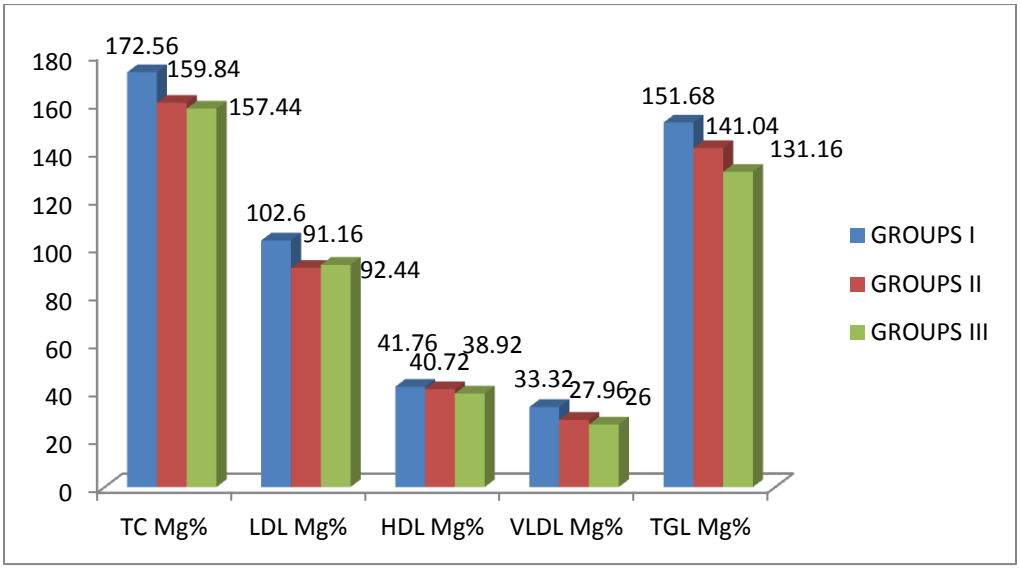
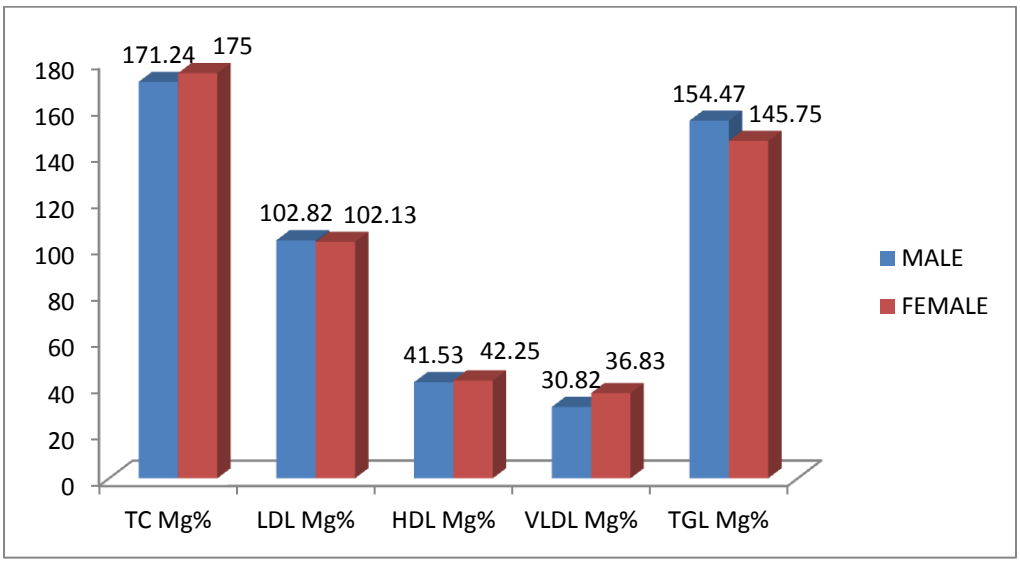


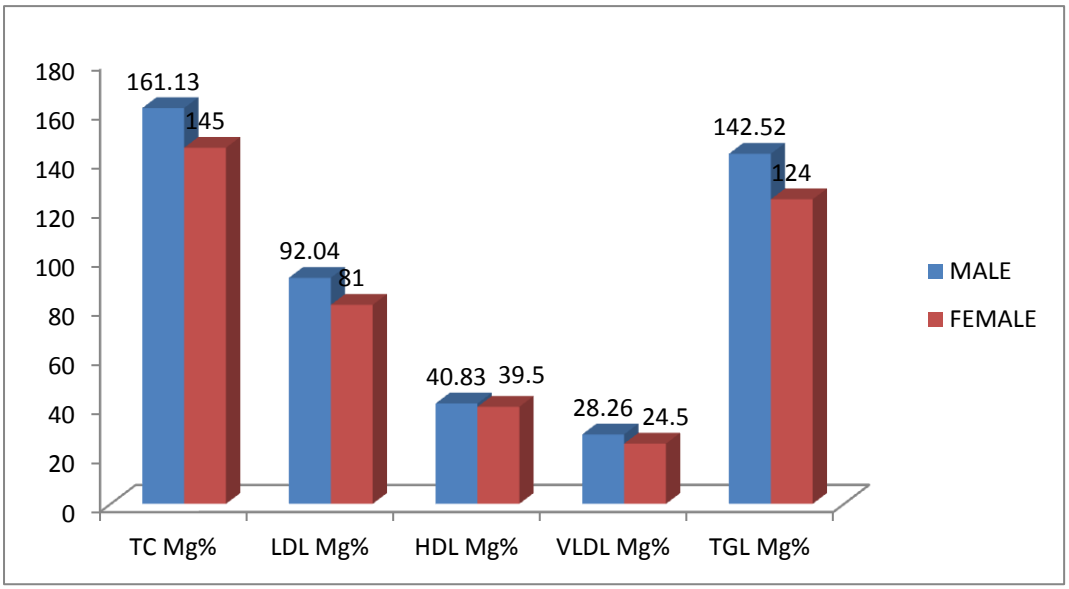
TABLE 9 LIPID PROFILE IN GROUP I,II,III



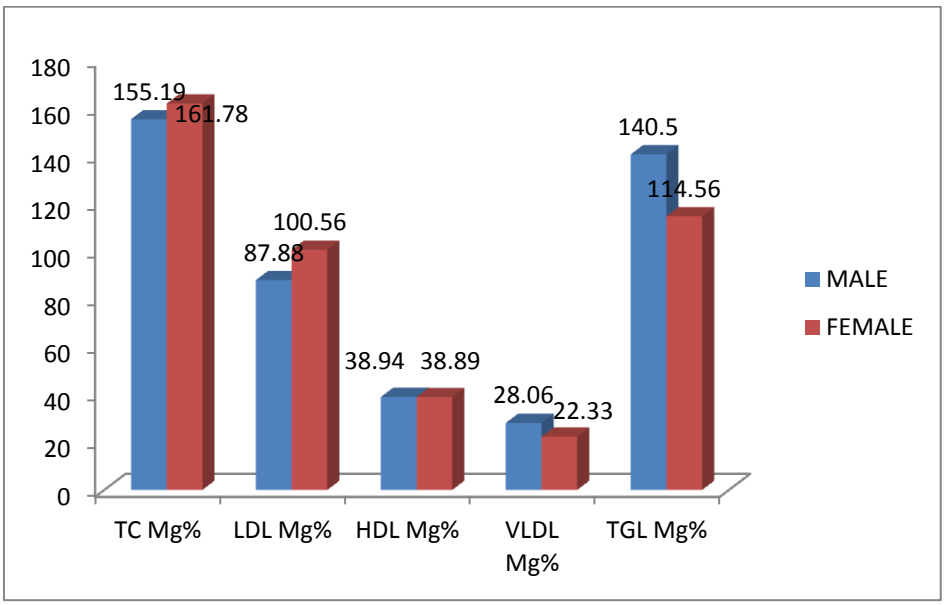
GRAPH 10 CORRELATION OF LIPID PROFILE WITH AGE IN GROUP I(CONTROL)



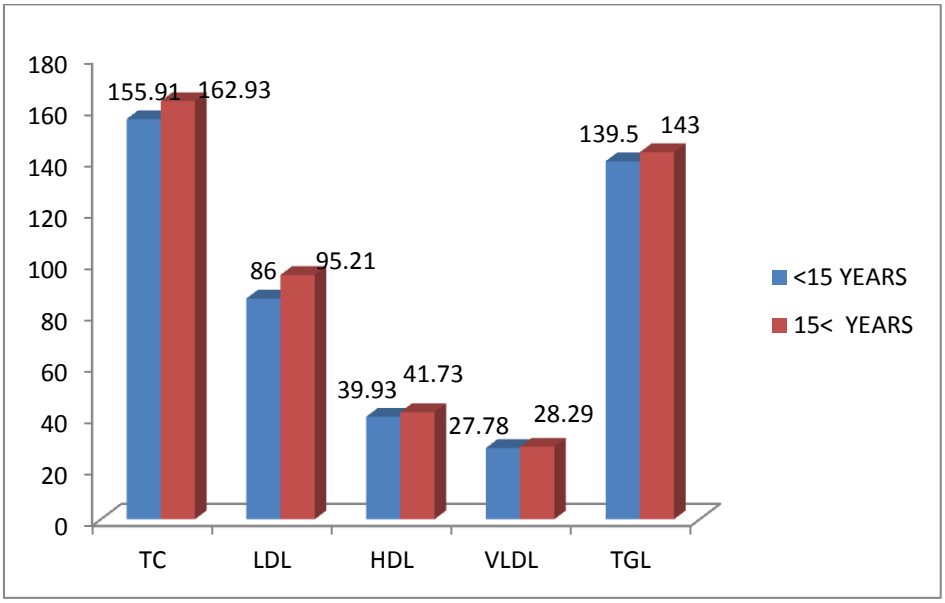
GRAPH 11 CORRELATION OF LIPID PROFILE WITH AGE IN GROUP II(PMD)



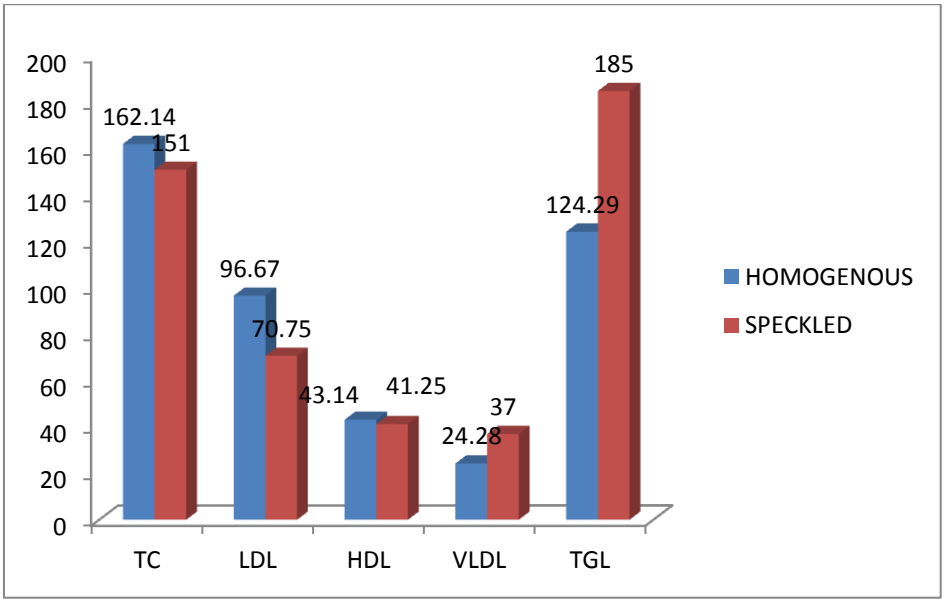
GRAPH 12 CORRELATION OF LIPID PROFILE WITH AGE IN GROUP III(OSCC)



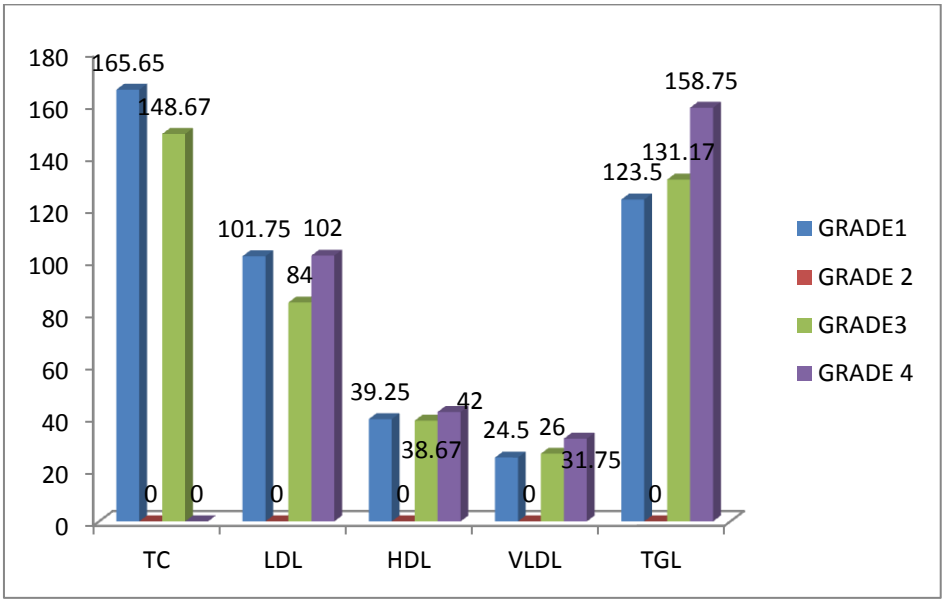
GRAPH 13 CORRELATION OF DURATION OF HABITS AND LIPID PROFILE IN PMD



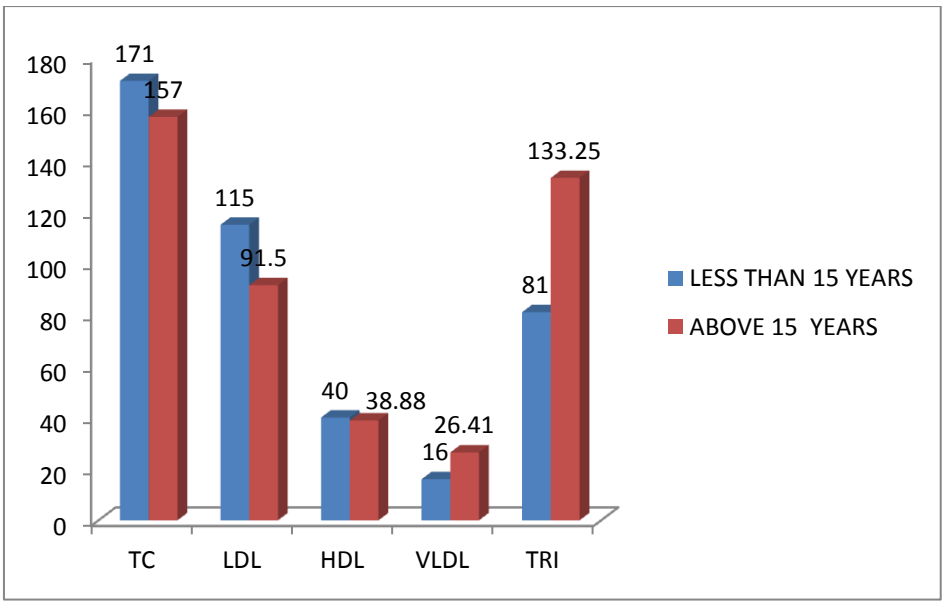
GRAPH 14 CORRELATION OF TYPES OF LEUKOPLAKIA AND LIPID PROFILE



GRAPH 15 CORRELATION OF GRADES OF OSMF AND LIPID PROFILE



GRAPH 16 CORRELATION OF DURATION OF HABITS AND LIPID PROFILE IN OSCC



GRAPH 17 CORRELATION OF STAGES OF OSCC AND LIPID PROFILE

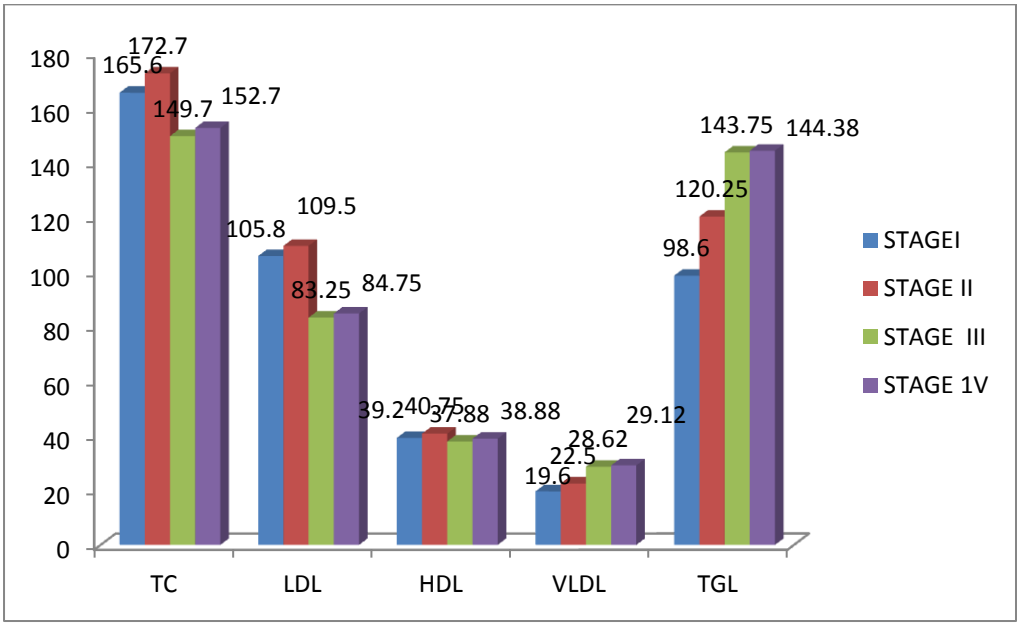


Table 1: Distribution of Subjects by Sex

SEX	GROUP I (controls)		GROUP II (oral potentially malignant disorders)		GROUP III (oral squamous cell carcinoma)		TOTAL	
MALE	17	68%	23	92%	16	64%	56	74.7%
FEMALE	8	32%	2	8%	9	36%	19	25.3%
TOTAL	25	100%	25	100%	25	100%	75	100%

p value 0.157 (not significant)

Table 2: Distribution of Subjects by Age

AGE (Years)	GROUP I (CONTROL)		GROUP II (OPC)		GROUP III (OSCC)		TOTAL	
21-30	9	36%	5	20%	0	0%	14	18.67%
31-40	7	28%	11	44%	0	0%	18	24.0%
41-50	2	8%	8	32%	4	16%	14	18.67 %
51-60	5	20%	1	4%	10	40%	16	21.33%
61-70	2	8%	0	0%	11	44%	13	17.33%
TOTAL	25	100%	25	100%	25	100%	75	100%

p value ≤ 0.001 (Highly significant)

Table 3: Age and Sex Wise Distribution of Subjects in Group-I (Control)

SNO	AGE	SEX
1	35	F
2	23	F
3	30	M
4	35	F
5	52	M
6	25	M
7	27	M
8	29	M
9	63	F
10	57	M
11	37	M
12	63	F
13	58	F
14	42	M
15	33	M
16	44	M
17	32	M
18	37	M
19	27	F
20	30	M
21	23	F
22	40	M
23	58	M
24	52	M
25	25	M

Age range : 23-63 Years **Mean age** –39.08 **Years**

Table 4: Age and Sex Wise Distribution of Subjects in Group-II

SNO	AGE	SEX
1	47	M
2	25	M
3	38	M
4	35	M
5	35	F
6	25	M
7	27	M
8	43	M
9	35	M
10	44	M
11	35	M
12	22	M
13	37	F
14	33	M
15	42	M
16	22	M
17	42	M
18	48	M
19	48	M
20	31	M
21	48	M
22	39	M
23	38	M
24	58	M
25	38	M

Age range: 22-58 Years **Mean age** –37.4 Years

Table 5: Age and Sex Wise Distribution of Subjects in Group-III

SNO	AGE	SEX
1	51	M
2	49	M
3	58	M
4	55	M
5	62	M
6	60	M
7	70	F
8	63	M
9	67	F
10	64	M
11	58	M
12	53	M
13	46	F
14	50	F
15	63	F
16	59	M
17	67	F
18	50	M
19	66	F
20	70	F
21	61	M
22	59	F
23	65	M
24	58	M
25	53	M

Age range : 46-70 Years **Mean age –**59.08**Years**

Table 6: Distribution of Subjects Based on Habits in Group I, Group II, Group III

HABIT/ GROUP	No Habits		Only Smoking		Only Chewing		Smoking+ Chewing		Smoking + Alcohol		Smoking + Chewing + Alcohol			Total
Group I	14	56%	7	28%	4	16%	0	0%	0	0%	0	0%	25	100%
Group II	0	0%	8	32%	14	56%	0	0%	3	12%	0	0%	25	100%
Group III	0	0%	0	0%	14	56%	7	28%	0	0%	4	16%	25	100%
Total	14	18.7%	15	20%	32	42.7%	7	9.3%	3	4%	4	5.3%	75	100%

p value ≤0.000 (**significant)**

Table 7: Distribution of Subjects According to Lesion

		GROUP – II		TOTAL	
LESION	OSMF	14	56%	14	56%
	LEUKOPLAKIA	11	44%	11	44%
TOTAL		25	100%	25	100%

Table 8: Distributions of Subjects According to the Grade of Oral Submucous Fibrosis

		GROUP – II		TOTAL	
OSMF GRADE	GRADE I	4	28.6%	2	28.6%
	GRADE II	0	0%	0	0%
	GRADE III	6	42.8%	5	42.8%
	GRADE IV	4	26.6%	4	28.6%
TOTAL		14	100%	14	100%

Table 9: Distribution of Subjects According to the Site of Leukoplakia

		GROUP – II		TOTAL	
LEUKOPLAKIA SITE	RETRO COMMISSURE AREA	5	45.5%	5	45.5%
	BUCCAL MUCOSA	5	45.5%	5	45.5%
	FLOOR OF THE MOUTH	1	9 %	1	9%
TOTAL		11	100%	11	100%

Table 10: Distribution of Subjects According to the Site of Carcinoma

	SITE	GROUP III	
CARCINOMA SITE	TONGUE	3	12%
	BUCCAL MUCOSA	12	48%
	ALVEOLAR MUCOSA	5	20%
	FLOOR OF THE MOUTH	1	4%
	PALATE	4	16%
TOTAL		25	100%

Table 11: Distribution of Subjects According to the Clinical Staging of Oral Squamous Cell Carcinoma

		GROUP – III	
CLINICAL STAGE	STAGE I	5	20%
	STAGE II	4	16%
	STAGE III	8	32%
	STAGE IV	8	32%
TOTAL		25	100%

Table 12: Lipid Profile in Group I, II, III

GROUPS	NUMBER OF SUBJECTS	TC Mg%	LDL Mg%	HDL Mg%	VLDL Mg%	TGL Mg%
I	25	172.56± 29.2	102.60± 24.2	42.76± 3.1	33.32± 9.4	151.68±20.5
II	25	159.84± 15.5	91.16± 17.0	40.72± 3.2	27.96± 10.7	141.04±53.4
III	25	157.44± 12.3	92.44± 14.6	38.92± 2.5	26.00± 26.9	131.16±44.7
ANOVA	F P	3.84 0.01	2.26 0.07	5.70 0.001	3.75 0.01	1.50 0.22

p<0.01-Significant **p<0.001-Highly significant**
p>0.05- Not significant

Table 13: Correlation of Total Cholesterol between Group I, II &Group III

GROUP(A)	GROUP(B)	Mean difference (A) - (B)	Test of significance(p)
GROUP-I	GROUP-II	12.60	0.01
	GROUP-III	14.88	0.01
GROUP-II	GROUP-I	-12.60	0.01
	GROUP-III	2.28	0.91
GROUP-III	GROUP-I	-14.88	0.01
	GROUP-II	-2.28	0.91

p<0.01-Significant **p>0.05- Not significant**

Table 14 : Correlation of LDL between the Groups I,II,III

GROUP(A)	GROUP(B)	Mean difference (A) - (B)	Test of significance(p)
GROUP-I	GROUP-II	11.44	0.09
	GROUP-III	10.16	0.15
GROUP-II	GROUP-I	-11.44	0.09
	GROUP-III	-1.28	0.97
GROUP-III	GROUP-I	-10.16	0.15
	GROUP-II	1.28	0.97

p>0.05- Not significant

Table 15 : Correlation of HDL Between the Groups I,II,III

GROUP(A)	GROUP(B)	Mean difference (A) - (B)	Test of significance(p)
GROUP-I	GROUP-II	1.04	0.05
	GROUP-III	2.84	0.001
GROUP-II	GROUP-I	-1.04	0.05
	GROUP-III	1.80	0.09
GROUP-III	GROUP-I	-2.84	0.001
	GROUP-II	-1.04	0.09

P<0.05-significant p<0.001- highly significant
p>0.05- Not significant

Table 16: Correlation of VLDL between the Groups I, II, III

GROUP(A)	GROUP(B)	Mean difference (A) - (B)	Test of significance(p)
GROUP-I	GROUP-II	5.36	0.13
	GROUP-III	7.32	<0.05
GROUP-II	GROUP-I	-5.36	0.13
	GROUP-III	1.96	0.75
GROUP-III	GROUP-I	-7.32	<0.05
	GROUP-II	-1.96	0.75

P<0.05-significant **p>0.05- Not significant**

Table 17: Correlation of TGL between the Groups I,II,III

GROUP(A)	GROUP(B)	Mean difference (A) - (B)	Test of significance (p)
GROUP-I	GROUP-II	10.64	0.64
	GROUP-III	20.52	0.19
GROUP-II	GROUP-I	-10.64	0.64
	GROUP-III	9.88	0.68
GROUP-III	GROUP-I	-20.52	0.19
	GROUP-II	-9.88	0.68

p>0.05- Not significant

Table 18: Correlation of Lipid Profile with Age in Group I (Control)

GROUPS	GENDER	NUMBER	TC mg%	LDL mg%	HDL mg %	VLDL mg%	TGL mg%
CONTROLS	MALE	17	171.24 ± 32.71	102.82 ± 27.27	41.53 ± 2.70	30.82± 7.00	154.47 ± 18.89
	FEMALE	8	175.00 ± 22.04	102.13 ± 18.77	42.25 ± 4.20	38.63± 12.06	145.75 ± 24.03
	MvS F	**T**	**2.97**	**0.655**	**0.52**	**0.561**	**0.998**
		P	**0.07**	**0.09**	**0.06**	**<0.05**	**0.38**

Table 19: Correlation of Lipid Profile with Age in Group II (PMD)

GROUPS	GENDER	NUMBER	TC mg%	LDL mg%	HDL mg%	VLDL mg%	TGL mg%
PMD	MALE	23	161.13± 15.55	92.04± 17.52	40.83± 0.3	28.26± 11.17	142.52± 55.11
	FEMALE	2	145.00± 1.41	81.00± 4.24	39.50± 0.71	24.50± 2.12	124.00± 9.90
	MvS F	**T**	**1.43**	**0.83**	**0.55**	**0.46**	**0.47**
		P	**0.16**	**0.06**	**0.16**	**0.20**	**0.19**

Table 20: Correlation of Lipid Profile with Age in Group III(OSCC)

GROUPS	GENDER	NUMBER	TC mg%	LDL mg%	HDL mg%	VLDL mg%	TGL mg%
OSCC	MALE	16	155.19± 11.76	87.88± 12.76	38.94± 2.93	28.06± 9.66	140.50± 48.59
	FEMALE	9	161.78± 12.99	100.56± 14.89	38.89± 2.03	22.33± 6.96	114.56± 33.03
	MvS F	**T**	**1.29**	**2.24**	**0.04**	**1.55**	**1.43**
		P	**0.20**	**0.35**	**0.95**	**0.16**	**0.12**

P<0.05- significant **p>0.05- Not significant**

Table 21: Correlation of Duration of Habits and Lipid Profile in PMD

DURATION	Number of cases	TC mg%	LDL mg%	HDL mg%	VLDL mg%	TGL mg%
LESS THAN 15 YEARS	14	155.91± 11.37	86.00± 17.69	39.93± 2.58	27.78± 9.56	139.50± 47.57
MORE THAN 15 YEARS	11	162.93± 17.96	95.21± 16.03	41.73± 3.77	28.18± 12.59	143.00± 61.67
T P		1.12 0.27	1.36 0.18	1.42 0.16	0.90 0.9	1.60 0.8

p>0.05- Not significant

Table 22: Correlation of Clinical Types of Leukoplakia and Lipid Profile

TYPES OF LEUKOPLAKIA	Number of cases	TC mg%	LDL mg%	HDL mg%	VLDL mg%	TGL mg%
HOMOGENOUS	7	162.14 ± 13.05	96.67 ± 11.88	43.14 ± 3.13	24.28 ± 5.82	124.29 ± 8.85
SPECKLED	4	151.00 ± 9.83	70.75 ± 14.24	41.25 ± 4.64	37 ± 18.34	185.00 ± 46.46
T P		1.47 0.17	3.25 0.15	0.907 <0.05	1.74 0.1	0.28 0.12

P< 0.05-Significant

Table 23: Correlation of Grades of OSMF and Lipid Profile

GRADES OF OSMF	Number of cases	TC mg%	LDL mg%	HDL mg%	VLDL mg%	TGL mg%
GRADE1	4	165.65± 18.26	101.75± 18.96	39.25± 1.25	24.50± 1.00	123.50± 7.32
GRADE 2	0					
GRADE3	6	148.67± 4.08	84.00± 4.24	38.67± 1.36	26.00± 3.57	131.17± 16.25
GRADE 4	4	175.75± 19.67	102.00± 20.51	42.00± 3.74	31.75± 17.74	158.75± 9.61
F P		4.56 0.36	2.47 0.12	2.77 0.10	.656 0.5	0.608 0.56

p>0.05- Not significant

Table 24 : Correlation of Duration of Habits and Lipid Profile in OSCC

DURATION	Number of cases	TC mg%	LDL mg%	HDL mg%	VLDL mg%	TGL mg%
LESS THAN 15 YEARS	1	171	115	40	16	81
ABOVE 15 YEARS	24	157± 12.31	91.5± 14.16	38.88± 2.66	26.41± 9.02	133.25± 43.43
T P		1.114 0.27	1.626 0.11	.417 0.68	1.131 0.27	1.152 0.26

p>0.05- Not significant

Table 25: Correlation of Stages of OSCC and Lipid Profile

GRADES OF OSCC	**Number of cases**	**TC mg%**	**LDL mg%**	**HDL mg%**	**VLDL mg%**	**TGL mg%**
STAGEI	5	165.6± 7.40	105.80± 13.33	39.20± 0.83	19.60± 4.92	98.60± 25.22
STAGE II	4	172.7± 2.63	109.50± 4.04	40.75± 1.70	22.50± 2.64	120.25± 16.64
STAGE III	8	149.7± 13.04	83.25± 12.78	37.88± 2.85	28.62± 12.81	143.75± 64.22
STAGE 1V	8	152.7± 6.79	84.75± 2.25	38.88± 3.18	29.12± 6.79	144.38± 32.37
F P		7.65 0.00	11.57 0.35	1.13 0.00	1.70 0.19	1.49 0.24

P=0.00- significant **p>0.05- Not significant**

In India, oral cancer is prevalent in most areas where tobacco related practices are observed. For development of oral cancer, tobacco is the single greatest risk factor. When this is combined with arecanut the risk increases many fold. Alcohol, viruses, genetic mechanisms, candida, chronic irritation and diet deficiency states are also implicated in the etiology.[84]

Cancer is a class of diseases in which a group of cells display uncontrolled growth , invasion and sometimes metastasis. These three malignant properties of cancers differentiate them from benign tumors, which are self-limited, and do not invade or metastasize**.** [11]

Head and neck malignancies rank among top three malignancies in our country for both males and females. The wide spread use of tobacco in various forms due to our cultural habits coupled with lack of awareness of it carcinogenic effects are responsible for their prevalence. Ignorance of early symptoms together with lack of proper diagnostic and treatment facilities at the gross root level lead to presentation of patients to cancer hospitals in advanced disease status in our country.[85]

Oral cancer is almost always preceded by benign lesions or conditions for varying lengths of time. Interestingly the benign lesions and conditions also share the same risk factors as the cancer, particularly the tobacco and the areca nut. Many of these have the potential to become cancer and are termed as precancerous lesions and conditions. [84]

Significant reduction in mortality can be achieved by advances in early diagnosis and implementation of multidisciplinary treatment

programmes leading to improvement of survivorship and better quality of life.

Among the oral tumors 90% are oral squamous cell carcinoma which arise from the mucosal lining. Inspite of significant advances in surgery, radiotherapy and chemotherapy the 5 year survival rate has remained at about 52% for the past few decades.

The development of oral cancer is a multistep process arising from pre-existing potentially malignant lesions. Leukoplakia is the most common precancer representing 85% of such lesion.[15]

Cholesterol is an amphipathic lipid and as such, is an essential structural component of all cell membranes and of the outer layer of plasma lipoproteins. It is present in tissues and in plasma lipoprotein either as free cholesterol or combined with a long-chain fatty acid, as cholesteryl ester. It is synthesized in many tissues from acetyl-CoA and is ultimately eliminated from the body in the bile as cholesterol or bile salts. Lipoprotein transports free cholesterol in the circulation, where it readily equilibrates cholesterol in other lipoproteins and in membranes. Of the lipoprotein fractions, LDL most clearly reflects the decrease in total cholesterol. The role of HDL and triglycerides in explaining the overall pattern of total cholesterol change is less clear. [81]

Regulation of cholesterol is mediated by lipoprotein receptors. Plasma triglycerides and cholesterol are packed into lipoproteins for transport. Cholesterol is an essential constituent of lipoprotein fractions like LDL,

HDL, and VLDL. Seventy five percent of the plasma cholesterol is transported in the form of LDL. Cells sequester cholesterol from LDL fraction of lipoproteins. High activity of LDL receptors attributes for lowering the serum cholesterol levels. The individuals having deficient or defective LDL receptors remove plasma LDL at much lower rate and have considerably elevated levels.

In some malignancies, serum cholesterol undergoes early and significant changes. Low levels of cholesterol in the proliferating tissues and in blood compartments could be due to the rapidly dividing cells in malignancies. The habit of tobacco consumption is a known etiological factor for development of oral precancerous disease and head and neck cancer. Patients with oral precancerous conditions have also been reported to show a significant tendency to develop cancer. It is believed that tobacco carcinogens and excessive use of areca nut induce generation of free radicals and reactive oxygen species, which are responsible for high rate of oxidation / peroxidation of polyunsaturated fatty acids. Because of lipid peroxidation there is greater utilization of lipids including total cholesterol, lipoproteins and triglycerides for new membrane biogenesis. Cells fulfill these requirements either from circulation, by synthesis through metabolism or from degradation of major lipoprotein fractions like VLDL, LDL, and HDL [5.]

The present study was done to validate Serum lipid changes as biological marker for Oral Potentially malignant disorders and Oral

squamous cell carcinoma. In the study the levels of serum lipid in subjects with untreated Oral Leukoplakia , Oral submucous fibrosis and Oral squamous cell carcinoma were determined

The Serum lipid levels were compared with Oral Potentially Malignant Disorders, Oral squamous cell carcinoma and with the control group Finally the relation between serum lipids with Oral Potentially Malignant Disorders and Oral squamous cell carcinoma were determined.

This is a cross sectional hospital based study conducted between March 2010 to March 2011, and the type of study is a case control study. The study subjects were categorized into three groups: Group I consisting of 25 normal controls, Group II consist of 25 patients who were suffering from Potentially Malignant Disorders like Leukoplakia and Oral submucous fibrosis; Group III, 25 patients suffering from Oral cancer.

STUDY ANALYSIS:

Age & Sex:

Among the 75 subjects 56(74.7%) were males and 19(25.3%) were females. The minimum age of the study subjects was 22 years and the maximum age was 70 years

HABITS

In the present study, among the 75 subjects 15(20%) had the habit of smoking, 32(42.7%) had the habit of chewing, 7(9.3%) had the habit of chewing and smoking, 3(4%) had the habit of smoking and alcohol consumption and 4(5.3%) had all three habits together with a p-value ≤

0.000 which is statistically significant. Thus a positive correlation between smoking, chewing, alcohol consumption and development of precancer and cancer has been established.

This is in accordance with various studies. **Sugár.L. et al** [16] made a follow-up study with 324 patients and concluded that there was a relationship between smoking and the frequency of leukoplakia. **Pindborg et al** [8] examined 1866 individuals and found a positive correlation between Preleukoplakia and leukoplakia and the habit of smoking. **Salonen et al**[45] reported a positive correlation between tobacco use and leukoplakia on his study on 920 individuals.

Shah N et al [33] reported that chewing of areca nut, quid and pan masala was directly related to oral submucous fibrosis and not a single case was found without any chewing habit in a study comprising 236 cases of oral submucous fibrosis which were compared with 221 control subjects matched for age, sex and socioeconomic conditions.

Sankaranarayanan [46] found a causal association between oral cancer and the chewing of betel quid containing tobacco leaves or stem and other tobacco habits.

Rajendran.R [30] reviewed the etiology and pathogenesis of Oral submucous fibrosis. He suggested that certain customs or habits (chewing) prevalent among the population groups in South East Asia might be possible etiological factors.

Shah N, Sharma PP [33] conducted a study to identify the role of chewing and smoking habit in the etiology of oral submucous fibrosis. In this study 236 cases of oral submucous fibrosis were compared with 221 control subjects matched for age, sex and socioeconomic conditions. It was found that chewing of areca nut, quid and pan masala was directly related to oral submucous fibrosis and not a single case was found without any chewing habit.

Crispian Scully et al [50] stated that the etiological factors of oral cancer include tobacco use, betel use (Bidi leaf, and often tobacco, plus spices, slaked lime, and areca nut) and alcohol consumption.

Zain et al [52] stated about the role of tobacco smoking, chewing of tobacco, areca nut, and betel quid and drinking of alcohol are established cultural risk factors of oral pre-cancer and oral cancer worldwide.

Saraswathi et al [12] stated that the habit of smoking, drinking and chewing tobacco products were common oral habits in India and these habits were positively related with development of oral lesion such as OSMF, leukoplakia and oral lichen planus which had potential for malignant transformation.

SITE OF LEUKOPLAKIA

In the present study, the most common site for leukoplakia was in the retro-commissure area with 5(45.5%) and buccal mucosa 5 (45.5%) and one in the floor of the mouth.

This is consistent with the study conducted by **Reichart PA and Kohn H in 1996** [86] in which they found the retrocommisure was the most commonly affected site upto 43.35 followed by 36.7% in buccal mucosa.

In a 10 year follow up study conducted in Mumbai **Napier SS and Speight PM.in 2008** [87] 80% lesions were found in retrocommisure and buccal mucosa and 5% found in tongue

CLINICAL GRADING

The present study showed all cases of OSMF in the buccal mucosa, with 6(42.8%) in Grade III and 4 each in Grades I and IV and none in Grade II.

This is consistent with the study done by **Shah et al** [33] stated that OSMF predominantly affects the buccal mucosa with the p-value <0.001.

This Grade III predominance of clinical presentation can be attributable to the fact that the presence of blanching and burning sensation, dryness of mouth, vesicles or ulcers in the mouth with restriction of mouth opening and palpable bands all over the mouth with out tongue involvement which causes major morbidity to the patient making them to seek dental advice.

SITE OF CARCINOMA

In the present study among the total of 25 (100%) subjects, 3(12%) had carcinoma in the tongue, 12(48%) had in the buccal mucosa, 5(20%) had in the alveolar mucosa, 1(4%) had carcinoma in the floor of the mouth and 4(16%) in the palate. Oral cancer was mostly seen in the buccal mucosa,

followed by tongue, alveolar mucosa, floor of the mouth and palate. This consistent with a study done by **Prabhu et al** [49] found the most common site of oral cancer was buccal mucosa followed by tongue and other sites.

Mehrota et al [53] stated that oral cancer was the commonest malignancy in Allahabad and buccal mucosa was the most common site of oral cancer.

CORRELATION OF LIPID PROFILE IN THE STUDY GROUPS

The present study found a mean TC in PMD and OSCC as 159.84 mg% and 157.56 mg% respectively .The present study also found a significantly reduced TC when both the groups were compared with control group with p value < 0.01. This is in accordance with studies conducted by **Patel et al** [5] who conducted study on 184 head and neck cancer patients, 153 patients with Oral precancerous conditions and 52 controls and found a mean TC of 167.59 mg/dl level in OSCC group and 168.42mg/dl in OPC group with p value of P=0.008 and P=0.014 respectively.

This is also consistent with another study conducted by **Lohe et al** [3] who conducted study on 70 Oral cancer patients, 70 patients with Oral precancerous conditions and 70 controls and found a mean TC of 178.73 mg/dl level in OSCC group and 179.17 mg/dl in OPC group with p value of P<0.001 when compared with controls . It was postulated that low levels of cholesterol in the proliferating tissues and in blood compartments could be due to the process of carcinogenesis.

The present study found a mean LDL in PMD and OSCC as 92.44 mg% and 91.16 mg% respectively .The present study could not find a significant result in LDL when both the groups were compared with control group with p value0.07. This is consistent with study conducted by **Lohe et al** [3] who found a mean LDL of 118.22 mg/dl level in OSCC group and 117.14 mg/dl in OPC group with p value of P=0.317 when compared with controls. This is also in consistent with study by **Chawda et al** [80] who didnot find a significant decrease in LDL.

The present study found a mean HDL in PMD and OSCC as 40.72 mg% and 38.92 mg% respectively .The present study also found a highly significantly reduced HDL when OSCC group was compared with control group with p value < 0.001 and significantly reduced HDL when PMD group was compared with control group with p value < 0.05. This is in accordance with studies conducted by **Patel et al** [5] who found a mean TC of 28 mg/dl level in OSCC group and 28.6 mg/dl in OPC group with p value of P=0.000 and P=0.000 respectively.

This is also consistent with another study conducted by **Lohe et al** [3] who found a mean TC of 40.35 mg/dl level in OSCC group and 39.5 mg/dl in OPC group with p value of P<0.001 when compared with controls . It was postulated that low HDL is an additional predictor of cancer and it might be a consequence of disease that is mediated by utilization of cholesterol for membrane biogenesis.

The present study found a mean VLDL in PMD and OSCC as 27.96 mg% and 26 mg% respectively .The present study found a significant reduced VLDL when OSCC group was compared with control group with p value <0.05. But there was no significant difference in VLDL when PMD group was compared with controls. This is consistent with study conducted by **Lohe et al** [3] who found a mean VLDL of 20.16 mg/dl level in OSCC group and 22.41 mg/dl in OPC group with P=0.002 when OSCC compared with controls and P=0.21 when PMD compared with controls. It is believed that tobacco carcinogens induce lipid peroxidation in which there is a greater utilization of lipids including total cholesterol, lipoproteins and triglycerides for new membrane biogenesis. Cells fulfill these requirements either from circulation, by synthesis through the metabolism or from degradation of major lipoprotein fractions like VLDL.

The present study found a mean TGL in PMD and OSCC as 141.04 mg% and 131.16 mg% respectively .The present study did not find a significantly reduced TGL with p =0.22 when both the groups were compared with control group. This is not in consistent with study conducted by **Lohe et al** [3] who found a significant decrease in TGL when OSCC was compared with control. But our study is in consistent with study conducted by **Alexopoulos et al** [4] who did not find a significant decrease in TGL in cancer patients. Our study did not find a significant difference due to decrease in sample size.

CORRELATION OF LIPID PROFILE WITH GENDER

When a correlation was done between lipid profile and gender in the present study, no significant differences were found. TC was more in males of PMD group when compared to females and lowest in males of OSCC group when compared to females. LDL was more in females of OSCC group and lowest in females of PMD group. HDL was more in males of PMD group when compared to females and almost same in males and females of OSCC group. VLDL was more in males of PMD and OSCC group when compared to females. TGL was more in males of PMD and OSCC group when compared to females .So, in brief men of PMD had higher TC,LDL,HDL,VLDL and TGL when compared to females. Men of OSCC group had lower TC, LDL and higher VLDL and TGL with HDL almost equal in both the gender. This is in accordance with a study by **Alexopoulos et al** [4] who found that cancer men had significantly lower TC and LDL but no significant difference in HDL. Though the present study had lower TC,LDL levels in cancer men ,there was no significant difference between the control. This could be attributed due to the smaller sample size.

CORRELATION OF DURATION OF HABITS AND LIPID PROFILE IN PMD

When a correlation was done between lipid profile and duration of habits in PMD group in the present study , no significant differences were found. TC, LDL, HDL,VLDL and TGL were more in subjects with

increased duration of habits. This could be a primary study where such a correlation is assessed.

CORRELATION OF CLINICAL TYPES OF LEUKOPLAKIA AND LIPID PROFILE

The present study found an increase in TC, LDL and decrease in VLDL and TGL in homogenous type when compared to speckled leukoplakia.HDL is found to be significantly reduced in Speckled leukoplakia ($p<0.05$). Speckled leukoplakia is reported to be asscociated with higher malignant transformation in about 20% of cases. Hence reduced cholesterol level is seen in Speckled type as the malignancy is likely to develop in this type. It could be used as a malignant marker or to assess the malignant transformation.

CORRELATION OF GRADES OF OSMF AND LIPID PROFILE

The present study found that TC,LDL,HDL,VLDL and TGL was highest in grade 4 ,1 followed by grade 3.There were no patients with grade 2.The present study could be a preliminary study which attempts to correlate the grades of OSMF with lipid profile. However we could not find a statistically significant difference, as the sample size may be small.

CORRELATION OF DURATION OF HABITS AND LIPID PROFILE IN OSCC

The present study found reduced TC, LDL,HDL and increased VLDL and TGL in subjects who used tobacco for a long time. Longer the duration of tobacco habit, increased chance of getting oral cancer. Hence

subjects with longer duration of habit, have reduced TC, HDL levels. However we could not find a statistically significant difference.

CORRELATION OF CLINICAL STAGES OF OSCC AND LIPID PROFILE

The present study found reduced TC,LDL, HDL and increased VLDL and TGL in subjects with stage III and stage IV oral cancer .This could be a preliminary study wherein such a correlation is made.

The present study titled "Evaluation of serum lipid profile in Patients with Oral Potentially Malignant Disorders and Oral Squamous Cell Carcinoma" was conducted in the Department of Oral Medicine and Radiology, Ragas Dental College, Uthandi, Chennai and Dr. Rai Memorial Medical and Cancer Centre, Chennai, to estimate the serum levels of TC,LDL,HDL,VLDL and TGL in patients with Potentially Malignant disorders like Leukoplakia and Oral submucous fibrosis, Oral cancer and to compare the values with the control subjects.

A total of 75 individuals were selected for the study. Among the study subjects 25 patients were suffering from Potentially Malignant Disorders, 25 patients were suffering from Oral Cancer, and 25 patients were normal controls. Informed consent was taken from all subjects before including them in the study.

The experimental subjects were made to sit comfortably on a Dental Chair. Sterile hand gloves were used during examination of the patients. Patients were examined under halogen lamp in the dental chair under aseptic conditions and relevant demographic data were collected. Clinical diagnosis was made and patients who showed characteristic features of Leukoplakia, Oral submucous fibrosis and Oral Cancer were prepared for sample collection. 5ml of blood from the patient was taken for the evaluation of lipid profile.

The study documents the following data:

- Among the 75 subjects 56(74.7%) were males and 19(25.3%) were females. The minimum age of the study subjects was 22 years and the maximum age was 70 years.
- Among the 75 subjects 15(20%) had the habit of smoking, 32(42.7%) had the habit of chewing, 7(9.3%) had the habit of chewing and smoking, 3(4%) had the habit of smoking and alcohol consumption and 4(5.3%) had all three habits together with a p-value of 0.000 which is statistically significant. Thus a positive correlation between smoking, chewing, alcohol consumption and development of precancer and cancer has been established.
- The most common sites for leukoplakia were in the retrocommissure area with 5 (45.5%) subjects followed by buccal mucosa 5(45.5%) and one in floor of the mouth.
- The present study showed all cases of OSMF in the buccal mucosa 6(42.8%) in Grade III and 4 each in Grades I and IV and none in Grade II.
- Among the total of 25 (100%) subjects, 3(12%) had carcinoma in the tongue, 12(48%) had in the buccal mucosa, 5(20%) had in the alveolar mucosa, 1(4%) had carcinoma in the floor of the mouth and 4(16%) in the palate. Oral cancer was mostly seen in the buccal mucosa, followed by tongue, alveolar mucosa, floor of the mouth and palate.

- There was a significant decrease in levels of serum TC, HDL which were observed in patients with Potentially Malignant Disorders like Leukoplakia and Oral submucous fibrosis. The mean TC in patients with PMD was 159.84±15.5 mg % ,the mean HDL was 40.72±3.2 mg % .LDL,VLDL and TGL were also reduced but not significant.
- There was a significant decrease in the serum TC, HDL, VLDL in patients with oral carcinoma. The mean TC in patients with OSCC was 157.44±12.3mg %, the mean HDL was 38.92±2.5 mg % , the mean VLDL was 26.00±26.9 mg%. LDL and TGL were also reduced but not significant.
- There were no significant relation between lipid profile in relation to gender, duration of habits, clinical types of leukoplakia, grades of OSMF and stages of OSCC.

Reduced lipid level may be attributed to the production of free radicals induced by tobacco carcinogens and excessive use of areca nut. It is believed that tobacco carcinogens and excessive use of areca nut induce generation of free radicals and reactive oxygen species, which are responsible for high rate of peroxidation of polyunsaturated fatty acids. Because of lipid peroxidation there is greater utilization of lipids including total cholesterol, lipoproteins and triglycerides for new membrane biogenesis. Cells fulfill these requirements either from circulation, by synthesis through metabolism or from degradation of major lipoprotein fractions like VLDL, LDL, and HDL.

To conclude an inverse relationship exists between serum lipid profile in Oral cancer and Oral Potentially Malignant disorders. The lower serum lipid status may be a useful indicator for initial changes occurring in neoplastic cells. The present findings are drawn by a smaller sample size but the findings strongly warrant an indepth study on a large sample size of oral cancer. Further study with larger sample size and additionally a long term follow up of PMD subjects with periodic estimation of lipid profile would be needed to establish correlation between a transformation from precancerous state to malignancy. Thus lipid profile may be used as a marker for malignant transformation in PMD and hence early detection of malignancy would give way to early treatment thereby increasing the survival rate in these patients.

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Group I

S.No	Name	Age	Sex	Habits	Duration	TC	LDL	HDL	VLDL	TRI
1	Mrs.Rajaamma	35	F	Nil		176	100	48	28	141
2	Mrs.Bethana	23	F	Nil		149	86	38	25	129
3	Mr .Selvam	30	M	Smoking	5	182	108	41	33	165
4	Mrs.Thendral	35	F	Nil		176	99	49	28	141
5	Mr.Sundar	52	M	Nil		160	87	40	33	165
6	Mr.Vinod	25	M	Chewing	4	170	103	39	28	143
7	Mr.Gajapathy	27	M	Nil		255	180	40	35	179
8	Mr.Senthil	29	M	Smoking	8	176	112	39	25	127
9	Mr.Mrajinder	63	F	Nil		212	133	41	38	194
10	Mr.Pandiyan	57	M	Nil		136	68	39	28	142
11	Mr.Sambasivam	37	M	Chewing	5	167	88	47	32	163
12	Mrs.Vijaya	63	F	Nil		159	79	41	39	197
13	Mrs.Daisy	58	F	Nil		190	116	43	31	159
14	Mr.Yogesh	42	M	Smoking	15	140	67	40	33	165
15	Mr.Saravanan	33	M	Chewing	7	182	108	41	33	165
16	Mrmani	44	M	Smoking	13	149	80	39	30	152
17	Mr.Naveen	32	M	Nil		189	115	46	28	141
18	Mr.Raja	37	M	Nil		139	70	45	24	123
19	Mrs.Amala	27	F	Nil		189	118	40	31	156
20	Mr .Ranjith	30	M	Smoking	11	176	106	42	28	141
21	Lakshmi	23	F	Nil		149	86	38	25	129
22	Mr .Basha	40	M	Chewing	11	182	104	45	33	165
23	Mr.Gopal	58	M	Smoking	20	190	116	43	31	159
24	Mr.Murugan	52	M	Smoking	15	212	133	41	38	194
25	Mr.Palani	25	M	Nil		170	103	39	28	143

GROUP II

Sno	Name	Age	Sex	Type Of Lesion	Habit	Duration	Site	OLType	OSMF Grade	TC	LDL	HDL	VLDL	TRI
1	Mr .Selvam	47	M	OL	S&A	20	RetroCommisure	Homogenous		167	100	44	22	114
2	Mr.Vijayakumar	25	M	OSMF	C	3			1	158	91	41	27	134
3	Mr .Mohamad	38	M	OSMF	C	12			4	187	126	41	20	100
4	Mr.Babu	35	M	OL	S	18	RetroCommisure	Homogenous		153	83	45	24	121
5	Mrs.Sathyapriya	35	F	OSMF	C	7			3	146	84	39	23	117
6	Mr.Faisal	25	M	OSMF	C	4			1	147	84	39	24	121
7	Mr.Sheik	27	M	OSMF	C	10			3	149	87	37	25	125
8	Mr.Murthy	43	M	OL	S	25	Buccalmucosa	Speckled		153	83	45	24	121
9	Mr.Hari	35	M	OSMF	C	13			3	153	90	39	24	124
10	Mr.Perumal	44	M	OL	S&A	18	RetroCommisure	Homogenous		149	90	37	22	110
11	Mr.Eshwaran	35	M	OSMF	C	17			4	176	112	42	21	107
12	Mr.Vijay	22	M	OSMF	C	11			1	167	105	38	24	117

13	Mrs.Sowmya	37	F	OSMF	C	14			3	144	78	40	26	131
14	Mr.Ahmad	33	M	OSMF	C	10			4	192	87	47	58	291
15	Mr.Prabhu	42	M	OL	S	15	Buccalmucosa	Homogenous		164	99	43	21	109
16	Mr.Saravanan	22	M	OSMF	C	5			1	190	127	39	24	122
17	Mr.Sekar	42	M	OSMF	C	16			4	148	83	38	27	137
18	Mr.Muthu	48	M	OL	S	23	Floor of Mouth	Speckled		142	70	39	33	168
19	Mr.Vasu	48	M	OL	S&Al	28	Buccalmucosa	Speckled		164	51	49	64	321
20	Mr .Abdul	31	M	OSMF	C	7			3	146	81	40	25	127
21	Mr.Sekar	48	M	OL	S	22	Buccalmucosa			148	83	38	27	137
22	Mr .Shankar	39	M	OSMF	C	12			3	154	84	37	32	163
23	Mr.Alayappan	38	M	OL	S	15	Retrocommissure	Homogenous		184	110	39	34	172
24	Mr.Mari	58	M	OL	S	27	Retrocommissure	Homogenous		170	112	42	21	107
38	Mr.Durai		M	OL	S	28	BuccalMucosa	Speckled		145	79	40	26	130

Group III

SNO	Name	AGE	SEX	HABITS	DURATION	SITE	CLINICAL STAGING	TC	LDL	HDL	VLDL	TGI
1	Ranganathan	51	M	S&C	20	BM	T3NIMX(3)	134	75	40	19	98
2	Radhakrishna	49	M	S&C	27	ALV RIDGE	T3N0MX(3)	159	70	34	55	277
3	Loganathan	58	M	C	19	BM	T3N1MX(3)	165	89	37	39	195
4	Ganesh	55	M	C	18	PALATE	T3N0MX(3)	144	71	41	32	158
5	Nahoor	62	M	S,C&AL	30	ALV RIDGE	T2N2MX(4)	142	84	38	19	99
6	Arulraj	60	M	S,C&AL	20	BM	T2N2MX(4)	155	88	39	27	138
7	Annama	70	F	C	30	PALATE	T3N1MX(3)	141	84	34	23	118
8	Sampath	63	M	C	25	BM	T2N1MX(3)	170	111	41	18	94
9	Dhanalakshmi	67	F	C	30	FOM	T1N0MX(1)	165	108	39	18	90
10	Venkatesan	64	M	S,C&AL	20	BM	T2N0MX(2)	175	112	43	20	99
11	Paramasivam	58	M	S&C	18	PALATE	T1NIMX(1)	155	85	38	27	137
12	Ramadoss	53	M	S&C	17	BM	T1N0MX(1)	163	102	39	22	110
13	Kamala	46	F	C	25	BM	T1N1MX(1)	174	119	40	15	75

14	Pushpa	50	F	C	15	TONG	T1N0MX(1)	171	105	40	15	75
15	Pushpalatha	63	F	C	28	BM	T2N2MX(2)	171	109	39	23	115
16	Sivasubramani	59	M	C	20	BM	T2N2MX(2)	170	104	40	26	133
17	Mangavalli	67	F	C	30	ALV RIDGE	T2N0MX(2)	175	113	41	21	134
18	Abdulshrif	50	M	C	16	BM	T4N0MX(4)	145	75	40	30	150
19	Visalam	66	F	C	32	ALV RIDGE	T2N2MX(4)	154	87	40	27	138
20	Bagyam	70	F	C	32	TONG	T3N1MX(3)	143	78	45	20	100
21	Muthu	61	M	S&C	23	BM	T4N0MX(4)	153	83	44	26	130
22	Naseran	59	F	C	22	TONG	T2N2MX(4)	162	86	38	36	180
23	Kannayirum	65	M	S,C&AL	32	BM	T4N0MX(4)	151	85	42	24	120
24	Arulnayagam	58	M	S&C	17	PALATE	T3N0MX(3)	142	83	37	22	110
25	Mustafa	53	M	S&C	19	ALVRIDGE	T4N0MX(4)	160	84	36	40	200

RAGAS DENTAL COLLEGE & HOSPITAL

2/102, East Coast Road, Uthandi, Chennai – 600119

DEPARTMENT OF ORAL MEDICINE & RADIOLOGY

CASE SHEET PROFORMA

Date:

S.No	:	
OP.No	:	
Study group	:	Group I / Group II / Group III
Name	:	
Age/Sex	:	
Address	:	
Phone number	:	
Occupation	:	
Monthly income	:	

Past medical /surgical/dental /history

HABITS	PRESENT	ABSENT	DURATION
Smoking			
Chewing			
Alcohol			

:

Leukoplakia :

Site :

Size :

Type :

Oral submucous fibrosis :

Grade :

Oral Squamous cell carcinoma

Site :

Size :

Type:

Clinical staging:

LIPID PROFILE:

PARAMETERS/ LESION	TOTAL CHOLESTEROL (TC) (mg%/)	LOWDENSITY LIPOPROTEIN (LDL) (mg%)	HIGHDENSITY LIPOPROTEIN (HDL) (mg%)	VERY LOWDENSITY LIPOPROTEIN (HDL) (mg%)	TRIGLYCERIDE (TGL) (mg%)
Potentially malignant disorders					
Oral Squamous Cell Carcinoma					

WRITTEN CONSENT OF THE PATIENT
CONSENT LETTER

I _____ the undersigned hereby give my consent for the performance of diagnostic test on myself to "Evaluation of Serum Lipid Profile in Patients with Oral Potentially Malignant Disorders and Oral Squamous Cell Carcinoma -A Case Control Study " conducted by Dr. S. Srividhya under the able guidance of Dr. S. Shanmugam MDS. Professor and HOD Dr. S. Elangovan MDS, Professor, Department of oral Medicine and Radiology, Ragas Dental College and Hospital, Chcnnai. I have been informed and explained the status of my disorder, evaluation procedure risk involved and likelihood of success. I also understand and accept this as a part of study protocol thereby voluntarily and unconditionally give my consent without any fear or pressure in mentally sound and conscious state to participate in the study.

Witness, Representative — Patient Signature

(if any) — Date:

ஒப்புதல் படிவம்

_____ என்கின்ற நான், சென்னை, ராகாஸ் பல்மருத்துவக் கல்லூரி மற்றும் மருத்துவமனையின் வாய் மருத்துவம் மற்றும் ஊடுகதிர் துறையின் பேராசியர் மரு. S. சண்முகம் மற்றும் பேர. மரு. கேப்டன், S. இளங்கோவன் அவர்களின் மேற்பார்வையில், முதுநிலை (M.D.S) பட்டப்படிப்பு பயிலும் மரு. எஸ். ஸ்ரீவித்யா அவர்கள் மேற்கொள்ளும், "வாய் புற்றுநோய் மற்றும் அதற்கான சாத்தியக்கூறு உள்ள நோய்களின் இரத்தத்தில் உள்ள கொழுப்பு அளவை கண்டறிதல்" என்கின்ற ஆராய்ச்சிக்கான பரிசோதனைகளுக்கு என்னை உட்படுத்துவதற்கு எனது மனமுவந்த பரிபூரண சம்மதத்தினை அளிக்கிறேன். மேலும் எனக்கு என்னுடையை நோயின் தன்மையைப் பற்றியும், அதனால் ஏற்படக்கூடிய விளைவுகளைப் பற்றியும் எடுத்துக் கூறப்பட்டுள்ளது எனவும், இந்த பரிசோதனைக்கு நான் எந்தவித அச்சமுமின்றி தன்னிச்சையாகவும், தெளிவான முழு மனதுடன் என்னுடைய பரிபூரண சம்மதத்தினை அளிக்கிறேன் என இதன் மூலம் தெரியபடுத்துகிறேன்.

சாட்சியாளர்கள் — இப்படிக்கு