MORPHOLOGICAL EVALUATION OF SOFT PALATE IN ORAL SUBMUCOUS FIBROSIS PATIENTS: A DIGITAL CEPHALOMETRIC STUDY

DISSERTATION

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In

ORAL MEDICINE AND RADIOLOGY

By

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DECLARATION BY THE CANDIDATE

I hereby declare that this dissertation entitled **"Morphological Evaluation of Soft Palate in Oral Submucous Fibrosis Patients: A Digital Cephalometric Study"** is a bonafide and genuine research work carried out by me under the guidance of **Dr. Deepak U.**, Professor, Department of Oral Medicine and Radiology, Babu Banarasi Das College of Dental Sciences, Babu Banarasi Das University, Lucknow, Uttar Pradesh.

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"A teacher is next only to God as he imparts the two most important attributes of life – Knowledge and wisdom"

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I beg forgiveness from those, whose name I have inadvertently missed but they should find solace that their knowledge has been extended to other by way of this thesis.

- Dr.SakshiVerma

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- BBDCODS :: BabuBanarasi Das College of Dental Sciences
- BBDU :: BabuBanarasi Das University
- OMR :: Oral Medicine and Radiology
- OSMF :: Oral Submucous Fibrosis
- BMF :: Buccal Mucosal Fibroblast
- CTGF :: Connective tissue growth factor
- INF-γ :: Interferon Gamma
- PAI :: Plasminogen activator inhibitor
- TGF :: Tumor growth factor
- MCH ::Major Histocompatibility complex
- TIMP :: Tissue inhibitor of matrix metalloproteinase
- tPA :: Tissue Plasminogen activator
- uPA ::Urokinase Plasminogen activator
- WHO :: World Health Organization
- OSA :: Obstructive sleep apnea
- CAD :: Computer- aided detection
- CBCT ::Cone beam computed tomography
- CRT :: Cathode ray tube
- CT :: Computed tomography
- DICOM :: Digital imaging and communications in medicine
- DLC :: Digitized lateral cephalograms
- GSDF :: Gray scale standard display function
- MRI :: Magnetic resonance imaging

BACKGROUND

Soft palate (velar) plays a significant role in various important functions in the head and neck region. Its diverse morphology is implicated in a variety of diseases. Knowledge about thevaried morphological pattern of soft palate in oral submucous fibrosis (OSMF) patients can give usa clear understanding about disease progress in the oropharyngeal region for a proper diagnosis andalso help in successful structural and functional corrections associated withthis disorder.

Oral submucous fibrosis (OSMF) is one of the most common premalignantconditions affecting the oral cavity of people consuming arecanut and gutka. Accordingto the available literature, as the disease progresses the morphology of the soft palatechanges.Soft palate morphologies vary among individuals, who may sometimes help in diagnosing various conditions such as oral submucous fibrosis (OSMF), cleft palate and obstructive sleep apnea (OSA).

AIM

To evaluate and correlate the morphology of soft palate in oral submucous fibrosis patients and healthy control using lateral cephalogram.

OBJECTIVES

To evaluate the morphology of soft palate in clinically diagnosed OSMF patient using digital lateral cephalogram.

To compare the morphological changes in oral submucous fibrosis patients with healthy controls.

MATERIALS AND METHODS

In the present study 100 patients (50 clinically diagnosed OSMF and 50 Control) were evaluated for soft palatal morphology. All the patients who were selected for the study were divided into two groups: Group A- had 50 patients with characteristic signs and symptoms of OSMF like, in tolerance to spicy foods, blanching and stiffness of oral mucosa, fibrous vertical bands palpable in oral mucosa and progressively inability to open the mouth. Group B- had 50 healthy subjects.The antero-posterior and supero-inferior dimensions of soft palate were measured on digital lateral cephalograms.The length of the soft palate was evaluated by measuring the linear distance from the posterior nasal spine (PNS) to the tip of the uvula of the resting soft palate. Supero-inferior dimension of soft palate was measured at the thickest area of soft palate. Morphology of soft palates was classified based on their morphology according to **You et al.** (2008) as Types: 1 (leaf-shaped), 2 (rat-tail

shaped), 3 (butt-like), 4 (straight line), 5 (S-shaped) and 6 (crook shaped). The data collected was statistically analysed using SPSS Version 16.0 statistical analysis software. The values were represented in number (%) and Mean±SD.

RESULTS

The results of present study revealed that type 6 (crook-shaped) soft palate was seen more common among theOSMF group. The anteroposterior dimension of soft palate in the OSMF group was 27.05±3.09 and in control group was 31.67±3.1 whereas the superoinferior dimension of soft palate in the OSMF group was 11.08±1.86 and in control group was 9.26±1.5. In both the parameters result was statistically significant.

CONCLUSION

It can be concluded that cephalometry can be efficiently used to assess the morphology of soft palate. There was diminution in anteroposterior length and increase in superoinferior measurement as the OSMF disease progressed.

Oral Submucous Fibrosis is a chronic condition of the oral mucosa, first described by Schwartz in 1952 among five East Africa women of Indian origin under the term, **atrophiaidiopathica (tropica) mucosae oris**. It is a premalignant condition that has received considerable attention in the recent past because of its chronic debilitating and resistant nature.[1]

Oral Submucous Fibrosis was defined by **Pindborg and Sirsat** as "An insidious, chronic disease affecting any part of the oral cavity and sometimes the pharynx. Although occasionally preceded by and/or associated with vesicle formation, it is always associated with juxta-epithelial inflammatory reaction followed by fibroelastic change of the lamina propria, with epithelial atrophy leading to stiffness of the oral mucosa and causing trismus and inability to eat."[2]

The disease is predominantly seen in Asian countries prevalence being more in India, Bangladesh, Bhutanand Pakistan occasionally in European countries. Recent epidemiological data indicate that the number of cases of OSMF has increased rapidly in India and majority seen in Bihar, Madhya Pradesh, Gujarat and Maharashtra.

Oral Submucous Fibrosis commonly seen among betel quid chewers. Clinically, the patient complains of burning sensation to spicy foods, blanching and stiffness of the oral mucosa, fibrous bands in the buccal or labial mucosa, and progressive inability to open the mouth.[3]

Oral Submucous Fibrosis occurs over a wide age range, majority of the patients diagnosed with age in the 2^{nd},3^{rd} and 4^{th} decade of life, individual less than 20 years seem to be more affected than individual in other age group.

Soft palate plays a very crucial role in velopharyngeal closure, that is, approximation of soft palate with pharyngeal walls. This sphincteric mechanism separates nasal and oral cavity during speech and deglutition.[4]

Clinical visualization of the soft palate becomes inadequate due to limited accessibility of the velopharyngeal region; therefore, it becomes mandatory to rely on other diagnostic methods for complete evaluation.[5]

The lateral skull view is by far the most valuable view for evaluation of the soft palate as it shows extensive bone and soft tissue images. Other views such as anteroposterior view, however, are useful in evaluation of the lateral pharyngeal walls and uvular deviation, but with the head in extension, the soft palate is projected above the hard palate.[6]

Lateral cephalogram is less expensive, more useful, easily achieved with reduced radiation. So, it can be used for morphometric evaluation of soft palate and its surrounding structures.[7]

Only few researches have reported on morphology of soft palate in OSMF patients, hence the need was felt to conduct a study to evaluate changes in soft palate using digital lateral cephalogram.

AIM

To evaluate and correlate the morphology of soft palate in oral submucous fibrosis patients and healthy control using lateral cephalogram.

OBJECTIVES

1. To evaluate the morphology of soft palate in clinically diagnosed oral submucousfibrosis patient using digital lateral cephalogram.

2. To compare the morphological changes in oral submucousfibrosis patients with healthy controls.

The soft palate is the posterior fibromuscular part of the palate that is attached to the posterior edge of the hard palate. The soft palate plays a large role in velopharyngeal closure, which refers to the normal apposition of soft palate with posterior and lateral pharyngeal walls. It participates in most oral functions, especially velopharyngeal closure which is related to the normal function of sucking, swallowing, and pronunciation.[8]

DEVELOPMENT OF SOFT PALATE[9]

New outgrowths from the medial edges of the maxillary prominences form the shelves of the secondary palate. These palatal shelves grow downward beside the tongue, at which time the tongue partially fills the nasal cavities. At about the ninth gestational week, the shelves elevate, make contact, and fuse with each other above the tongue.

Fusion of palatal shelves requires alterations in the epithelium of the medial edges that begin prior to elevation. These alterations consist of cessation of cell division, which appears to be mediated through distinct underlying biochemical pathway, including a rise in cyclic AMP levels. There is also loss of some surface epithelial (peridermal) cells and production of extracellular surface substances, particularly glycoproteins that appear to enhance adhesive between the shelf edges as well as between the shelves and inferior margin of the nasal septum.

The ultimate fate of these remaining epithelial cells is controversial. Some of them appear to undergo cell death and eventually are phagocytized, but recent studies indicate that many undergo direct transformation in mesenchymal cells. The fate of cells in the epithelial seam of the primary palate is also questionable. Some of the epithelial cells remain indefinitely in clusters (cell rests) along the fusion line. Eventually, most of the hard palate and all of the soft palate form from the secondary palate.

ANATOMY OF SOFT PALATE[10]

Soft palate is a movable, muscular fold, suspended from the posterior border of the hard palate. It separates the nasopharynx from the oropharynx, and is often looked upon as traffic controller at the crossroads between the food and air passages.

The soft palate has two surfaces, anterior and posterior; and two borders, superior and inferior. The anterior (oral) surface is concave and is marked by a median raphe. The posterior surface is convex, and is continuous superiorly with the floor of the nasal cavity. The superior border is attached to the posterior border of the hard palate, blending on each side with the pharynx. The inferior border is free and bounds the pharyngeal isthumus. From the middle, there hands a conical projection, called the uvula. From each side of the base of the uvula, two curved folds of mucous membrane extend laterally and downwards. The anterior fold is called the palatoglossal arch or anterior pillar of fauces. It contains the palatoglossus muscle and reaches the side of the tongue at the junction of its oral and pharyngeal parts. This fold forms the lateral boundary of the orophayngeal isthumus or isthumus of fauces. The posterior fold is called the palatopharyngeal arch or posterior pillar of fauces. It contains the palatopharyngeal muscle. It forms the posterior boundary of the tonsillar fossa, and merges inferiorly with the lateral wall of pharynx.

Muscles of the soft palate are: [10]

1. Tensor palate (tensor veli palatine)
2. Levator palate (levator veli palatini)
3. Musculus uvulae
4. Palatoglossus
5. Palatopharyngeus

Nerve supply of the soft palate:[10]

1. Motor nerves: all muscles of the soft palate except the tensor veli palatine are supplied by the pharyngeal plexus. The fibers of this plexus are derived from

the cranial part of the accessory nerve through the vagus. The tensor veli palatine is supplied by the mandibular nerve.

2. General sensory nerves are derived from:
    a) The middle and posterior lesser palatine nerves, which are branches of the maxillary nerve through the pterygopalatine ganglion.
    b) The glossopharyngeal nerve
3. Special sensory or gustatory nerves carrying taste sensations from the oral surface are contained in the lesser palatine nerves.
4. Secretomotor nerves are also contained in the lesser palatine nerves.

Blood supply:[10]

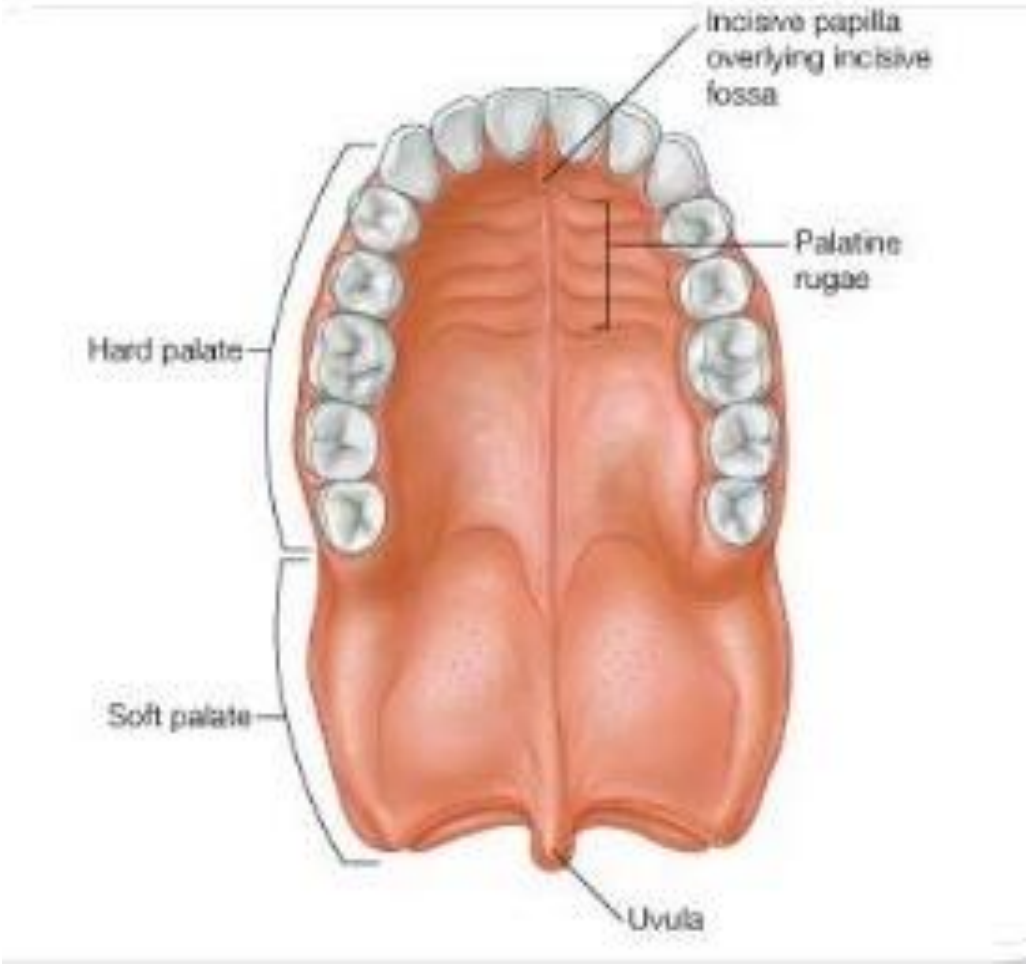
Arteries-1. Greater palatine branch of maxillary artery

2. Ascending palatine branch of facial artery

3. Palatine branch of ascending pharyngeal artery

Veins- They pass to the pterygoid and tonsillar plexuses of veins

Lymphatics- Drain into the upper deep cervical and retropharyngeal lymph node.



Photograph: 1 Anatomy of Soft Palate

MORPHOLOGY OF SOFT PALATE

Six basic types of basic shapes of the soft palate were seen. This was in accordance with the classification given by **You*et al.***[7] viz.

• **Type 1: Leaf shaped/lanceolate shaped** - the middle portion of the soft palate was slightly elevated to than the nasal and the oral ends.

• **Type 2: Rat-tail shaped** - the soft palate with bulged anterior portion and constricted free margin.

• **Type 3: Butt-like** soft palate which showed a shorter and fatter appearance with no distinct difference in width from anterior portion to the free margin.

• **Type 4: Linear shaped.**

• **Type 5: S-shaped/twisted/distorted soft palate.**

• **Type 6: Crooked appearance** - the soft palate in which the posterior most portion of the soft palate hooked up anterior superiorly.

According to **Guttal *et al.***[11] study **(2012),** there were two additional variants of soft palate was found, viz.

• **Type 7: U-shaped soft palate** - variety of Type 2, with blunt end.

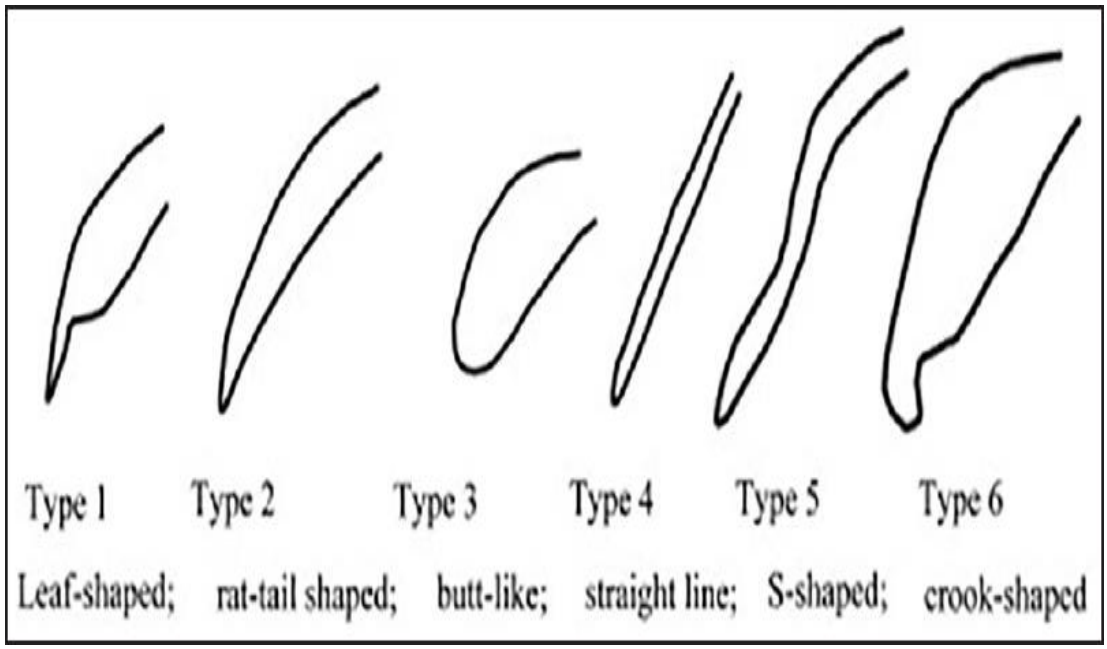
• **Type 8:** Variants which did not fit into either of the above-mentioned categories.

In addition to the above-mentioned types, three different types were found in **Nagaraj et al.**[12]study **(2016),***viz*.

• Type 9: Cone Shaped.

• Type 10: Triangular shape.

• Type 11: V shaped.



Photograph2: Schematic representation of different types of soft palate according to You et. al. classification(2008)

ORAL SUBMUCOUS FIBROSIS

HISTORICAL REVIEW

A condition resembling OSMF was described as early as "600" BC by **Sushruta** and it was named as **"VIDARI"** having features of progressive narrowing of the mouth, depigmentation of oral mucosa and pain on taking food.[13]

OSMF was first described by **Schwartz** in 1952 while examining five Indian women from Kenya, to which he ascribed the descriptive term "**atrophia idiopathica (tropica) mucosae oris".** Later in 1953, **Joshi** from Bombay (Mumbai) coined the term **"submucous fibrosis of palate and pillars"**[14]

Different authors have used different terms for OSMF like, **idiopathic scleroderma of the mouth** (Su et al. in 1954), **idiopathic palatal fibrosis** (Rao et al. in 1962), **sclerosing stomatitis** (Behl et al. in 1962), **and Juxta epithelial fibrosis (**Pindborgh et al. in 1966)**.**[15]

In 1966, **Pindborg** defined OSMF as "an insidious, chronic disease affecting any part of the oral cavity and sometimes the pharynx. Although occasionally preceded by and/or associated with vesicle formation, it is always associated with a juxta-epithelial inflammatory reaction followed by a fibroelastic change of the lamina propria, with epithelial atrophy leading to stiffness of the oral mucosa and causing trismus and inability to eat."[15]

EPIDEMIOLOGY

Numerous published reports on OSMF suggest that the disease predominantly affects people of South East Asian origin. It affects between 0.2% and 1.2% of urban population in India. The cases have also been reported among Indians living in Kenya, Malaysia, Uganda, South Africa, Fiji Islands, and UK. Sporadic cases have been reported in other ethnic groups from countries such Taiwan, Nepal, Thailand, South Vietnam and Srilanka.[16]

An epidemiological assessment of OSMF among Indian villagers, based on baseline data, recorded a prevalence of 0.2% (n=10071) in Gujarat, 0.4% (n=1027) in Kerala, 0.04% (n=10169) in Andhra Pradesh, and 0.07% (n=20388) in Bihar. The prevalence among 101,761 villagers in the state of Maharashtra (central India) was 0.03%. In a 10-year follow up study of oral precancer, Gupta et al. in 1980 observed that the incidence of OSMF in Ernakulum, Kerala was 8 for men and 19 for women per 100,000.[17]

There is wide variations in the prevalence figure between different studies, and may probably due to differences in the clinical criteria for diagnosis, differences in abusive habits, differences in frequency of habit, differences in geographic distribution and differences in races & other causes. While some investigators adhere to the initial signs and symptoms, other looked for fibrous bands as the diagnostic criterion.[18]

Worldwide estimate in 1996 indicate that 2.5 million people are affected by the disease. In 2002, the statistics for OSMF from Indian subcontinent alone was about 5 million people.[19]

AETIOLOGY

The etiology of OSMF still remains obscure. In past, many authors have proposed various hypotheses with a multifactorial origin for this particular condition. The factors that have been discussed as possible aetiological factors to data are areca nut, capsaicin in chillies, micronutrient deficiencies of iron, zinc and essential vitamins. In addition, a possible autoimmune basis to the disease with demonstration of various auto-antibodies and an association with specific HLA antigens has been proposed. This raises the possibility of a genetic predisposition of some individuals to develop OSMF.[20]

Areca nut

OSMF is thought to be a disease of collagen metabolism secondary to betel nut usage. The betel quid is placed in the buccal vestibule for about 15 minutes to an hour and repeated several times a day which leads to constant contact between the mixture and oral mucosa. The alkaloids from the quid are absorbed into the mucosa and undergoes metabolism. Microtrauma produced by the friction of coarse fibers of areca nut also facilitates diffusion of the alkaloids into the subepithelial connective tissue resulting in juxtaepithelial inflammatory cell infiltration.[20]

Betel nut contains alkaloids, flavonoids, and copper, all of which in turn are thought to affect collagen synthesis and breakdown. Four alkaloids: arecoline, arecaidine, guvacine, and guvacoline, are all involved in stimulating fibroblasts to produce collagen. In addition, flavonoids (tannins and catechins) are found to inhibit collagenase, decreasing collagen breakdown. Betel quid also causes localized mucosal inflammation, causing a recruitment of activated T cells and macrophages locally, resulting in an increase in cytokines and tumor growth factor beta (TGF- β). TGF- β is found to significantly increase collagen production by activating procollagen genes, elevating procollagen proteinase levels, and upregulating lysyl oxidase activity (LOX). TGF- β also inhibits collagen degradation by activating the tissue inhibitor of matrix metalloproteinase (TIMP) gene and activating the plasminogen activator inhibitor (PAL). Activation of TIMPs and PAI genes in turn result in a decrease in collagenase activity, in turn resulting in a decrease in collagen degradation. Areca nut has a high copper content and copper has been found to stimulate LOX, an enzyme essential to the final crosslinking of collagen fibers. All

of this results in a significant increase in collagen production and decrease in collagen breakdown.[21]

M.K. Gupta et al (2008) studied on literature on etiology of OSMF and made conclusion based on various available data suggests that the main causative agents for OSMF are the constituents of areca nut, mainly arecoline and tannin may have a synergistic role. Arecoline will interfere with the molecular processes of deposition and/or degradation of extracellular matrix molecules such as collagen. Due to this interference, phagocytic capacity of fibroblastis reduced, because of up or down regulation of key enzymes such as lysyl oxidase and alteration in expression of various ECM molecules. The process may also be influenced by increased secretion of inflammatory cytokines, growth factors and decreased production of anti-fibrotic cytokines. Although the above mechanisms may explain the induction, maintenance and progression of fibrosis in OSMF. Nutritional deficiencies may not play a primary role but it could synergize the symptomatology by contributing to epithelial atrophy.[22]

Vinit Aher et al (2011) conducted study on patients with the limited mouth opening and associated blanched oral mucosa with palpable fibrous bands to evaluate the effect of frequency, duration and type of areca nut products on the incidence and severity of oral submucous fibrosis and concluded that occurrence of OSMF is related to areca nut and its products. The duration and frequency of its use and type of areca nut products has effect on the incidence and severity of OSMF. Gutkha and pan masala have more deleterious and faster effects on oral mucosa. The gutkha chewing habit along with the other habits does not have any significant effect on the rate of occurrence and incidence and severity of the OSMF.[23]

Gunjan Shah et al (2012) study on the role of Areca nut as an emerging etiology of oral cancers and concluded that neither single agent is responsible nor single pathway can produce carcinogenesis and OSMF is related with the carcinogenesis.[24]

A Shukla et al (2015) reviewed on etiology of OSMF and found, the constituents of areca nut are well established cause of stimulation and proliferation of fibroblasts. Evidences suggest that OSMF is multi-factorial with certain effects on specific subpopulations of fibroblasts, genetic predisposition and molecular mechanism which could render the oral mucosa more susceptible to chronic inflammatory changes on exposure to carcinogens.[25]

Chilli

The use of chillies (Capsicum annum and Capsicum frutescence) has been thought to play an etiological role in OSMF. Capsaicin, which is vanillylamide of 8-methyl-6-nonenic acid, is the active ingredient of chillies, play an etiological role in oral submucous fibrosis.[26]

Seedat and Van Wyk (2014) studied that no positive correalation. Chilli hypothesis do not hold in places like Mexico and South America where chilli is widely used and OSMF is not found. The overall assessment is that there is no evidence substantiating the etiologic role of chillies in OSMF.[27]

Misi

Misi is a black colored powder that is used more commonly by women in rural areas of Uttar Pradesh. It contains washing soda, borax, charcoal of myrobalan, and fuller's earth in varying proportions. Misi is used as a cosmetic to keep the teeth shiny and clean. These substances are thought to be a causative factor of OSMF among these women.[26]

Nutritional Deficiencies

Several investigators have reported nutritional deficiencies in patients with OSMF. The serum total protein and albumin level, hemoglobin and serum iron in OSMF patients have been found to be significantly lower than in normal patients. In the same study it was found that total iron binding capacity was elevated and the percentage saturation of transferrin was significantly lower.[26]

Genetic Predisposition

Although betel nut chewing is widely practiced in some geographical regions, only a minority of genetically predisposed individuals are susceptible to OSMF. The frequency of HLA antigens and haplotypic pairs in patients with OSMF and ethnically matched non consanguineous controls was investigated. The haplotypic pairs A10/DR3, A10/B8 and B8/D3 showed an increased frequency in the patients, but the latter two were not statistically significant. In South Africa, HLA typing was carried out on OSMF patients of Indian origin. The HLA antigen patterns as reported by **Cannif et al** were not encountered in patients with oral submucous fibrosis or in persons practicing the betel habit without the disease. However, it was also noted that there were inconsistencies in the presentation of the disease, with some patients

having severe OSMF associated with a short duration of the betel habit and a low frequency. In Taiwan, a significant increase in HLA phenotype B76 and haplotype pairs of HLA-B52/CW7, B62/CW7 and B48/CW7 was seen. All these studies suggest that some subjects with particular HLA haplotypes are more prone to develop OSMF.[13]

Autoimmunity

Several characteristics indicate that OSMF may be an autoimmune disease. A high incidence of autoantibodies has been reported in Taiwanese subjects with OSMF. This study demonstrated a significantly higher positive ANA (23.9%), SMA (23.9%), and GPCA (14.7%) in OSMF patients compared to healthy controls (9.2%, 7.3%, 5% respectively) which is suggestive of OSMF being an autoimmune condition.[13]

Suspicion of an autoimmune explanation for OSMF from certain similarities of this condition with other collagen disorders, namely scleroderma, which is presumed to have an autoimmune pathogenesis.Because of the similarities of clinical features between OSMF and scleroderma, earlier it was thought as oral scleroderma.[28]

DEFECTIVE IRON METABOLISM

Divya Bhardwaj et al (2012) conducted study on 120 subjects out of them 40 subjects with the OSMF, 40 with the iron deficiency anemia without tobacco chewing habit, 40 healthy control subjects without OSMF and iron deficiency anaemia. They found that statistically significant difference in serum iron and haemoglobin level in all three groups and there is a progressive decrease in serum iron and haemoglobin levels from stage I of OSMF to the stage IV of OSMF so it can be used as an auxillary test in assessment of prognosis of the disease.[29]

ETIOPATHOGENESIS

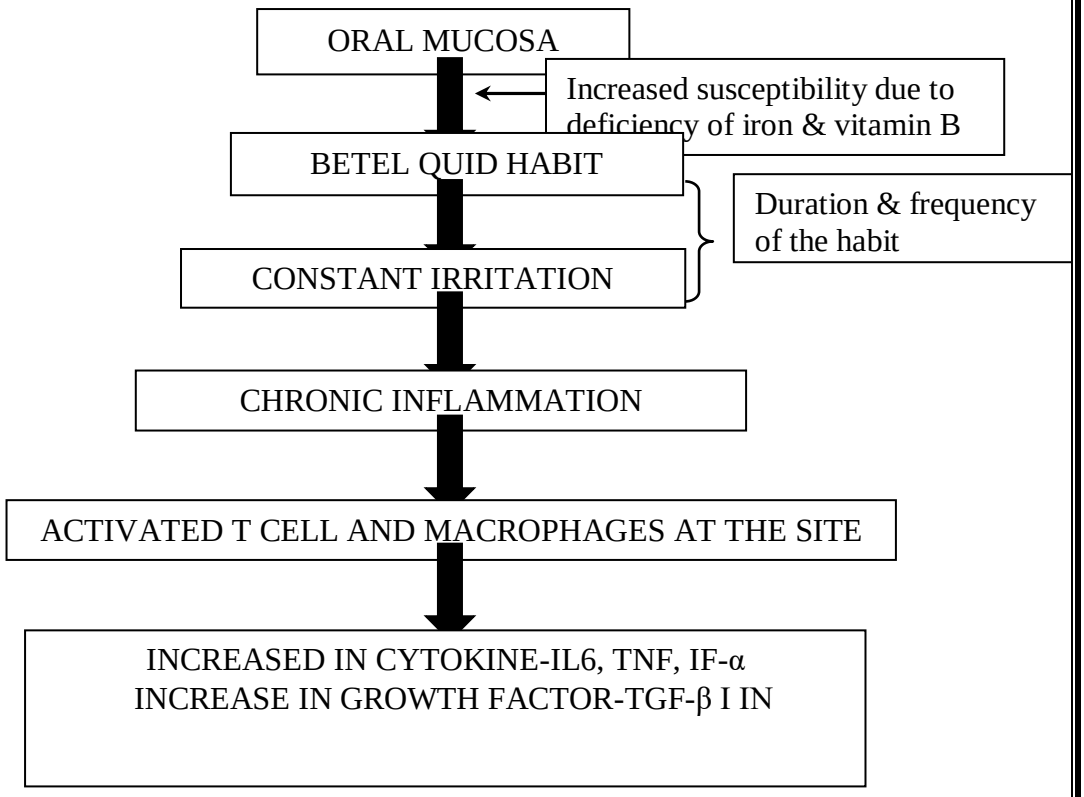
The pathogenesis of OSMF is believed to be multifactorial. Factors that trigger the disease include consumption of chillies, chewing areca nut, nutritional deficiencies, and immunologic processes. The most important risk factor however is the chewing of betel quid (containing areca nut, tobacco and lime) and this has been supported by epidemiologic studies as well.

In iron deficiency anemia the oral epithelium becomes atrophic with reduced maturation compartment but an increased keratin compartment. Cell kinetics have shown an increased cell production indicating that despite atrophy, the epithelial

turnover is rapid. From this it can be presumed that there may be increased susceptibility to chemical carcinogens due to an increased population of dividing cells and also to a more permeable epithelium, leading to development of oral precancer including OSMF. Decrease in the levels of iron and ascorbate has been reported in patients with OSMF.[26]

The disease is multifactorial but the exact pathogenesis is not well established. The mechanism responsible for the pathogenesis are**increased collagen accumulation, increased expression of fibrogenic cytokines, genetic polymorphisms and autoimmunity.** The increased collagen accumulation results from increased collagen production and stabilization or decreased breakdown of collagen. Fibroblasts are changed into different phenotypes under the influence of areca nut alkaloids which secrete more amount of collagen. Increased fibrosis is also thought to be due to increased cross-linking of collagen through up-regulating of lysyl oxidase (present in copper which is present in betel nut) activity in OSMF fibroblasts. Thus OSMF is now considered a collagen metabolic disorder. Stabilization of collagen structure is produced by catechin and tannins from the areca nut.[30]

The role of the constituents of areca nut in the pathogenesis of OSMF has been studied in detail over last two decades. It is apparent that fibrosis and hyalinization of subepithelial tissues account for most of the clinical features encountered in this condition. Moreover substantial amount of research on elucidating the etiology and pathogenesis appear to have been focused on changes in the extracellular matrix. It is logical to hypothesize that the increased collagen synthesis or reduced collagen degradation as possible mechanisms in the development of the disease. There are numerous biological pathways involved in the above processes and it is likely that the normal regulatory mechanisms are either down regulated or up regulated at different stages of the disease.[31]



Figure–1: Initial events of the disease process of oral mucosa which is in direct contact with the betel quid due to the habit, is the site of constant irritation (Rajalalitha and Vali, 2005)

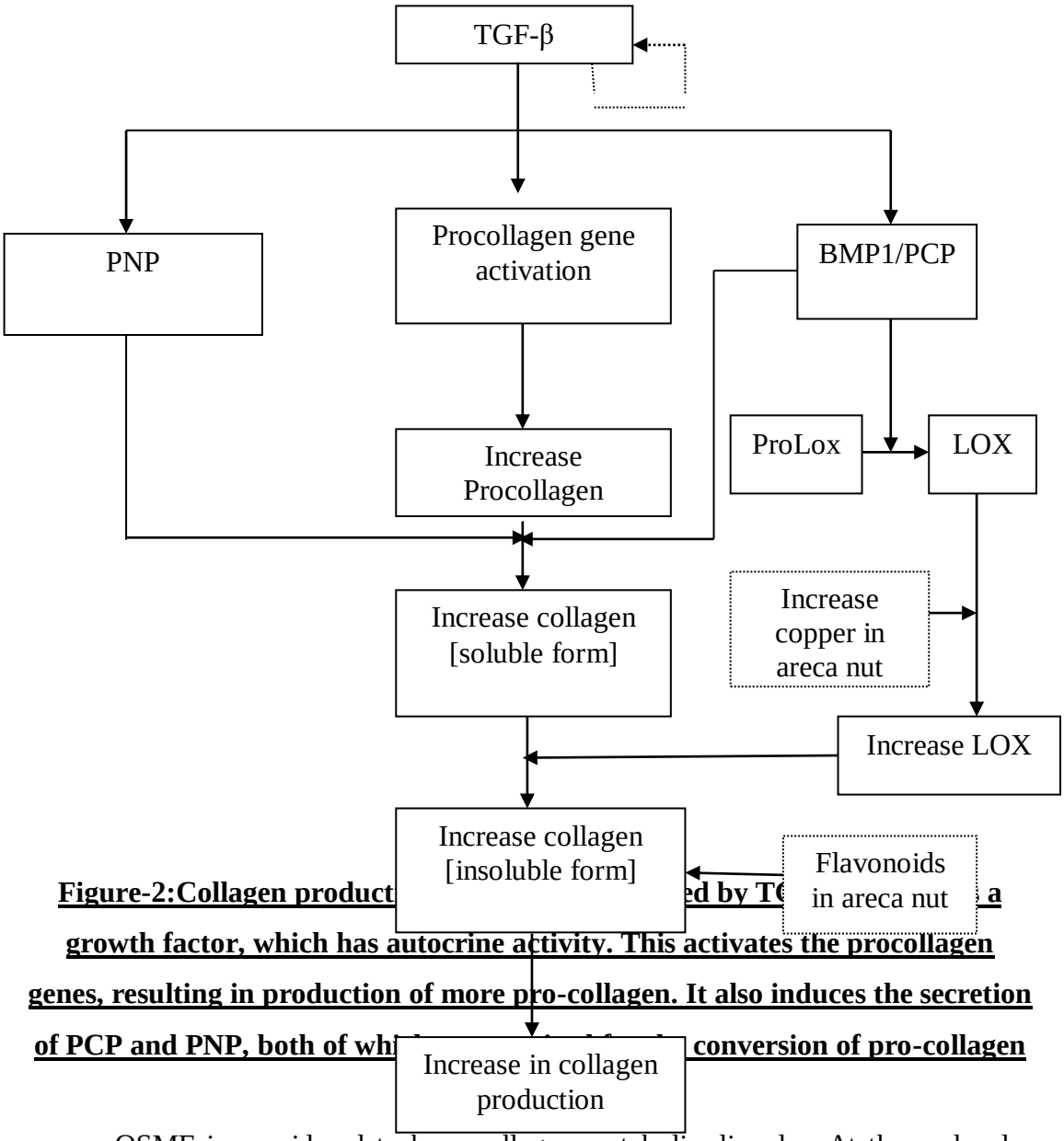


Figure-2:Collagen product ed by TG a growth factor, which has autocrine activity. This activates the procollagen genes, resulting in production of more pro-collagen. It also induces the secretion of PCP and PNP, both of wh conversion of pro-collagen

OSMF is considered to be a collagen metabolic disorder. At the molecular level the collagen production and collagen degradation are regulated by transforming growth factor-beta (TGF-β) and the flavonoids present in areca nut. There are three main events modulated by TGF-β, which favor collagen production:

1. Activation of procollagen genes.
2. Elevation of procollagen proteinase levels
3. Upregulation of lysyl oxidase (LOX) activity.

The transcriptional activation of procollagen genes by TGF-β causes an increased expression of procollagen genes and hence contributing to increased collagen level in OSMF. N- and C- procollagen proteinases play an important role in processing procollagen into collagen fibrils. LOX is dependant on copper and is an essential

enzyme for final processing of collagen fibers into a stabilized, covalently cross linked mature fibrillar form that is resistant to proteolysis. Areca nuts have been shown to have a high copper content. Trivedy et al have reported a high copper content in oral tissues of patients with OSMF. Copper has been implicated in tissue fibrogenesis via the copper dependant enzyme lysyl oxidase (LOX)which has a crucial role in the cross linking of collagen and elastin fibers. LOX has also been implicated in other fibrotic disorders such as hepatic and pulmonary fibrosis and scleroderma.[16]

1. ACTIVATION OF PROCOLLAGEN GENES

Collagen plays a critical role as a structural element of connective tissue. About 27 types of collagen have been recognized, which can be grouped into seven broad classes. Major class is fibrillar collagen, among them types I, III and VI form a major part of connective tissue. Collagen type VII forms the anchoring fibrils of oral mucosa. The distinguishing feature is a unique type of triple helix, stabilized by unusual crosslinks. The processing of fibrillar collagen occurs in a stepwise manner. Procollagen genes are transcribed and translated to form procollagen monometric chains (procollagen precursor). Three of these monomers assemble into a trimer triple helix. This is aided by disulphide bridge formation. Trimeric procollagen chains are then acted upon by N- and C-terminal proteases (PCP and PNP), to cleave the terminal domains. After this cleavage the collagen units form spontaneously into fibrils. The newly formed fibrils are then covalently stabilized through cross-linking to form a stable mature structure of collagen. The genes COL1A2, COL3A1, COL6A1, COL6A3, and COL7A1 have been identified as definite TGF-β targets. These are early induced genes in fibroblasts. They were identified by differential hybridization of cDNA array. The transcriptional activation of types I and VII collagen gene expression by TGF-β has been demonstrated. This transcriptional activation of procollagen genes by TGF-β is causing an increased expression of procollagen genes and hence contributing to increased collagen level in OSMF.[25]

2. ELEVATION OF PROCOLLAGEN PROTEINASE LEVELS[25]

Procollagen proteinases play an essential role in processing. There are two types of proteinases that cleave the N- and C-terminal respectively.

1. **PROCOLLAGEN N PROTEINASE (PNP)**

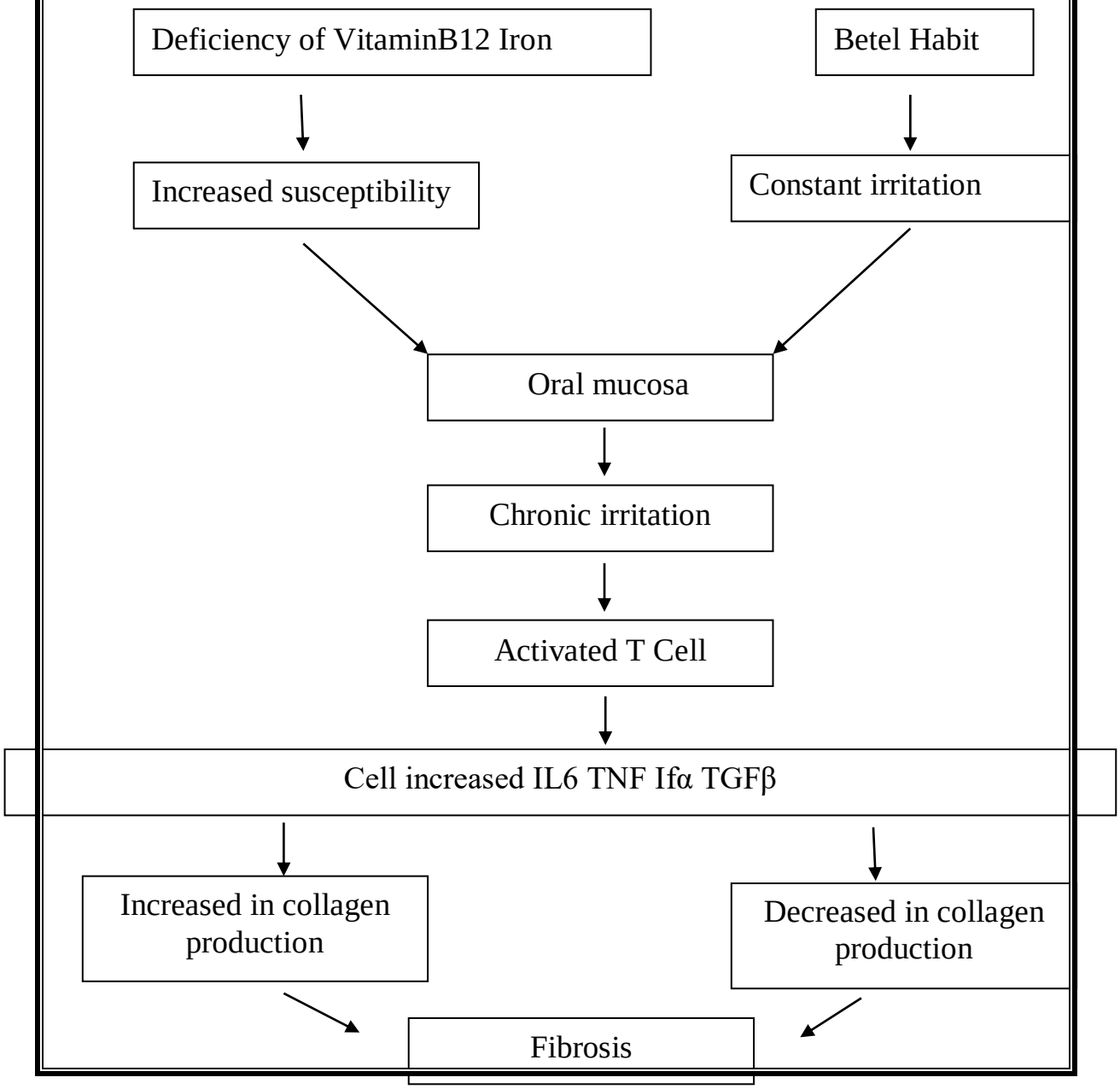
2. PROCOLLAGEN C PROTEINASE (PCP)

1. PCP and BMP1 have been shown to be the same protein that cleaves the C-terminal of procollagen precursor. TGF-α has been found to induce BMP1 at the transcriptional and translational levels in different cell types such as the osteosarcoma cells and fibrogenic cell cultures.
2. PNP-It cleaves the N-propeptide of procollagen precursor. There are two types of PNPs, PNP I and III, they are classified based on the type of procollagen fibers on which they act. TGF- β treated cells have been shown to have an elevated level of PNP. Thus, not only is procollagen gene expression increased by TGF-α, but also their processing into fibrils is enhanced by increased levels and activities of the PNP and PCP.[31]

3. UPREGULATION OF LYSYL OXIDASE (LOX) ACTIVITY

The copper content of areca nut is high and the levels of soluble copper in saliva may rise in volunteers who chew areca quid **(Trivedy et al.,1997).**The same group showed that the oral mucosa of areca nut chewers had significantly raised levels of copper when compared with the control subjects **(Trivedy et al., 2000).** The association between copper and OSF has been linked on the basis that excess copper is found in tissues of other fibrotic disorders- Wilson's disease, Indian childhood cirrhosis and primary biliary cirrhosis. The enzyme lysyl oxidase is found to be upregulated in OSF **(Trivedy et al., 1999).** This is a copper dependent enzyme **(Kagen and Trackenman, 1991)** and plays a key role in collagen synthesis and its cross linkage. The possible role of copper as a mediator of fibrosis is supported by the demonstration of up regulation of this enzyme in OSF biopsies **(Trivedy et al., 1999)** and in OSF fibroblasts compared to normal fibroblasts grown in culture **(Ma et al., 1995).**Copper added at various concentrations in vitro has also been shown to increase proliferation of fibroblasts in culture **(Trivedy et al., 2001).** The fibroblasts in OSF have not only increased lysyl oxidase activities but also specific growth characteristics. This was evident with the reported cell doubling time of 3.2 days for OSF and 3.6 days for normal fibroblasts **(Ma et al., 1995).**OSF fibroblasts grew more rapidly than normal. However, another study based on ultrasound

investigations of visceral organs in OSF patients reported that there was no evidence of fibrotic changes elsewhere **(Rajendran et al., 2003).** As the oral mucosa is directly exposed to the copper challenge in chewers its effect may well be local. These different growth characteristics may either be due to the direct effects of ingredients of areca nut or secondary to inflammatory factors mediated by areca nut such as IL-1, TGF- β, IGF, EG **(Haque et al., 2000).** The LOX activity is important of insoluble collagen due to cross linking. The process of cross linking gives tensile strength and mechanical properties to the fibers as well as makes the collagen fibersresistant to proteolysis tilting the balance toward a fibrotic condition as present in OSMF.[32]



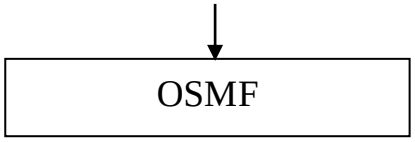


Figure3 : Pathogenesis of OSMF

COLLAGEN DEGRADATION PATHWAY

There are two main events modulated by TGF-β which decreases collagen degradation-

1. Activation of tissue inhibitor of matrix metalloproteinases gene (TIMPs).

2. Activation of plasminogen activator inhibitor (PAI) gene.

Matrix metalloproteinases (MMPs) are a set of structurally related matrix proteases. TIMPs are specific inhibitors of MMPs and control their local activities in tissues. An increased expression of TIMPs has been reported in oral tissues of patients with OSMF by **Chang et al and Sheih et al.** TGF-β activates TIMP gene which increases the tissue level of TIMPs. The TIMPs inhibit activated collagenase thereby decreasing collagen degradation. Type 1 plasminogen activator inhibitor is a 50kDa glycoprotein belonging to the serine protease superfamily. Plasminogen activators and their inhibitors are thought to play a key role in the balance of proteolytic and anti proteolytic activities that regulate matrix turnover. Yang et al in their study demonstrated that arecoline was capable of stimulating PAI 1 mRNA, and PAI 1 expression was elevated in OSMF specimens compared to normal buccal mucosa. TGF-β activates PAI genes which increase synthesis of PAI; PAI inhibits conversion of plasminogen to plasmin which decreases collagen degradation. Another explanation of fibrosis is that chewing areca nut leads to muscle fatigue. Over activity of the muscle results in excessive glycogen consumption, leading to glycogen depletion. The increased muscle activity and diminished blood supply following connective tissue changes owing to extensive OSMF leads to degeneration and fibrosis of the muscle. The collagen that is synthesized is mostly insoluble and in cross linked form. Besides stimulating fibroblast proliferation and collagen synthesis, areca nut alkaloids are also thought to inhibit fibroblast phagocytosis

which leads to fibrosis. Tsai et al investigated phagocytosis of collagen and fibronectin coated beads by fibroblast cultures in the presence of areca nut alkaloids with an in vitro model system. They found that arecoline and arecaidine caused a dose dependent inhibition of phagocytosis. Thus OSMF lesions appear to contain fibroblasts with marked deficiencies in collagen and fibronectin phagocytosis. The flavonoids tannin and catechin render the collagen fibers resistant to degradation by stabilizing the collagen fibers. Oral submucous fibrosis may affect persons of any age and sex. No caste or religion is specifically affected. It has a slow and insidious onset. It may take two to five years for the disease to become clinically apparent. Any site in the oral cavity may be involved.[26]

DIFFERENT CLASSIFICATION, STAGING AND GRADING SYSTEMS

The different classification systems existing in literature can be broadly categorised as follows:

A: Classifications based on clinical aspects of the disease[33]:

1. Desa J. V (1957)
2. Wahi P.N. and KapurV.L. et al (1966)
3. Ahuja S.S. and Agarwal G.D. (1971)
4. Bhatt A. P. and Dholakia H.M. (1977)
5. Gupta D.S. and Golhar B.L. (1980)
6. Pindborg J.J (1989)
7. Katharia S.K. et al (1992)
8. Bailoor D.N. (1993)
9. Racher S.K (1993)
10. Lai D.R. et al (1995)
11. Maher R.et al(1996)
12. Haider S.M. et al(2000)
13. Ranganathan K. et al (2001)
14. Rajendran R. (2003)
15. Bose T. and Balan A. (2007)
16. Kumar K. et al (2007)
17. Mehrotra D. et al (2009)
18. More C.B. et al (2011)
19. Kerr A.R.et al(2011)
20. Patil S. and Maheshwari S. (2014)

21. Prakash R. et al (2014)

B: Classifications based on histopathological aspects of the disease: [33]

1. Pindborg J.J. and Sirsat S.M. (1966)
2. Utsonumiya H. et al (2005)
3. Kumar K. (2007)

C: Classifications based on clinical and histopathological aspects of the disease:[33]

1. Khanna J.N. and Andrade N.N. (1995)

A: CLASSIFICATIONS BASED ON THE CLINICAL ASPECTS OF THE DISEASE[33]:

1. **Desa J.V.** divided OSMF into 3 stages:

Stage I: Stomatitis and vesiculation

Stage II: Fibrosis

Stage III: As its sequelae

2. **Wahi P.N. and Kapur V.L.** et al classified OSMF based on the clinical features, severity and extent of involvement into 3 groups:

Group I: Usually there are no symptoms referable to mucosal involvement. The lesion affects one or other commonly involved anatomical site, is focal in character, shows pallor or whitish coloration, wrinkling of mucosa and minimal induration.

Group II: Cases present with symptoms like soreness of mucosa or increased sensitivity to chillies. The lesion is diffuse, white, extensive and indurated, involving one or more anatomical sites.

Group III: symptoms are mostly due to restricted mobility like trismus, stretching at the angles of the mouth altered pronunciation and inability to protrude the tongue. Firm submucosal bands are palpable. Surface may be fissured or ulcerated.

3. **Ahuja S.S. and Agarwal G.D.** classified based on the extent and type of fibrosis as:

Class I: Localised fibrous bands in the cheek extending from the superior to the inferior fornix on one or both sides. In order of frequency, the bands are mostly found on the lips, the premolar region or the second molar region.

Class II: Generalised diffuse hardening of the sub epithelial tissues extending from the cheek and hard palate to the soft palate, uvula and the faucial pillars. Occasionally, the hardening might extend to the lining mucosa of the pharynx.

Class III: Combination of the above two types where the fibrous bands are associated with a generalised diffuse form of submucous fibrosis.

4. **Bhatt A. P. and Dholakia H.M.** clinically grouped the patients into three grades as:

Grade I: Comprised of mild and early cases with a very slight fibrous bands and little closure of the mouth.

Grade II: Moderately pronounced symptoms with fibrous bands extending from the cheek to the palate.

Grade III: Excessive amount of fibrosis involving the cheek, palate, uvula, tongue and the lips with narrow opening of the mouth.

5. **Gupta D.S. and Golhar B.L.** classified into four stages based on the increasing intensity of trismus as:

Very early stage: The patients complain of burning sensation in the mouth or ulceration without difficulty in mouth opening.

Early stage: Along with burning sensation, the patients complain of slight difficulty in opening the mouth.

Moderately advanced stage: The trismus is marked to such an extent that the patient cannot open his/her mouth more than two fingers width therefore experiencing difficulty in mastication.

Advanced stage: Patient is undernourished and has a marked degree of trismus.

6. **Pindbor J.J** divided OSMF into 3 stages as:

Stage I: Stomatitis includes erythematous mucosa, vesicles, mucosal ulcers, melanotic mucosal pigmentations and mucosal petechiae.

Stage II: Fibrosis occurring in the healing vesicles and ulcers is the hallmark of the stage.

- Early lesions demonstrate blanching of the oral mucosa.
- Older lesions include vertical and circular palpable fibrous bands in the buccal mucosa and around the mouth opening or lips resulting in mottled

marble like appearance of the mucosa because of the vertical thick fibrous bands in association with blanched mucosa.

- Specific findings include reduction of mouth opening, stiff and small tongue, blanched and leathery floor of the mouth, fibrotic and depigmented gingiva, rubbery soft palate with decreased mobility, blanched and atrophic tonsils, shrunken bud like uvula and sunken cheeks, not commensurate with age or nutritional status.

Stage III: Sequelae of OSMF as follows:

- Leukoplakia is found in more than 25 % of the individuals with OSMF.
- Speech and hearing defects may occur due to involvement of the tongue and eustachian tubes.

7. **Katharia S.K. et al** described a scoring system based on the mouth opening present between upper and lower central incisors as:

Score 0: Mouth opening is greater than 41 mm
Score 1: Mouth opening between 37 to 40 mm
Score 2: Mouth opening between 33 to 36 mm
Score 3: Mouth opening between 29 to 32 mm
Score 4: Mouth opening between 25 to 28 mm
Score 5: Mouth opening between 21 to 24 mm
Score 6: Mouth opening between 17 to 20 mm
Score 7: Mouth opening between 13 to 16 mm
Score 8: Mouth opening between 09 to 12 mm
Score 9: Mouth opening between 05 to 08 mm
Score 10: Mouth opening between 00 to 04 mm

8. **Bailoor D.N.** classified on the basis of diagnosis as:

Stage I: Early OSMF

- Mild blanching.
- No restriction in mouth opening (normal distance between central incisor tips: Males 35 to 45 mm, Females 30 to 42 mm).
- No restriction in tongue protrusion (normal mesioincisal angle of the upper central incisor to the tip of the tongue when maximally extended with the mouth wide open: Males 5 to 6 cm, Females 4.5 to 5.5 cm).

- Cheek flexibility: CF= V1-V2 where V2 is a point measured between at one-third the distance from the angle of the mouth on a line joining the tragus of the ear to the angle of the mouth. The patient is then asked to blow his cheeks fully and the distance between the two points is marked on the cheek as V1. Mean values for cheek flexibility: Males 1.2 cm and Females 1.08 cm.
- Burning sensation on taking spicy or hot foods only.

Stage II: Moderate OSMF

- Moderate to severe blanching.
- Mouth opening reduced by 33%.
- Cheek flexibility also demonstrably reduced.
- Burning sensation in absence of stimuli.
- Palpable bands felt.
- Lymphadenopathy either unilateral or bilateral.
- Demonstrable anaemia on haematological examination.

Stage III: Severe OSMF

- More than 66% reduction in the mouth opening, cheek flexibility and tongue protrusion.
- Tongue may appear fixed.
- Severe burning sensation, patient is unable to do day to day work.
- Ulcerative lesions may appear on the cheek.
- Thick palpable bands.
- Bilateral lymphadenopathy.

9. **Racher S.K** classified into 3 stages based on habits as:

Stage I: Stage of Stomatitis and Vesiculation

- Characterised by recurrent stomatitis and vesiculation. Patient complains of burning sensation in the mouth and inability to eat pungent food.
- The examination reveals vesicles on the palate that may rupture and a superficial ulceration may be seen. Some amount of fibrosis can be seen.

Stage II: Stage of fibrosis

- There is inability to open the mouth completely and stiffness in mastication. As disease advances, there is difficulty in blowing the cheeks and protruding the tongue.

- On examination, there is increasing fibrosis in the submucosal. Mucosa is blanched and white. Lips and cheeks are stiff. Dorsum of the tongue may show atrophy of papillae. Blanching and stiffness of the mucosa of the floor of the mouth is less marked than that seen in the lips, cheeks and palate. Larynx is free from disease and respiration is not affected.

Stage III: Stage of sequelae and complications

- Leukoplakia changes in the mucosa.
- An ulcerating malignant lesion may be seen involving the cheeks, oropharynx or the tongue.
- Patients are predisposed to develop oral cancer under the influence of carcinogens.

10. **Lai D.R.** grouped OSMF on the basis of interincisal distance as:

Group A: Interincisal distance greater than 35 mm.

Group B: Interincisal distance 30 to 35 mm.

Group C: Interincisal distance 20 to 30 mm.

Group D: Interincisal distance less than 20 mm.

11. **Maher R**. et al classified on the basis of area of involvement in the oral cavity. He divided the intra-oral regions into eight sub regions viz palate, posterior one-third of the buccal mucosa, middle one-third of the buccal mucosa, anterior one-third of the buccal mucosa, upper labial mucosa, tongue and floor of the mouth and looked for disease involvement in each to assess the extent of clinical disease. This was further grouped into three categories as:

1. Involvement of one-third or less of the oral cavity

2. Involvement of one-third to two-third of the oral cavity (if 4 to 6 intra-oral sites are involved)

3. Involvement of greater than two-third of the oral cavity.

12. **Haider S.M.** classified on the basis of severity of disease taking objective parameters like mouth opening into consideration.

I: Clinical staging

1. Faucial bands only.
2. Faucial and buccal bands.
3. Faucial, buccal and labial bands.

II: Functional staging

1. Mouth opening greater than 20 mm.

2. Mouth opening between 11 to 19 mm.

3. Mouth opening less than 10 mm.

13. **Ranganathan K. et al** divided OSMF based on mouth opening as follows:

Group I: Only symptoms with no demonstrable restriction of mouth opening.

Group II: Limited mouth opening 20 mm and above

Group III: Mouth opening less than 20 mm.

Group IV: OSMF advanced with limited mouth opening. Precancerous or cancerous changes are seen throughout the mucosa.

14. **Rajendran R.** reported the clinical features of OSMF as follows:

Early OSMF: Comprises of burning sensation in the mouth, blisters especially on the palate, ulceration or recurrent generalized inflammation of oral mucosa, excessive salivation, defective gustatory sensation and dryness of mouth.

Advanced OSMF: Comprises of blanched and slightly opaque mucosa, fibrous bands in the buccal mucosa running in vertical direction. Palate and faucial pillars are the areas first involved with gradual impairment of tongue movement and difficulty in mouth opening.

15. **Bose T. and Balan A**. classified based on clinical features as:

Group A: Mild cases

Only occasional symptoms, pallor, vesicle formation, presence of one or two solitary palpable bands, loss of elasticity of mucosa, variable tongue involvement with protrusion beyond vermillion border. Mouth opening is greater than 3 cm.

Group B: Moderate cases

Symptoms of soreness of mucosa or increased sensitivity to chillies, diffuse involvement of the mucosa, blanched appearance, buccal mucosa tough and inelastic fibrous bands palpable, considerable restriction of mouth opening (1.5 to 3 cm) and variable tongue movement.

Group C: Severe cases

Symptoms are more severe, broad fibrous bands palpable, blanched opaque mucosa, rigidity of mucosa, very little opening of mouth (less than 1.5 cm), depapillated tongue and protrusion of tongue very much restricted.

16. **Kumar K. et al** categorized OSMF based on mouth opening as follows:

Stage I: Mouth opening greater than 45 mm.

Stage II: Mouth opening between 20 to 44 mm.

Stage III: Mouth opening less than 20 mm.

17. **Mehrotra D. et al** suggested a clinical grading of the disease and treatment methods as:

Grade I: Stomatitis, burning sensation in the buccal mucosa and with no detection of fibres. Suggested treatment is abstinence from habit and medicinal management.

Grade II: Symptoms of grade I, palpable fibrous bands, involvement of soft palate and maximal mouth opening of 26 to 35 mm. Suggested treatment is abstinence from habit and medicinal management.

Grade III: Symptoms of grade II, blanched oral mucosa, involvement of tongue and maximal mouth opening of 6 to 25 mm. Suggested treatment is abstinence from habit and surgical management.

Grade IV: Symptoms of grade III, lip fibrosis and mouth opening of 0 to 5 mm. Suggested treatment is abstinence from habit and surgical management.

18. **More C.B. et al** gave the following classification based on clinical and functional parameters as:

I: Clinical staging:

Stage 1 (S1): Stomatitis and/or blanching of oral mucosa.

Stage 2 (S2): Presence of palpable fibrous bands in buccal mucosa and/or oropharynx, with/without stomatitis.

Stage 3 (S3): Presence of palpable fibrous bands in buccal mucosa and/or oropharynx, and in any other parts of oral cavity, with/without stomatitis.

Stage 4 (S4):

A: Any one of the above stage along with other potentially malignant disorders e.g. oral leukoplakia, oral erythroplakia, etc.

B: Any one of the above stage along with oral carcinoma.

II: Functional staging:

M1: Inter-incisal mouth opening up to or greater than 35 mm.

M2: Inter-incisal mouth opening between 25 to 35 mm.

M3: Inter-incisal mouth opening between 15 to 25 mm.

M4: Inter-incisal mouth opening less than 15mm

19. **Kerr A.R. et al** gave the following grading system for OSMF as:

Grade 1: Mild: Any features of the disease triad for OSMF (burning, depapillation, blanching or leathery mucosa) may be reported and inter-incisal opening greater than 35 mm.

Grade 2: Moderate: Above features of OSMF and inter-incisal limitation of opening between 20 to 35 mm.

Grade 3: Severe: Above features of OSF and inter-incisal opening less than 20 mm.

Grade 4A: Above features of OSMF with other potentially malignant disorders on clinical examination.

Grade 4B: Above features of OSMF with any grade of oral epithelial dysplasia on biopsy.

Grade 5: Above features of OSMF with oral squamous cell carcinoma.

20. **Prakash R. et al** assessed the morphologic variants of soft palate by conducting a clinic-radiological study. The authors based on these variants assessed the severity of OSMF to establish it as a basis for staging of OSMF. Six morphologic variants were delineated as follows:

Type 1: Leaf shaped

Type 2: Rat tail shaped

Type 3: Butt shaped

Type 4: Straight line

Type 5: Deformed S

Type 6: Crook shaped

It was observed that type 1 variant was the most common, seen in stage 2 OSMF (based on More C.B. et al classification42) and type 3 variant was common in stage 3 OSMF. The authors concluded that in OSMF, type 1 and 2 are commonly seen but as the diseases advances, these are replaced by type 3 and 6 variants.

21. **PatilS. and Maheshwari S.** suggested a new classification based on cheek flexibility. Here, cheek flexibility was measured as a distance in millimetres, from

maxillary incisal midline to the cheek retractor during retraction. Normal cheek flexibility observed was: Males 35 to 45 mm, Females 30 to 40 mm.

Grade 1 (Early): Cheek flexibility of 30 mm and above.

Grade 2 (Mild): Cheek flexibility between 20 to 30 mm.

Grade 3 (Moderate): Cheek flexibility less than 20 mm.

Grade4 (Severe): Any of the above condition without concurrent presence of potential malignant lesions.

Grade 5 (Advanced): Any of the above condition with concurrent presence of oral carcinoma.

B: CLASSIFICATIONS BASED ON HISTOPATHOLOGICAL ASPECTS OF THE DISEASE: [33]

1. **Pindborg J.J. and Sirsat S.M.**

Very early stage: Finely fibrillar collagen dispersed with marked oedema with plump young fibroblasts containing abundant cytoplasm. Blood vessels are dilated and congested. Inflammatory cells, mainly polymorphonuclear leukocytes with occasional eosinophils are found.

Early stage: Juxta-epithelial area shows early hyalinization. Collagen is still in separate thick bundles. Moderate numbers of plump young fibroblasts are present. With dilated and congested blood vessels. Inflammatory cells are primarily lymphocytes, eosinophils and occasional plasma cells.

Moderately advanced stage: Collagen is moderately hyalinised. Thickened collagen bundles are separated by slight residual oedema. Fibroblastic response is less marked. Blood vessels are either normal or compressed. Inflammatory exudate consists of lymphocytes and plasma cells.

Advanced stage: Collagen is completely hyalinised. A smooth sheet with no separate bundles of collagen is seen. Oedema is absent. Hyalinised area is devoid of fibroblasts. Blood vessels are completely obliterated or narrowed. Inflammatory cells are lymphocytes and plasma cells.

2. **Utsonumiya H. et al** divided OSMF based on the concept of Pindborg J.J. and Sirsat S.M. and modified it as follows:

Early stage: Large number of lymphocytes in the sub epithelial and connective tissue zones along with myxedematous changes.

Intermediate stage: Granulation changes close to the muscle layer and hyalinization appears in sub epithelial zone where blood vessels are compressed by fibrous bundles. Reduced inflammatory cells in sub epithelial layer are seen.

Advanced stage: Inflammatory cell infiltrate hardly seen. Number of blood vessels dramatically less in the sub epithelial zone. Marked fibrous areas with hyaline changes extending from sub epithelial to superficial muscle layers are seen. Atrophic, degenerative changes start in muscle fibres.

3. **Kumar K. et al** graded OSMF as follows:

Grade I: Loose, thick and thin fibres.

Grade II: Loose or thick fibres with partial hyalinisation.

Grade III: Complete hyalinisation.

C: CLASSIFICATIONS BASED ON CLINICAL AND HISTOPATHOLOGICAL ASPECTS OF THE DISEASE:[33]

1.**Khanna J.N. and Andrade N.N.** developed a group classification system to aid in the surgical management of OSMF. It is the most accepted classification by the clinicians.

Group I: Very early cases:

Clinically**:** Common symptom is burning sensation in the mouth, acute ulceration and recurrent stomatitis and not associated with mouth opening limitation.

Histology: Fine fibrillar collagen network interspersed with marked oedema, blood vessels dilated and congested,large aggregate of plump young fibroblasts present with abundant cytoplasm, inflammatory cells mainly consist of polymorphonuclear leukocytes with few eosinophils. The epithelium is normal.

Group II: Early cases

Clinically: Buccal mucosa appears mottled and marble like, widespread sheets of fibrosis palpable, interincisal distance of 26 to 35 mm.

Histology: Juxta-epithelial hyalinization present, collagen present as thickened but separate bundles, blood vessels dilated and congested, young fibroblasts seen in moderate number, inflammatory cells mainly consist of polymorphonuclear leukocytes with few eosinophils and occasional plasma cells, flattening or shortening of epithelial rete-pegs evident with varying degree of keratinization.

Group III: Moderately advanced cases

Clinically: Trismus, interincisal distance of 15 to 25 mm, buccal mucosa appeal's pale firmly attached to underlying tissues, atrophy of vermilion border, vertical

fibrous bands palpable at the soft palate, pterygomandibular raphe and anterior faucial pillars.

Histology: Juxta-epithelial hyalinization present, thickened collagen bundles, residual edema, constricted blood vessels, mature fibroblasts with scanty cytoplasm and spindle-shaped nuclei, inflammatory exudate which consists of lymphocytes and plasma cells, epithelium markedly atrophic with loss of rete pegs, muscle fibres seen with thickened and dense collagen fibres.

Group IVA: Advanced cases

Clinically: Severe trismus, interincisal distance of less than 15 mm, thickened faucial pillars, shrunken uvula, restricted tongue movement, presence of circular band around the entire lip and mouth.

Group IVB: Advanced cases

Clinically: Presence of hyperkeratoticleukoplakia and/or squamous cell carcinoma.

Histology**:** Collagen hyalinised smooth sheet, extensive fibrosis, obliterated mucosal blood vessels, eliminated melanocytes, absent fibroblasts within the hyalinised zones, total loss of epithelial rete pegs, presence of mild to moderate atypia and extensive degeneration of muscle fibres.

The authors are of the view that patients in group I and group II can be managed by symptomatic treatment, whereas those in group III and group IV definitely require surgical management.

CLINICAL FEATURES

AGE GROUP

Majority of the patients diagnosed with OSMF are between the ages 20-40 years. **Anuradha,Priyanka et al in 2009** reported describes a case of OSMF presenting in a young Indian child of 9 years.[34]

Vinay gupta et al in 2009 reported two cases of OSMF in 11-year-old Indian Muslim girl and 10-year-old Indian Muslim boy.[35]

Rohit Mehrotra in 2013 found in their study that OSMF mostly seen in 2nd to 6th decades[36]

SEX

Vijayalaxmi et al in 2014 reported in their review literature that study shows in regional variations in OSMF undertaken in Ernakulam and Pune, 72% of the patients were females in Ernakulam and 46 % in Pune. In a study comprising 44 subjects of Asian origin in UK, the female to male ratio was found to be 4.5:1.[26]

Herman Guild et al in 2016 conducted study on 4000 patients who attended two major tertiary care centers of South Kerala were examined and found that out of the 4000 patients, 2048 (51.2%) were females and 1952 (48.8%) males.[37]

Jazib Nazeer et al in 2017 conducted study on 200 OSMF cases and found that the male to female ratio of OSMF cases was 5:1[38]

SIGN AND SYMPTOM

SIGNS[26]

a) Early Signs

The early signs of the disease are a mild to moderate blanching of the oral tissues. Fibrosis may not be evident, or they may be seen arching from the anterior faucial pillars into the soft palate as a delicate reticulum of interlacing white strands which later become confluent. Slight rigidity may be felt in the oral tissues in the early stages and the bands are diffuse and mild in the early stages. The occurrence of vesicles has been reported in some patients in the early stages of the disease which later form ulcers.

b) Late Signs

Gradually, as the disease progresses the mucosa gets a mottled or marble like appearance where dense pale areas alternate with areas of normal appearing mucosa or areas of melanin pigmentation. Occasionally fiery red areas appear. Appearance of petechiae has been reported in some cases. As the disease progresses, thick fibrous bands appear in the submucosal layer of the oral soft tissues. The fibrous bands run vertically in the buccal mucosae, and horizontally on the soft palate and rima oris. The bands become dense and confluent causing rigidity and stiffness of the oral tissues leading to restricted movement. Deposition of fibrous bands in the cheeks causes flattening of the cheeks. Recurrent ulceration may be present due to repeated trauma to the buccal mucosa from rubbing against buccal surfaces of the teeth. The

fibrosis is usually bilateral. When there is unilateral involvement, fibrosis of pterygomandibular raphe on the affected side may produce mandibular deviation in later stages. Circular bands may be palpable around the lips causing them to appear thin or distorted. The faucial pillars become short, thick and extremely hard. Tonsils become pressed between the pillars and appear blanched. When the soft palate is involved, the bands radiate from the median raphe to the anterior faucial pillars. The voice becomes nasal and the uvula shrunken and bud like, and mobility is restricted. Sometimes fibrosis may spread down to involve the pharynx and pyriform fossa. Fibrosis of the tongue is less advanced than the buccal mucosa or the lip and is associated with reduced mobility of the tongue. Papillary atrophy is present in later stages. The floor of the mouth is blanched and leathery; the gingiva is fibrotic, depigmented and devoid of its normal stippled appearance. A marked reduction has been seen in buccal and lingual vestibular sulci.

Kiran Kumar K et al in 2003 conducted a study on 75 OSMF cases who visited hospital in Chennai from 2000-2013 and found clinical features of OSMF were difficulty in opening the mouth and associated blanched oral mucosa with palpable fibrous bands.[39]

Hazarey V.K. et al in 2007 conducted study on total of 1000 OSMF cases and their clinical findings were reduced mouth opening, altered salivation and taste sensation were found to be significantly more prevalent in women when compared with men.[40]

Ajit Auluck et al in 2008 studied a case of OSMF in 23-year-old man and found the clinical feature including burning sensation in the buccal mucosa while chewing spicy food. His mouth opening was normal. Intraoral examination revealed that his entire oral mucosa was pale, specially the buccal mucosa, which showed areas of erosion and the hard palate, which was completely blanched. His tongue, uvula and soft palate was normal. No fibrotic bands were palpable in the oral cavity.[41]

Anshula, Shital et al in 2013 reported a case of a 14-year-old Indian girl presented with difficulty in mouth opening and burning sensation while eating. On examination, blanching of the oral mucosa with diffuse white pigmented lesion of size 3.5 to 2cm along with melanotic pigmentation was seen on the left buccal mucosa posteriorly. The patient was diagnosed with OSMF.[42]

Asha et al in 2017 reported a case of 35 years with the chief complaint of inability to open mouth, burning sensation on having spicy food, reduced cheek

blowing capacity and tongue protrusion and restricted mouth opening. Marble stone appearance of mucosa was seen. Pale blanched appearance of soft palate, faucial pillars was also observed. Bud shaped uvula was present.[43]

SYMPTOMS

a) Early Symptoms

The early symptoms include burning sensation. The burning sensation is usually present only while eating spicy food. This is accompanied by an increased salivation. Some patients may have an itching sensation as reported by **Bhatt and Dholakia[25]** which is probably due to release of histamine from mast cells.

b) Late Symptoms

As the disease progresses, there is a gradual increase in stiffening of the oral tissues. The patients start experiencing increasing difficulties in chewing, swallowing and speaking and most consistently complain of inability to tolerate even non spicy food.

The deposition of collagen fibers around the minor salivary glands and salivary gland ducts leads to xerostomia in later stages. As the disease progresses there is dysphagia, restricted mouth opening, restriction in tongue protrusion and cheek flexibility.

Patients may rarely complain of nasal regurgitation or nasal intonation to their speech. Defective gustatory function has been reported in these patients, which may be due to reduced contact surface of the tongue mucosa while chewing, atrophy of taste buds, or perineural fibrosis. There may be earache and relative loss of auditory acuity due to stenosis of the opening of the Eustachian tube.[26]

HISTOPATHOLOGY

An evaluation of the epithelial changes in the different grades of OSMF shows that increase in the clinical severity of the disease may be accompanied by epithelial hyperplasia or atrophy, which is associated with an increased tendency for keratinizing metaplasia. The epithelial atrophy reports by **Pindborg** and associates is one of the marked changes in OSMF, which contrasts with the predominantly hyperplastic epithelium reported by **Sirsat & Khanolkar** and by **Wahi and associates**. This disparity may be due to the selection of cases and also to the sites of biopsy in the various studies. **Wahi et al** correlated the type of keratinizing

metaplasia with the site of the lesion and the habits of the patients. Lesions involving the palate showed predominantly orthokeratosis and those of the buccal mucosa, parakeratosis. The high mitotic count in parakeratotic epithelia, which is more common with OSMF, and the association with parakeratotic leukoplakia predispose to carcinoma. A useful histological grading in conjunction with the clinical progression of the disease was proposed by **Pindborg et al.** it is still not clear whether the epithelial atrophy, as reported by various workers, is the aftermath of heavy fibrosis in the underlying connective tissue or is a result of malnutrition. Atleast a few hold the view that the epithelium has become stretched and thinned by the changes in the underlying connective tissue. Whatever the cause, it has been stated that atrophic changes in the mucosa predispose to malignant changes in the epithelium.[44]

Histological changes in cases of OSMF can be dealt with under following headings:

1. Changes in the epithelium.

2. Changes in subepithelial tissue.

1. Changes in the Epithelium

The epithelial changes in oral submucous fibrosis have been variously described by different authors as normalepithelium with flattening of the retepegs; acanthosis and parakeratosis; marked thickening and acanthosis; hypertrophicepithelium with occasional areas of atrophy and liquefaction of the basal layer; normal but somewhat atrophicepitheliumand thickened squamous epithelium with deep invaginations of retepegs into the lamina propria.Increased mitotic activity and coexistent squamous cell carcinoma has also been reported in biopsy specimens.A marked reduction in melanin pigment in the basal cell layers has been seen which apparently has been displaced into theupper part of lamina propria where it accumulates in clumps.[26]

2. Changes in Subepithelial Tissue

A marked epithelial atrophy has been reported by many authors and it is suggested that marked atrophy of the epithelium is probably due to changes in the underlying epithelium namely fibroelastic transformation of the lamina propria, and hyalinised tissue around the blood vessels resulting in reduced nutrition to the epithelium and atrophy.[26]

Four consecutive stages, based upon sections stained with hematoxylin and eosin, have been described in connective tissue in patients with OSMF-

The Very Early Stage

Characterized by a finely fibrillar collagen, dispersed with marked edema. The fibroblastic response is strong, with plump young cells containing abundant cytoplasm. The blood vessels are sometimes normal, but more often they are dilated and congested. Inflammatory cells mainly polymorphonuclear leukocytes with occasional eosinophils are present.[26]

Van Wyk CW et al in 1990 studied a comparison of the electron-microscopic features of 11 examples of submucous fibrosis in its moderately advanced and advanced stages with 15 control specimens revealed no obvious abnormality of the collagen fibrils. The notable feature of the collagen in this disease is the densely packed bundles in the lamina propria, reaching close to the epithelial-connective tissue junction, to blood vessel walls, salivary glands and muscle fibers. The width and the periodicity of fibrils vary in both groups of specimens, noticeably so, next to the junction and close to blood vessels, salivary glands and muscles. This is due to the presence of the thinner Type III collagen fibrils in these sites and the natural variation of Type I fibrils. Immunofluorescent microscopy and special staining with sirius red and polarization microscopy demonstrate both types, confirming that Type I collagen forms the bulk of the collagen and that Type III is localized in the sites mentioned above. It is concluded that although there is an excessive increase of collagen, especially Type I, in submucous fibrosis, the fibrils are still morphologically normal.[27]

The Early Stage

The juxta-epithelial area shows early hyalinization. The collagen is still seen as separate bundles, which are thickened. Plump young fibroblasts are present in moderate numbers. The blood vessels are often dilated and congested. The inflammatory cells are mostly mononuclear lymphocytes, eosinophils, and occasional plasma cells.[26]

The Moderately Advanced Stage

Collagen is moderately hyalinized. The amorphous change starts from the juxta-epithelial basement membrane. Occasionally, thickened collagen bundles are still seen separated by slight residual edema. The fibroblastic response is less marked, the cells present being mostly adult fibrocytes with elongated spindle

shaped nuclei and scanty cytoplasm. Blood vessels are either normal or constricted as a result of increased surrounding tissue. The inflammatory exudate consists of lymphocytes and plasma cells, although occasional eosinophils are seen.[26]

The Advanced Stage

The collagen is completely hyalinized and is seen as a smooth sheet, with no separate bundles discernible. Edema is absent. The hyalinized areas are devoid of fibroblasts, although a thin, elongated cell or vestigial nucleus is seen at rare intervals along the fiber bundle. Blood vessels are completely obliterated or narrowed. The inflammatory cells are lymphocytes and plasma cells. Apart from connective tissue repair process, vascular response due to inflammation has been very commonly found in OSMF. Normal dilated and constricted blood vessels, often in combination, have been observed in the same section. The melanin containing cells in the lamina propria become surrounded by dense collagen, which explains the clinically observable loss of pigment. Metachromatic areas are also observed. A rise in mast cells occurs in the earlier stages of the disease, but in more advanced cases the counts are similar to those seen in normal mucosa or even lesser.[26]

S. Anil et al in 1993 reported a case of OSMF in a 12-year-old girl discusses its etiopathogenesis, clinical features, and histopathological findings of the condition and highlights strong association of areca nut chewing as the potential factor in the etiology of this condition.[45]

Usha Isaac et al in 2008 study was carried out on 35 biopsy specimens from patients presenting Oral Submucous Fibrosis. Histopathological analysis was carried out to confirm the disease and to evaluate the microscopic features of Oral Submucous Fibrosis (OSMF). They found that diffuse nonspecific chronic inflammation with fibrosis was present in all specimens (100%). Classical picture of OSMF was found in 20 (57.4%) of specimens while 16 (45.7%) showed Lichenoid reaction as well. OSMF with ulceration was present in 14 (40%) specimens. Pseudoepitheliomatous hyperplasia was recorded in 9 (25.7%). Dysplastic changes were seen in 3 (8.6%) specimens. This study gives a detailed account of the histological changes along with the frequency of their occurrence and describes a new finding of Lichenoid reaction occurring in OSMF.[46]

Yesha V Jain et al in 2016 aim to study was to devise the staging system which is suggestive of treatment strategies based on the clinical and histopathological staging and they consist 100 OSMF patients categorized into

clinical stages of Andrade and Khanna's staging system and histological grading of Andrade and Khanna's grading system and they conclude that new staging system for OSMF with objective clinical and histopathological criteria which provide guidance for treatment plan.[47]

PRECANCEROUS NATURE AND MALIGNANT TRANSFORMATION

The possible precancerous nature of OSMF was first described by Paymaster in 1956 when he observed slow growing squamous cell carcinoma (SCC) in one third of the cases of OSMF.[26]

The precancerous nature of OSMF was first postulated by **Paymaster JC** who described the development of carcinoma in 1/3 of OSMF cases attending Tata Memorial Hospital, Mumbai. Malignant transformation in OSMF cases has been reported by many workers.[48]

In an observation of biopsy specimens from OSMF patients, **Pindborg** found hyperchromatism, increased mitoticactivity, and shift in nuclear: cytoplasmic ratio. To substantiate the precancerous nature of the condition he listed fivecriteria:

1. High occurrence of oral submucous fibrosis in patients with oral cancer.
2. A higher incidence of oral cancer among patients with oral submucous fibrosis.
3. Histologic diagnosis of oral cancer without any clinical suspicion among oral submucous fibrosis cases.
4. High frequency of epithelial dysplasia.
5. Higher prevalence of leukoplakia among OSMF cases.[26]

M Mcgurk et al in 1984 reported three cases of OSMF, two of which were associated with oral carcinoma and concluded that condition is not as rare amongst Asian immigrants as the small number of reported cases might suggest that early detection and follow up are important because of the risk of neoplasia.[49]

P R Miuty et al in 1985 conducted study on 66 patients with OSMF were followed up for a period of 17 years (median observation 10 years) in Emakulam district Kerala, India. Oral cancer developed in 5 (7.6%) patients, the malignant transformation rate in the same sample was 4.5% over a 15 year observation period (median 8 years). So they found that these findings impart a high degree of malignant potential to this condition.[50]

P S ho et al in 1986 studied on total of 148 male patients with OPMDs in Medical hospital in Kaohsiung, Taiwan. The mean follow up period was 37.8 months. They found that Oral squamous cell carcinoma could be preceded by clinically evident oral potentially malignant disorders (OPMDs). The malignant transformation rate was highest in subjects diagnosed with oral epithelial dysplasia. In this group the transformation rate was 7.62 per 100 persons-year. The rate in the group with verrucous hyperplasia (VH) was 5.21 per 100 persons-year, and in those with hyperkeratosis or epithelial hyperplasia was 3.26 per 100 persons-year. The reported discrepancies of malignant transformation of OPMDs involve the follow-up time to cancer development and hence it is preferable to use a time-to-event estimation for comparison that malignant transformation of OPMDs involving the tongue was significantly higher than in other anatomical subsites after adjusting for the clinicopathological type or lifestyle factors at diagnosis.[51]

Wang et al in 1986 studied on 5071 patients with PMD- epithelial dysplasia with OSMF, epithelial dysplasia with hyperkeratosis/epithelial hyperplasia, hyperkeratosis epithelial hyperplasia, OSMF, Lichen planus and verrucous hyperplasia between 2001 and 2010 for malignant transformation. They found that two hundred nineteen of these 5071 OPMD patients (202 men, 17 women; mean age: 51.25 years; range: 30–81 years) developed oral cancers (179 squamous cell carcinomas; 40 verrucous carcinomas) in the same sites as the initial lesions at least 6 months after their initial biopsies. The overall transformation rate was 4.32% (mean duration of transformation: 33.56 months; range: 6–67 months). Additionally, the mean time of malignant transformation was significantly shorter for lesions with than without epithelial dysplasia. The risk of malignant transformation was 1.89 times higher for epithelially dysplastic than non-dysplastic lesions. The anatomical site of OPMD and the presence of epithelial dysplasia were significantly associated with malignant transformation. The hazard rate ratio was 1.87 times larger for tongue lesions than for buccal lesions. Patients with OPMDs require long-term follow up.[52]

SOFT PALATE ANOMALIES

Clefts of the soft palate in the presence of an intacthard palate exist in a spectrum of anatomic severity,from the *forme fruste* submucous variant to a completeseparation of both sides extending forward to thehorizontal shelves of the palatine bones and finallyinto the palatal shelves of the maxilla. Careful examination of the anatomyof the submucous cleft, as compared with that of thenormal soft

palate, can yield valuable insights into theembryologic defects responsible for this deformity.The developmental field model provides a rationale for surgical approaches to its repair.[53]

The submucous cleft and indeed all other variationsof soft palate clefts share three invariable features:(1) deficiency of the posterior border of thehorizontal palatine shelf proper, causing universalabsence of posterior nasal spine, (2) concomitantdeficiency of the palatine aponeurosis causinganterior foreshortening and anterior displacementof soft palate muscle, and (3) anomalous insertionof levator veli palatini (LVP) into horizontal plate ofthe palatine bone. All three conditions are grosslyabnormal.[53]

KaiWermker,Susanne Jung,Ulrich Joos,and Johannes Kleinheinzin 2012 aimed to evaluate cephalometrically the nasopharyngeal development of patients with complete unilateral cleft lip and palate. Influencing factors were evaluated and cleft to non-cleft subjects were compared to each other. The lateral cephalograms of 66 patients with complete cleft lip and palate were measured and compared retrospectively to the cephalograms of 123 healthy probands. Measurements were derived from a standardized analysis of 56 landmarks. Significant differences between cleft and control group: the cleft patients showed a maxillary retroposition and a reduced maxillary length; the inclination of the maxilla was significantly more posterior and cranial; the anterior nasopharyngeal height was reduced; the nasopharyngeal growth followed a vertical tendency with reduced sagittal dimensions concerning hard and soft tissue. The velum length was reduced. In the cleft group, an accumulation of mandibular retrognathia and an anterior position of the hyoid were observed. Skeletal configuration and type of growth were predominantly vertical.[54]

V Deepa, Chaya M David, BK Ramnarayan in 2013 identified the morphological varieties of the soft palate on a digital lateral cephalogram in the normal individuals with age and gender and also to assess if there exists any morphological variations in the soft palate among cleft palate and obstructive sleep apnea (OSA) groups. A total of 120 normal subjects, 15 cleft palate patients and 15 OSA patients, whose ages ranged from 5 years and above were included. The morphology of the soft palate was classified into six types with an additional ungrouped type. There was a significant increase in the length of soft palate with age. In cleft palate patients, the predominant type of soft palate was type-3 with

shorter velar length, while the predominant type of soft palate in OSA patients was type-1 with the length of the soft palate longer than that of the normal group, no significant difference was observed between males and females with respect to the mean length in normal group, cleft palate group and OSA group.[55]

Kaur S, Rai S, Sinha A, Ranjan V, Mishra D, Panjwani S. in 2015 studied the interaction between craniofacial structures and pharyngeal airway space along with soft palate and tongue in patients withdifferent anteroposterior skeletal patterns using lateral cephalogram. The correlation of upper airway and soft-tissuemeasurements with neck circumference (NC) and body mass index (BMI) was elucidated to evaluate the predictorson lateral cephalogram, in order to determine the etiology of obstructive sleep apnea (OSA)s. Lateral cephalograms of45 subjects were used to measure the pharyngeal airway and were divided into three groups (each group included15 subjects) according to ANB angle: Class I (ANB angle 2°-4°), Class II (ANB angle >4°), and Class III (ANB angle<2°). Velar morphology along with its length was also analyzed and categorized into different types. The NC andBMI of all the patients were also calculated. Student's t-test for paired samples was used to compare the meanvalues of the study variable vital parameters. Significant reduction was found in pharyngeal airway in ANBgroup II. The soft palate and tongue size increased with increasing BMI and NC.[56]

Tanya Khaitan, Arpita Kabiraj, Uday Ginjupally, Ramaswamy P in 2015 discussed that Soft palate (velum) represents the posterior fibro-muscular portion of the palate. Its dimensions and active relations participate in most of the oral functions, particularly in velopharyngeal closure which is associated with the normal functions of sucking, swallowing, respiration, phonation and pronunciation. This also helps to control nasal airflow and any disturbance in this mechanism may cause problems in phonation. Such disorders may include obstructive sleep apnoea,cleft palate,malocclusion and oral submucous fibrosis. The anatomical and radiological correlation of the velum mayaid in the research of the velopharyngeal closure and etiological study of these conditions.[57]

DIAGNOSTIC CRITERIA FOR MORPHOLOGICAL EVALUATION OF SOFT PALATE

The diagnosis in most of the cases is made from the history of repetitive exposure to causative agents, clinical appearance and the texture of tissue. The

presence of palpable fibrous bands in a restricted mouth opening are diagnostic criterion for oral submucous fibrosis further diagnosis and prognosis of OSMF can be established by means of biopsy.[58]

No specific test will confirm a suspected diagnosis of OSMF. **Haider et al**. study stated that velar is the first tissue to be affected in OSMF; there is a need to analyze its morphology in OSMF patients. Merely three such studies are reported in the literature by **Shankar et al., Mohan et al.,** and **Tekchandani et al.** to evaluate the morphological variants of velar in OSMF.[59]

Biopsy is an invasive, time-consuming procedure and causes psychological trauma to some patients. Thus the need of the hour is that the technique for evaluation the soft palate ought to be simple, less invasive, less time consuming, easy to interpretation, economical and yet quite confirmatory for the diagnosis and prognosis. So apart from histopathological other diagnostic and prognostic methods such as cephalometric analysis are of great importance.[60]

CEPHALOMETRY:

Lateral cephalometric radiographs are important in growth analysis, diagnosis, treatment planning, therapy monitoring, and evaluation of treatment outcome. Digital dental radiography is used in dental office today for the acquisition, measurement, and analysis of cephalometric images.[61]

A lateral cephalometric radiographs is needed routinely. Lateral cephalograms have two purposes: (1) they reveal details of skeletal and dental relationships that cannot be observed in other ways, and (2) they allow a precise evaluation of response to treatment. In many instances, an adequate orthodontic

diagnosis can be made without a cephalometric radiograph; however, accurate assessment of a patient's response to treatment is practically impossible without comparing cephalometric films before, during and after treatment. For this reason, lateral cephalometric films are needed even for patients whose dental and skeletal relationship seems perfectly straight forward (e.g., class I crowding problems).Treating skeletal malocclusion without cephalometric evaluation is serious error.[62]

Use of Cephalograms

Cephalometrics has established itself as one of the pillars of comprehensive orthodontic diagnosis. It is also a valuable tool in treatment planning and follow up of patients undergoing orthodontic treatment. The following are some of the applications of cephalometrics in orthodontics.

a) Cephalometric help in orthodontic diagnosis by enabling the study of skeletal, dental and soft tissue structures of the cranio-facial region.

b) It helps in classification of the skeletal and dental abnormalities and also helps in establishing facial type.

c) Cephalometrics helps in planning treatment for an individual.

d) It helps in evaluation of the treatment results by quantifying the changes brought about by treatment.

e) Cephalometrics helps in predicting the growth related changes and changes associated with surgical treatment.

f) Cephalometrics is a valuable aid in research work involving the cranio-dentofacial region.[63]

FACTOR AFFECTING CEPHALOMETRIC RADIOGRAPHS:

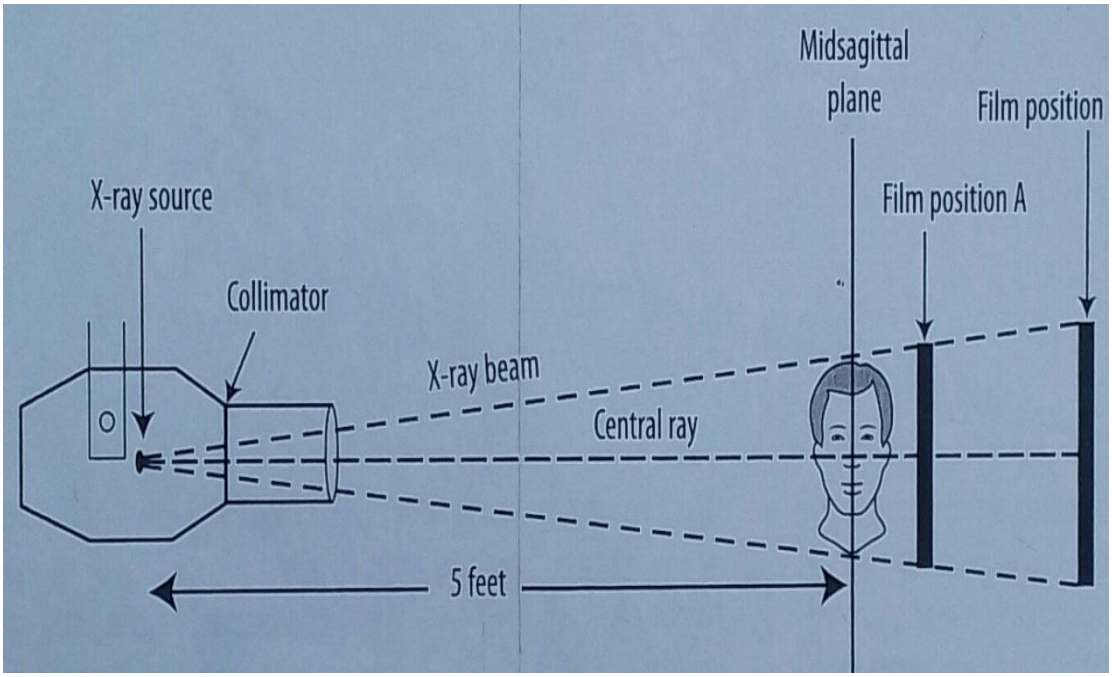
Patient positioning and X-ray tubehead settings are the two most critical factors in consistently producing cephalometric images of high diagnostic quality.

Generally, patients are positioned within the cephalostat using adjustable bilateral ear rods placed within each auditory meatus, usually while the patient is standing. The midsagittal plane of the patient is vertical and perpendicular to the x-ray beam. The patient's Frankfort plane is oriented parallel to the floor. Positioning

for the PA cephalogram is identical to that for the lateral cephalogram except that the patient is rotated 90 degrees, i.e. facing the film.[63]

Radiographic Magnification:

The x-ray emanating from the source have a divergent pattern, there is a variation in the amount of magnification of the object in any radiograph. To reduce the magnification in lateral cephalometric radiographs, one should increase the distance between the source of x-ray and the object to be radiographed in order to take advantage of the central beam, which is flatter, and also decrease the distance between the object and the radiographic film. It is recommended a distance of 152.4 cm between the x-ray source and the sagittal plane, considering that increasing the distance would result in loss of penetration of rays. According to Weens magnification of craniofacial structures varies from almost 0% upto 24% in objects close to the film or objects in the exact center of the rays. This magnification is not constant for all possible sagittal plane of patient. Structures located closer to the film will present lower magnification comparing to those closer to the rays. As mentioned earlier, another variable, considering the magnification factor, would be the distance between the midsagittal plane of the individual and the film. To minimize variations between different patients and obtain consistent measurements in an individual's over time, it is recommended to maintain constant this distance. An average distance of 15 cm is often used; although it would be ideal to position the frame as close to the patient's head as possible to reduce the magnificatio



Photograph 3- Relationship of x-ray source, patient and film for lateral cephalometric radiographs.

PATIENT POSITIONING:[61]

Lateral Cephalometric radiograph

The lateral cephalometric radiograph displays numerous cranial, facial, and oral anatomic structures imaged from the lateral aspect. Additionally, structural points of reference leading to angular and distance measurements may be visualized to assess growth patterns.

The visualization of the structures in the radiographic image is dependent on proper alignment of the x-ray beam and the patient. Proper alignment of the x-ray beam relative to the cephalostat may be evaluated by exposing a test film of the head-stabilizing ear rods without a patient positioned in the cephalostat. Proper alignment is assured if the radiopaque circle representing the film-side ear rod is reasonably centered within the image of the beam-side ear rod. This helps to ensure that the midsagittal plane will be perpendicular to the x-ray beam once the patient is placed within the ear rods.

An 8 x 10- inch film cassette/digital sensor equipped with the appropriate film and intensifying screens is placed either horizontally or vertically in the cephalostat cassette holder. The proper x-ray beam collimator must be selected depending on the film cassette's orientation. The anterior border of the film should be placed so that the soft tissue outline of the nose will be captured on the film image. The patient is then positioned within the cephalostat ear rod, exerting moderate pressure on the external auditory meatus. Excessive horizontal movement of the head within the cephalostat will create variations in beam-object alignment, thus causing inaccurate image analysis and comparison when cephalometric superimpositions are made.

The patient's Frankfort plane is placed parallel to the floor. Some x-ray technicians prefer to place the patient's canthomeatal line upward 10 degree relative to the floor. Either method of placement will result in the patient's occlusal plane being in the proper downward orientations. A locking nasal positioner is then secured against the bridge of the patient's nose to eliminate rotation around the ear rod in the sagittal plane and for future reference in subsequent exposures. As this point the film cassette is moved to the desired distance from the patient's midsagittal plane. The central ray of the x-ray beam will enter and exit the patient near the horizontal axis of the auditory meatus.

The amount of x-ray energy necessary to penetrate certain dense areas of the human skull will, in most cases, “burn out” the soft tissue of the nose, lips, and chin, thus resulting in excessive density in those areas. Imaging the patient’s soft tissue profile without the loss of bony details may be accomplished by attenuating or blocking out some of the beam’s energy with a soft tissue shield. This shield is often a wedge of aluminum placed on the x-ray film cassette so that it primarily covers the area behind the patient’s soft tissue profile. In some machine, a small aluminum attenuator is placed within the x-ray beam inside the tube-head, which has the additional benefits of reducing the radiation dose to the soft tissues and producing a less-distinct wedge image than when the shield is placed in direct contact with the film cassette. Care must always be taken not to reduce the beam energy to the point of obliterating the opaque image of the nasal bone, anterior nasal spine, and the long axis of the maxillary and mandibular incisors located near the shielded area.

Once properly positioned, the patient should be instructed to close to centric position, swallow, and hold the body of the tongue in the posterior area of the soft palate. This will reduce the radiolucent band in the resulting image representing the pharyngeal air space commonly superimposed across the angle of the mandible. The patient should then be instructed to remain still throughout the exposure.

Verma SK, Maheshwari S, Gautam SN, KC Prabhat, Kumar S (2012)[65] reviewedthe Frankfort horizontal is a useful compromise for studying skulls but not for orienting the natural head position (NHP) in the living because it is normally distributed around a true extracranial horizontal. Nonetheless, orthodontists dealing with living subjects, rather than inert crania, have used this Frankfort horizontal faithfully in cephalometry. Because the cant or inclination of all intracranial reference lines is subjected to biologic variation, they are unsuitable for meaningful cephalometric analysis. Registration of head posture in its natural position has the advantage that an extracranial vertical or a horizontal perpendicular to that vertical can be used as reference line for cephalometric analysis.

Shetty D, Bagga DK, Goyal S, Sharma P (2013)[66]studied on a cephalometric study of various horizontal reference planes in natural head position. For the present study, 100 subjects (50 males and 50 females) were selected between the age group of 17-25 years having pleasing profile with competent lips with angles class I molar relationship and normal overjet and overbite with no history of taking

any form of orthodontic treatment. The study concluded that among all the reference plane studied, the Frankfort horizontal plane was closest to the true horizontal and thus could be recommended as a reference plane, when radiographs were not recorded in natural head position.

DIGITAL IMAGING TECHNOLOGY:

Technical advances in computer science have made it possible to perform cephalometric tracing both through the use of digitizers and directly on screen-displayed digital images. First-generation computer-based analysis systems used digitizer pads for tracing conventional cephalometric films and software programs to compute the measurements, whereas second-generation systems use scanners or digital cameras to export cephalometric images to measurement programs. Recently, third-generation systems have been introduced that transmit digital radiographs directly to a computer database through the use of photostimulable phosphor plates, charge-coupled device receptors, or direct digital systems. The use of direct digital images offers several advantages, such as instant image acquisition, reduction of radiation dose, facilitated image enhancement and archiving, elimination of technique-sensitive developing processes, and facilitated image sharing.Both digital radiography and conversion of conventional analogue film to a digital format require less storage space than conventional cephalometric film. Digital archiving is also a valuable method for overcoming the problem of film deterioration, which has been a major source of information loss in craniofacial biology. Several drawbacks such as the inability to perform structural superimposition and the need for a digital cephalometric radiographic machine and a software program are also present.[67]With the rapid evolution of computer radiography, digital tracing has slowly replaced the manual tracing methods. Three techniques are commonly reported:8 the first uses digitizer pads for tracing conventional cephalometric films and software programs to compute the measurements; the second uses scanners or digital cameras to export cephalometric images to measurement programs; and the third transmits digital radiographs directly to a computer database. The use of both digital radiography and conversion of manual film to a digital format offers several advantages—it is easy to use, allows several analyses to be performed at a time, promises convenience when generating treatment predictions, takes up less storage space, allows superimposition of images, provides the option to manipulate the size and contrast of the image and

provides the ability to archive and improve access to images to overcome the problem of film deterioration, which has been a major source of information loss in craniofacial biology. Moreover, patients benefit from reduced radiation dose and elimination of chemicals and associated environmental hazards if a direct digital cephalograph is used for image capture. However, several drawbacks are also present, such as difficulty in landmark identification related to the 2D representation of a 3D structure, superimposition of bilateral structures and the need for a digital cephalometric radiographic machine as well as a software program. Furthermore, the quality of digital images is affected by their resolution, pixel size, shades of grey (bit) and compression format.[68] For digital cephalometry to be a better tool in clinical orthodontics, the cephalometric analysis, represented by widely used linear and angular measurements, must be as a comparable and reliable as it is on a conventional radiographic film.[69]

FACTORS AFFECTING DIGITAL IMAGE QUALITY:

Image quality is affected by a number of factors, beginning with the acquisition process and device and including the manner in which images are displayed. In digital systems, the functions of acquisition and display are clearly separable, so that the evaluation and optimization of image quality can take place at both ends of this imaging continuum. The analysis of image quality also depends on the particular type of imaging task. Digital radiography is used in a wide variety of imaging tasks (eg, chest, musculoskeletal), but there are basic image-quality parameters that can be defined that are applicable to all of these tasks.[70]

Matrix Size and Display Size

Soft-copy displays should render images with sufficient pixel density to allow viewing of the whole image with sufficient spatial detail at a normal viewing distance of approximately 30 to 60 cm (with eyeglasses specifically selected for this distance when required). Matrix size should be as close to the for-processing image data as possible or attainable with magnification. A 5-megapixel (MP) (2,048 x 2,560 pixels) monitor (usually in portrait mode with a diagonal dimension of 54 cm [21 in]) exceeds the matrix size stipulated by the ACR's standard of a resolution of at least 2.5 lp/mm at the detector plane when acquiring a 35 x 43 cm image (equivalent to 14 x 17 in), and thus is sufficient for viewing all types of computed radiographic

and digital radiographic images in a single view. Note that the US Food and Drug Administration recommends that only monitors that have been approved for digital mammography be used for interpreting digital mammography images. A 1-MP (1,024 x 1,280 pixels), 2-MP (1,200 x 1,600 pixels), or 3-MP (1,536 x 2,048 pixels) monitor will not permit full simultaneous viewing of 35 x 43 cm images at a detector plane resolution of 2.5 lp/mm. For those images, zooming and roaming display functions are required to achieve a correspondence between the detector element matrix and the display pixel matrix so that the resolution of the display monitor does not limit the resolution of the partially displayed image. This is true for any size image for which the detector element matrix size exceeds the display pixel matrix size.[70]

Luminance and Contrast

The luminance of a display can affect image quality significantly, so the appropriate range of luminance should be maintained. The ratio of maximum luminance to minimum luminance of a display device for images (other than for mammography) should be at least 100. The maximum luminance of gray-scale monitors used for viewing digital conventional radiographs should be at least 200 cd/m^2. Smaller ranges could lead to inadequate levels of contrast in displayed images, and larger values could lead to poor visualization of details at the extremes of the luminance range because of the limited range of the contrast sensitivity of the human eye. The contribution of ambient light reflected from the display surface should be included in luminance measurement considerations, because some level of ambient light is always present. Luminance should be as uniform as possible across the entire display. The contrast response of a display should comply with the AAPM Task Group 18 recommendations. A high display contrast ratio with a low minimum luminance level (0.5 cd/m^2) is most desirable. Contrast response should not deviate from the DICOM Gray scale Standard Display Function (GSDF) contrast values by more than 10%.[70]

Bit Depth

It is necessary for a soft-copy display device to render image details with sufficient luminance quantification to prevent the loss of contrast details or the appearance of contour artefacts. Thus, a minimum of 8-bit luminance resolution (bit

depth) is required. Nine-bit resolution or higher is recommended if the for-processing image data are greater than 8-bit. In general, the higher the luminance ratio of the display, the larger the bit-depth resolution that is recommended.[70]

Display Calibration

All monitors and corresponding video graphics cards used for primary diagnosis or for image adjustment and evaluation (e.g., a technologist review monitor) must provide a means to be calibrated to and conform to the current DICOM GSDF perceptual linearization methods.

The intent of the DICOM GSDF is to allow images transferred using the DICOM standard to be displayed on any DICOM-compatible display device with a consistent gray-scale appearance. Additional factors to consider when characterizing a soft-copy display for interpreting medical images include the modulation transfer function and noise. The modulation transfer function at the Nyquist frequency of the display should be greater than 35%, as recommended by the AAPM Task Group 18 documents. A display device also should not add more than a third of the noise of a typical image, limiting the display relative noise to 0.6% to 0.8%. Desirable display calibration features include remote performance monitoring, calibration, and quality control. Monitor set matching of contrast ratio, brightness, and color are generally accomplished with the DICOM GSDF, although color does not have a standard calibration method to date.[70]

Glare and Reflections

Veiling glare or the spread of light within the display can reduce contrast, so the glare ratio should be greater than 400 for primary displays. Reflections from ambient light sources should be kept at a minimum. Indirect and backlight incandescent lights with dimmer switches rather than fluorescent lights are recommended. Light-colored clothing and laboratory coats can increase reflections and glare. The intrinsic minimum luminance of a device should not be smaller than the ambient luminance (minimum luminance should be at least 2.5 times ambient light). Cathode ray tube (CRT) displays typically have antiglare coatings that can help reduce these effects, but not eliminate them. Protective shields on liquid crystal displays (LCDs) add to reflections and should not be used if possible.[70]

Colour Tint and Colour Displays

Both monochrome and colour displays have a colour tint that is a function of where the manufacturer sets the white point. The tint of the display can affect the comfort of the user. The color tint of the display (blue, gray, yellow, etc.) is based on user preference but should be uniform across the display area, and monitor pairs should be matched from the same manufacturing batch. Currently, most colour displays have lower luminance and thus lower contrast ratios than monochrome displays and are generally not recommended for viewing certain radiographic modalities (chest, bone, and mammography). There are currently no accepted standards or guidelines available for calibrating color displays when viewing gray-scale radiographic images, so care should be taken. The DICOM GSDF can be applied to color displays but does not fully address this issue of calibration of color displays.[70]

TRACING TECHNIQUE:

Before any attempts are made to trace a cephalometric head film, the clinician should become thoroughly familiar with the gross anatomy of the head, in particular the bony components of the cranium and face. Access to a dry skull also is helpful initially as an aid in identifying the various bony landmarks.

It is important to recognize that a two-dimensional cephalogram represents a three-dimensional object and that bilateral structures are projected onto the film. The clinician should be able to distinguish bilateral structures and trace them independently because, in most instances, left-to-right outlines will not be perfectly superimposed due to facial asymmetry, greater magnification in the image on the side of the skull farthest from the film, and imperfect positioning of the patient in the cephalostat.

By convention, bilateral structures (e.g., the rami and inferior borders of the mandible) are first traced independently. A broken line is then drawn by visual approximation to represent the average of these lines.

All bilateral landmarks that are present are located on the “average” outline of a specific bone such as the mandible.[61]

General Considerations for tracing:

Start by placing the cephalogram on the view box with the patient’s image facing to the right. (By convention, the lateral head plate faces right for most

orthodontic analyses) Tape the four corners of the radiographs to the view box. With a fine felt-tipped black pen, draw three crosses on the radiograph, two within the cranium and one over the area of the cervical vertebrae. These registration crosses allow for reorienting the acetate tracing on the film for later verification or in the event the film becomes displaced during the tracing procedure, a not infrequent occurrence. Next, place the matte acetate film over the radiographs and tape it securely to the radiograph and the view box. (The shiny side of the acetate film is placed down, against the radiograph.) After firmly affixing the acetate film, trace the three registration crosses. Print the patient's name, record number, age in years and months, the date the cephalogram was taken, and your name in the bottom left-hand corner of the acetate tracing. Use smooth continuous pressure on the pencil; whenever possible, trace image lines without stopping and/or lifting the pencil from the acetate film. Avoid erasures. Consult dental casts when outlining molar and incisor teeth, taking care to depict left and right teeth.

The faint shadow lines in the outline of the soft tissue profile (e.g., anterior nasal spine, nasion) can be more readily visualized by masking the light, radiopaque areas of the radiograph with one or more sheets of black cardboard paper.

For certain applications such as serial or post treatment studies, it is helpful to trace as much anatomy as possible in the areas of the skull base, palate, and mandible (including, when visible, the mandibular canal) to provide a better basis for super positioning serial radiographs.[61]

Paixao MB, Sobral MC, Vogel CJ, Telma Araujo T.M.D (2010)[71]studied on comparative study between manual and digital cephalometric tracing using Dolphin imaging software with lateral radiographs. The study sample consisted of 50 lateral cephalometric radiographs. One properly calibrated examiner performed 50 manual and 50 digital cephalometric tracing using eight angular measurements [FMA, IMPA, SNA, SNB, ANB, 1.NA, 1.NB, Y-Axis] and six linear measurements [1-NA, 1-NB, Co-Gn, Co-A, E Line –Lower lip and LAFH]. Results were assessed using student's t-test. The results showed no statistically significant differences in any of the assessed measurements ($p > 0.05$).

Agarwal N, Bagga DK, Sharma P (2011)[69]took up a comparative study of cephalometric measurements with digital versus manual methods. The study include

digital photographs of 32 cephalograms were imported into the Nemotec digital imaging software. Digital measurements of 41 hard and soft tissue variables generated by the software were compared to those obtained by manual tracings. Reproducibility for each method was assessed using pearson's correlation coefficients by repeating measurements of all radiographs at an interval of 3 months. A paired t-test was used to detect differences between the manual and digital method. The study showed digital measurements obtained with the Nemotec digital imaging software using digital photographs of analogs cephalograms were found to be reproducible and comparable to the manual method for most of the variables used in clinical practice except a few which could not be measured accurately with the digital method.

Ghoneima A, Albarakati S, Baysal A, Uysal T and Kula K (2012)[72]conducted a study on Measurements from conventional, digital and CT-derived cephalograms. The study sample consisted lateral cephalometric radiographs of 30 patients were manually traced. The radiographs were subsequently scanned and traced using Dolphin imaging software 11. The CT- created lateral cephalograms were also traced using the same software. Sixteen (10 angular and 6 linear) measurements were performed. Cephalometric measurements obtained from conventional, digital and CT- created cephalograms were statistically compared using repeated measures analysis of variance (ANOVA). The study showed there are statistically- significant differences in measurements produced using a traditional manual analysis, a direct digital analysis or a 3D CT-derived cephalometric analysis of orthodontic patients. These differences are, on average, small but because of individual variation, may be of considerable clinical significance in some patients.

Navarro RDL, Oltramari-navarro PVP, Fernandes TMF, et al.[73] **(2013)** studied on comparison of manual, digital and lateral CBCT cephalometric analyses. The study material consist of conventional pretreatment lateral cephalograms and cone beam computed tomography (CBCT) scans from 50 subjects from a radiological clinic were selected in order to test the three method: manual tracing (MT), digitized lateral cephalograms (DLC), and lateral cephalograms from CBCT (LC- CBCT). The lateral cephalograms were manually analyzed through the Dolphin imaging 11.0 software. Twenty measurements were performed under the same conditions, and retraced after a 30-days period. Paired t- tests and the Dahlberg

formula were used to evaluate the intra-examiner errors. The pearson's correlation coefficient and one-way analysis of variance (ANOVA) tests were used to compare the differences between the methods. The result showed that all evaluated methodologies are reliable and valid for scientific research, however, the method used in the lateral cephalograms from the CBCT proved the most reliable.

Mahto RK, kharbanda OP, Duggal R, Sardana HK (2016)[74]took up comparison of cephalometric measurements obtained from two computerized cephalmetric software's with manual tracing. The study sample consisted 50 pretreatment lateral cephalgrams were selected from the archives of a postgraduate orthodontic clinic. The digital images of each cephalogram were imported directly into softwares Dolphin and AutoCEPH for onscreen digitization. While for manual tracing digital images were printed using a compatible x-ray printer. After images were standardized and calibrated 34 commonly used anatomical landmarks were plotted on each cephalogram. These landmarks were then utilized to evaluate 35 cephalometric parameters. Intraclass correlation coefficient (ICC) was used to determine both intrarater reliability for repeated measurements and agreements between linear and angular measurements obtained from all parameters while comparing three methods, i.e., manual tracing versus AutoCEPH, manual tracing versus Dolphin and AutoCEPH versus Dolphin. The study concluded that a high level of agreement (ICC<0.9) for cephalometric measurements was obtained from both the computerized software Dolphin and AutoCEPH in comparison with manual tracing.

Identification of cephalometric Landmarks[61]

First, the most common cephalometric landmarks must be defined

ANS: Anterior nasal spine. The anterior tip of the sharp bony process of the maxilla at the lower margin of the anterior nasal opening.

Ar: Articulare. A point at the junction of the posterior border of the ramus and the inferior border of the posterior cranial base (occipital bone)

Ba: Basion. The lowest point on the anterior rim of the foramen magnum.

Bo: Bolton point. The intersection of the outline of the occipital condyle and the foramen magnum at the highest point on the notch posterior to the occipital condyle.

Go: Gonion. A point on the curvature of the angle of the mandible located by bisecting the angle formed by lines tangent to the posterior ramus and the inferior border of the mandible.

Gn: Gnathion. A point located by taking by taking the midpoint between the anterior (pogonion) and inferior (menton) points of the bony chin.

Me: Menton. The lowest point on the symphyseal shadow of the mandible seen on the lateral cephalogram.

N: Nasion. The most anterior part on the frontonasal suture in the midsagittal plane.

Or: Orbitale. The lowest point on the inferior rim of the orbit.

PNS: Posterior nasal spine. The posterior spine of the palatine bone constituting the hard palate.

Pog : Pogonion. The most anterior point on the chin.

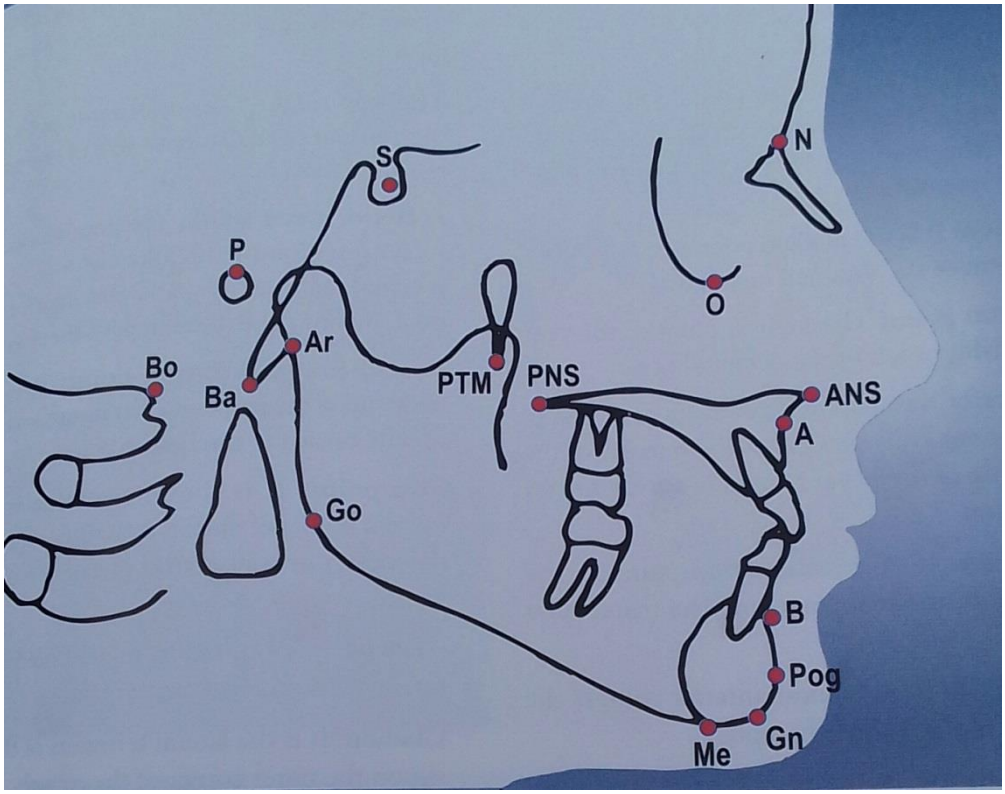
Po: Porion. The most superiorly positioned point of the external auditory meatus located by using the ear rods of the cephalostat (mechanical Po)

Point A: Subspinale. The most posterior midline point in the concavity between the ANS and the prosthion (the most inferior point on the alveolar bone overlying the maxillary incisors)

Point B: Supramentale. The most posterior midline point in the concavity of the mandible between the most superior point on the alveolar bone overlying the mandibular incisors (infradentale) and Pog.

PTM: Pterygomaxillare. The contour of the pterygomaxillary fissure formed anteriorly by the retromolar tuberosity of the maxilla and posteriorly by the anterior curve of the pterygoid process of the sphenoid bone. The lowest point of the opening is used.

S: Sella. The geometric center of the pituitary fossa.



Photograph-4 : Cephalometric Landmarks

CLINICAL REVIEWS

BN Praveen, Sunita Amrutesh,Sumona Pal, Shubhasini AR, Syed Vaseemuddin. in 2011[75] aimed to investigate various shapes of soft palate in normal individuals. The study comprised of 80 individuals requiring orthodontic treatment but without any speech abnormality, whose age ranged from 9 to 31 years. Velar shape was examined on digital lateral cephalograms and was allocated to one of the six patterns as described by You M et al. The difference in proportion of each type and also difference between genders were studied. The normal soft palate can be classified into six types based on its shape. Type 2—rat-tail shape is most common in both the genders. There is no significant difference in proportion of various shapes of soft palate between genders.

D. Kalyan Kumar, DR. K. Saraswathi Gopal. in 2011[76]investigated the variation of the velar morphology. In this study, the sample comprised 100 normal subjects whose ages ranged from 15–35 years. The morphology of the soft palate on lateral cephalometry were examined and classified into six types. The variation of the soft palate between gender groups were also studied. The morphology of the soft palate were classified into six types. There was a significant difference in the morphology of soft palate and also between male and female groups in proportion to velar type.

Mohan RS, Verma S, Singh U, Agarwal N. in 2014[77]evaluated the morphological variants of soft palate in oral submucous fibrosis (OSMF) patients using digital lateral cephalometry. A total number of 100 patients who were a part of this study were divided in two equal Groups. Group 1 comprised of 50 patients clinically diagnosed with OSMF and Group 2 included 50 routine patients. Six different morphological variants of soft palate were found. Among the study Groups, type 1soft palate was most commonly seen (56%) whereas type 5 was the least common variant. Majority of patients belonged to stage II OSMF and type 1soft palate was commonly seen in this stage of disease whereas butt shaped soft palate (type 3) was more common in stage III OSMF. In OSMF, type 1 and 2 are commonly seen but as the diseases advances, these are replaced by type 3 and 6 variants. In OSMF patients, there in reduction in the anterio-posterior dimension of soft palate.

Shankar V.N., Hegde K., Ashwini N.S., Praveena V. in 2014[78] conducted study to evaluate the morphology of soft palate in Oral Submucous Fibrosis (OSF) patients using digital lateral cephalogram. A total number of 70 patients were included in the study (Control group had 35 patients and Study group had 35 OSF patients) were evaluated for soft palate by digital lateral cephalogram. The anterio-posterior length and superio-inferior length of soft palate were measured. The morphology of soft palate was categorized as type 1, to type 6. Different types of soft palate were compared with stages of OSF. Among the Study group (35 patients) 62.9% had Stage 2 OSF. Leaf shaped (Type 1) soft palate was seen commonly in stage 2 OSF whereas butt shaped (Type 3) in stage 3 OSF. In the present study there was statistically significant difference in length (anterio-posterior) of Type 1 soft palate of OSF patients. In the present study as the OSF progressed to advanced stage there was gradual change from Type 1 and Type 2 variety of Soft palate to Type 3

and Type 6 variety of soft palate. The study observed that there was gradual reduction in the length of soft palate in anterior-posterior direction in OSF patients.

Khaitan T, Pachigolla R, Uday G, Balmuri PK, Chennoju SK, Pattipati S. in 2015[5]conducted study to investigate the variation in the morphology of the soft palate. A total of 200 patients belonging to both the genders, in the age group 5-55 years, were selected from the outpatients visiting the Department of Oral Medicine and Radiology. All the study samples were subjected to lateral cephalogram and the morphology of the soft palate was categorized as described by You *et al*. Any additional finding was further differentiated as type 7 and so on. The length of soft palate was also evaluated using Sidexis next generation software. The data obtained were tabulated and subjected to statistical analysis. The morphology of soft palate was categorized into eight types. Type 1 was the commonest type observed. The relationship between the different types of soft palate in various age groups was found to be non-significant. The mean length of the soft palate was found to be more in group V (46-55 years). The mean length of soft palate was found to be higher in males. There was a positive correlation between age and type of soft palate. The present study was done to investigate the variation in the morphology of the soft palate.

Tekchandani V, Thakur M, Paive D, Mohale D, Gupta R in 2015[79]conducted study to evaluate and correlate the morphology of soft palate in Oral submucous fibrosis (OSMF) patients to the clinical and histopathologic grade, using digital lateral cephalogram. A total of 80 patients (40 OSMF and 40 Control) were evaluated for soft palatal morphology. The antero-posterior and supero-inferior dimensions of soft palate were measured on digital lateral cephalogram, categorized as Type 1 to Type 6 and were then compared to clinical and histopathologic grade. In this study, Type 1 (leaf-shaped) soft palate was found to be the most common followed by Type 6 (crook-shaped) and Type 3 (butt-like) varieties. The study observed that there was gradual reduction in antero-posterior length of soft palate in OSMF patients and with advancing OSMF, an increasing incidence of Type 6 soft palate was seen**.**

Deshmukh RA, Bagewadi AS. in 2015[60] evaluated and compare the morphology of soft palate in individuals with and without OSMF, using digital lateral cephalogram. Sixty male individuals were selected and divided into three groups, Group I-20 individuals (habit group), Group II-20 individuals (OSMF

group), and Group III-20 individuals (individuals with no habit and/or OSMF group). The morphology of soft palate was assessed using digital lateral cephalogram. Statistical analysis was carried out using Scheffe multiple comparison test. The superoinferior dimension of soft palate was increased with statistically significant difference in the habit and OSMF groups. The anteroposterior dimension was reduced in the habit group as compared to normal individuals, with statistically significant difference in the OSMF group. The type of soft palate more common in normal individuals and habit group was type 1 and 2, while type 6 was seen more commonly in OSMF group.

Santosh VK, Singh P, Pagare SS. in 2015[80]aimed to investigate the variations in the velar morphology and to analyze the variations of length and density of the soft palate. In this study, a sample of 100 normal digital lateral cephalograms was analyzed for the variations in morphology of the soft palate and evaluated for analysis of length and density of the soft palate. The morphology of the soft palate showed seven different morphological types. There was a significant difference in length of the soft palate between preadult and adult age groups. Males showed significantly longer and denser soft palate than the females.

Chintamaneni Raja Lakshmi, Dharmavaram Ayesha Thabusum, and Sujana Mulk Bhavana in 2016[81]aimed to evaluate the morphology of soft palate in normal individuals and OSMF patients using lateral cephalometry and to compare and correlate these variants of soft palate with different stages of OSMF. 100 subjects were included in the study, who were divided into two groups. Group I included 50 subjects with clinical diagnosis of OSMF and Group II included 50 normal subjects (control group). Using digital lateral cephalometry, velar length and width were measured and soft palatal patterns were categorized based on You et al.'s classification. Leaf and rat-tail patterns of soft palate were predominant in control group, whereas butt and crook shaped variants were more in study group. Anteroposterior (A-P) length of soft palate was significantly greater in stage I OSMF, while superoinferior (S-I) width was greater in stage III OSMF. Interestingly, a negative correlation was observed in staging of OSMF and A-P dimensions. As the staging of OSMF advances, the A-P length of soft palate decreases, but S-I width increases.

Tejavathi Nagaraj, Rahul Dev Goswami, Leena James, N. Sreelakshmi, Bhavana T. Veerabasavaiah, R. Shruthi in 2016[82]aimed to assess the shape of the

soft palate in normal individuals, classify the soft palate and investigate the differences in the size and shape of velar morphology in both the genders and age groups. The study was conducted using 200 lateral cephalograms which were taken with digital orthophos XG machine. Radiographs were collected and soft palate morphologies were analyzed using Sirona software. Soft palate length and thickness were also calculated. Increase in soft palate length was observed till the age of 30 years and showed a decrease thereafter. Velar width was more in males and showed variation in different age groups. Three additional morphological variants of soft palate were found. The soft palate length and width was significantly higher in males than females.

Ashwini Nerkar, Rajeev Gadgil, Ajay Bhoosreddy, Chetan Bhadage, Priyanka Vedpathak in 2017[83]investigated morphometric variation of the soft palate on lateral cephalogram in different stages of Oral submucous fibrosis. The radiographic velum length, velum width, angle/inclination of velum and pharnygeal depth divided by velum length giving Need's ratio in different morphological types of soft palate and different stages of OSMF and to determine correlation of all metric parameters with respect to staging of OSMF. Also, correlation of staging of OSMF with respect to different types of soft palate was evaluated. Lateral cephalographs of 80 cases with age range 18-45years irrespective of gender were evaluated. Soft palatal patterns were categorized based on You et al. et al's classification & staging of OSMF was done according to Kiran Kumar et al's classification. Total 80 cases were divided into two groups such as Group A (OSMF = 40) and Group B (Control =40). The length, width, angle of inclination and need's ratio was evaluated in each type of soft palate. Mann-Whitney est. and Kruskal Wallis test was used for statistical analysis. Results: The mean age of the 80 cases was 40.5years. The highest incidence of soft palate seen in group A and B was type 1, whereas the lowest incidence was type 5 in Group A and type 6 in Group B. The mean and Standard deviation of length, width, angle of inclination and need's ratio in group A was 22.43 + 0.76, 23.91 + 0.94, 127.72° + 1.21 and 0.8+ 0.57 respectively and that of control group was 24.47 + 1.10, 21.60 + 0.58, 131.6° + 0.75 and 0.63+ 0.97 respectively. Stage 1 OSMF subjects had maximum type 2 soft palate (4%), Stage 2 had type 1 (45%) and stage 3 had type 6 (5%). With OSMF staging advancement, length and angle of inclination of soft palate shows negative, whereas width and the need's ratio shows positive correlation.

Patil BM, Ara SA, Katti G, Ashraf S, Roohi U. in 2017[84]evaluated the morphological variations of soft palate in OSMF patients using digital lateral cephalogram and the morphological variations of soft palate with respect to the different clinical stages of OSMF patients. A total number of 300 patients were included in the study (150 participants each in study and control group), evaluated clinically, and subjected for digital lateral cephalogram for evaluating velar morphological variants. The data were statistically evaluated using SPSS 11.5 software with Student's t-test, Chi-square test, and ANOVA. Among Group I, 34 participants had Stage I OSMF, 90 participants had Stage II OSMF, and 26 participants had Stage III OSMF. Type I velar was commonly seen in Stage I OSMF, Type VI velar in Stage II OSMF, and Type III velar in Stage III OSMF. There was statistically highly significant decrease in anterior-posterior (AP) length and increase in width of superior-inferior (SI) measurement, as compared to the Group II. There was diminution in AP length and increase in SI measurement as the OSMF disease progressed.

MATERIALS AND METHODS

The presentstudy was conducted in Department of Oral Medicine and Radiology of BabuBanarasi Das College of Dental Sciences, Lucknow (UP). Ethical clearance for the study was obtained from the institutional ethical committee.

The study population was drawn from the patients attending the outpatient Department of Oral Medicine and Radiology. The study sample consisted of 100 patients, which is divided into 2 groups. Group A consist of 50 subjects with clinically diagnosed OSMF and Group B consist of 50 healthy subjects. All the patients were subjected to cephalometric radiographs.

MATERIALS AND EQUIPMENTS USED

1. Dental chair with illuminating facility.
2. A pair of sterile disposable gloves and mouth mask.
3. Stainless steel kidney tray, mouth mirror, straight probe, tweezers and explorer.
4. Sterile gauze piece and cotton swab
5. Digital Vernier caliper

INCLUSION CRITERIA

- Subjects who are well oriented to time, place and person.
- Subjects of either sex aged between 18-55 yrs.
- Subjects with positive history of chewing areca nut or one of its commercial preparations.
- Subjects with clinical features based on Nagesh&Bailoor (1993) classification.

EXCLUSION CRITERIA

- Subjects who have undergone any treatment for Oral submucous fibrosis (OSMF).
- Subjects suffering from any systemic disease.
- Subjects with known history of surgery of palate, cleft lip and palate, scleroderma patients.

- Subjects failing to give their consent

EXAMINATION OF THE PATIENT

The study subjects were made to sit comfortably on dental chair. Patients were examined under artificial illumination. The clinical examination was carried out following the methods described by **Kerr, Ash & Millard[85], SR Prabhu**and **Shafers[3].** A complete personal history was recorded in a predesigned format. Special reference was given to the frequency and duration of habits of betel quid, tobacco and pan/pan masala chewing and smoking. Each patient was informed about the protocol and was given appropriate instructions after obtaining a written consent.

MOUTH OPENING

Mouth opening was assessed by measuring the interincisal distance from the mesioincisal edge of the upper left central incisor tooth to the mesioincisal edge of the lower left central incisor tooth. The measurement was made using a digital vernier caliper and was recorded in millimeters.

BURNING SENSATION

The intensity of burning sensation was determined using a Visual Analogue Scale (VAS) of 0-100, where 0 is no burning sensation and 100 is the worst possible burning sensation. All the relevant data was entered in the case history proforma.

All the patients who were selected for the study were randomly divided into two groups-

Group A–50 OSMF patients

Group B –50 normal individuals

All the enrolled subjects were evaluated for burning sensation and intolerance to spices using a Visual Analouge scale (VAS) and then subjected for digital cephalometric radiographs.All the standard protocol for radiation protection was followed.

- Digital Lateral Cephalometric machine

[PlanmecaProline XC, SN: XC430638, 180-240V, 50 Hz, 68KVp, 5mA]Installed in AERB (Atomic Energy Radiation Board) certified quality assurance facility.

- PlanmecaRomexis 2.9.2.R software

- Participants were positioned in the cephalostat with Frankfurt horizontal plane parallel to the floor. With upper and lower teeth in centric occlusion, with oropharyngeal musculature relaxed, digital lateral cephalogram was shot.
- Antero-posterior and supero-inferior dimensions as well as morphology of soft palate were analyzed from the cephalograms.
- The length of the soft palate i.e. antero-posterior dimension was evaluated by measuring the linear distance from the posterior nasal spine (PNS) to the tip of the uvula of the resting soft palate.
- Supero-inferior dimension of soft palate was measured at the thickest area of soft palate. Morphology of soft palates was classified based on their morphology according to You et al. (2008) as Types: 1 (leaf-shaped), 2 (rat-tail shaped), 3 (butt-like), 4 (straight line), 5 (S-shaped) and 6 (crook shaped).

Following the accomplishment of the diagnosis, each patient were educated about the nature of the condition, its precancerous potential and motivated to discontinue the use of areca nut, tobacco, or any abusive habit in any form.

All the data was tabulated on spread sheets and subjected to stastistical analysis.

STATISTICAL ANALYSIS

The results are presented in frequencies, values, percentages and mean ± SD. Chi-square test and t-test was used to compare the categorical variables. The p-value <0.05 was considered significant. All the analysis was carried out on SPSS 16.0 version (Chicago, Inc., USA).

Formula

- **Mean and standard deviation**

  Thesample mean is the average and is computed as the sum of all the observed outcomes from the sample divided by the total number of events. We use “x” as the symbol for the sample mean. In math terms:-

$$\bar{x} = \frac{\sum x_i}{n}$$

Where “n” is sample size and the “x” corresponds to the observed valued.

We define the ***variance*** to be:-

$$s^2 = \frac{\sum (X - \bar{X})^2}{N - 1}$$

The ***standard deviation (SD)*** is the positive square root of the variance, calculated as:-

$$s = \sqrt{\frac{\sum_{i=1}^{n} (x_i - \bar{x})^2}{n - 1}}$$

n= number of observations

The ***standard error se*** of the difference between the two means is calculated as:

$$se(\bar{x_1} - \bar{x_2}) = s \times \sqrt{\frac{1}{n_1} + \frac{1}{n_2}}$$

- **Chi-square test**

This test is applied to a single categorical value variable from two or more different populations. It is used to determine whether frequency counts are distributed identically across different populations.

$$\chi_c^2 = \sum \frac{(O_i - E_i)^2}{E_i}$$

O=observed frequency

E=expected frequency

- **Paired “t” test**

To compare the change in a parameter at two different time intervals paired “t” test was used.

$$t = \frac{\bar{d}}{\sqrt{s^2/n}}$$

d = mean difference; s = standard deviation; n = number of pairs

- **Student "t" test**

  To test the significance of two mean the student "t" test was used.

$$t = \frac{(x_1 - x_2)}{\sqrt{\frac{(s_1)^2}{n_1} + \frac{(s_2)^2}{n_2}}}$$

x1, x2 = group 1 and group 2, n = no. of observation; s = standard deviation

- **Level of significance: "p"**

In statistical hypothesis testing, the *p*-value or probability value or asymptotic significance is the probability for a given statistical model that, when the null hypothesis is true, the statistical summary (such as the sample mean difference between two compared groups) would be the same as or of greater magnitude than the actual observed results. The use of *p*-values in statistical hypothesis testing is common in many fields of research. The smaller the *p*-value, the higher the significance.

- $p > 0.05$ :: Not significant
- $p < 0.05$:: Significant
- $p < 0.01$:: Highly significant
- $p < 0.001$ :: Very highly significant

- **Pearson Correlation Coefficient**

  Correlation between sets of data is a measure of how well they are related. The most common measure of correlation in stats is the Pearson Correlation (r). The full name is the Pearson Product Moment Correlation or PPMC. It shows the linear relationship between two sets of data.

$$r = \frac{n(\Sigma xy) - (\Sigma x)(\Sigma y)}{\sqrt{[\, n\Sigma x^2 - (\Sigma x)^2 \,][\, n\Sigma y^2 - (\Sigma y)^2 \,]}}$$

Predictive values were calculated using the following calculation:

Screeningtest result	Diseased	Not diseased	Total
Positive	a (true positive)	b (false positive)	a+b
Negative	c (false negative)	d (true negative)	c+d
Total	a+c	b+d	a+b+c+d

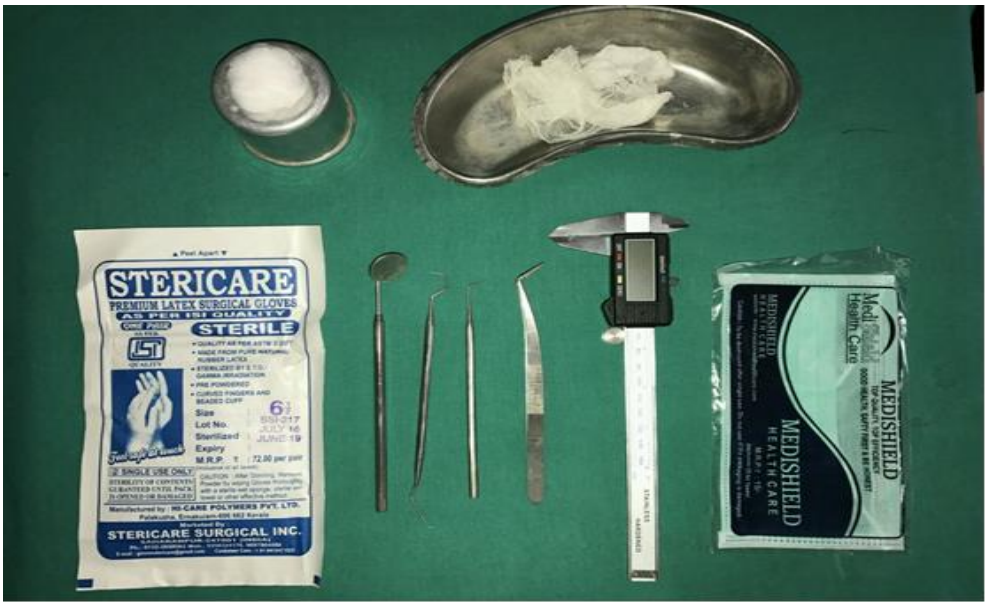
Evaluation of screening test:

a) Sensitivity =a/(a+c)X100

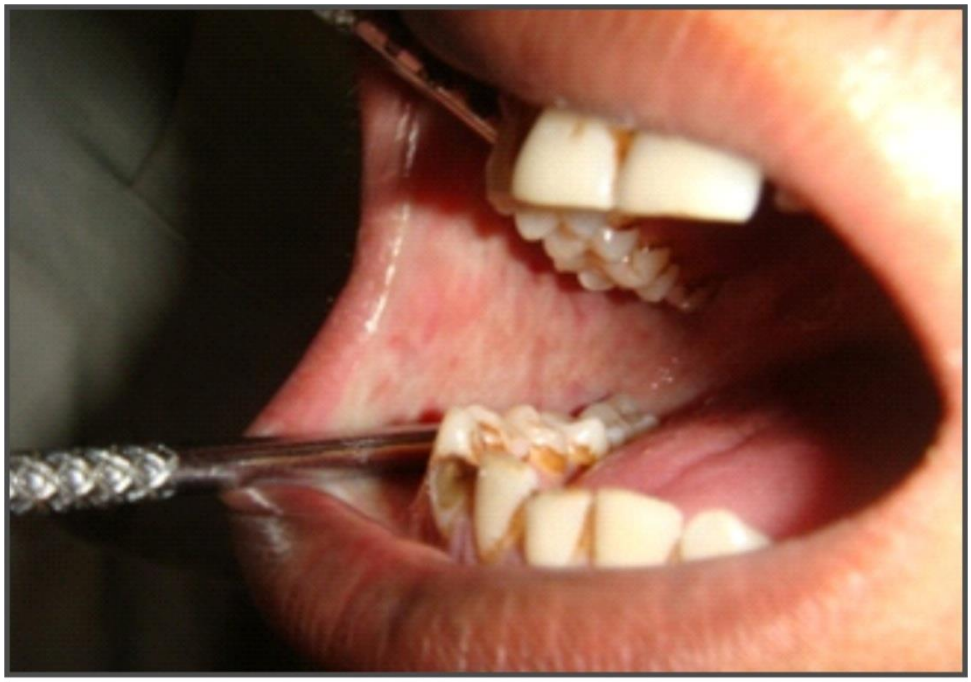
b) Sensitivity =d/(b+d)X100

c) Positive predictive value=a/(a+b)X100

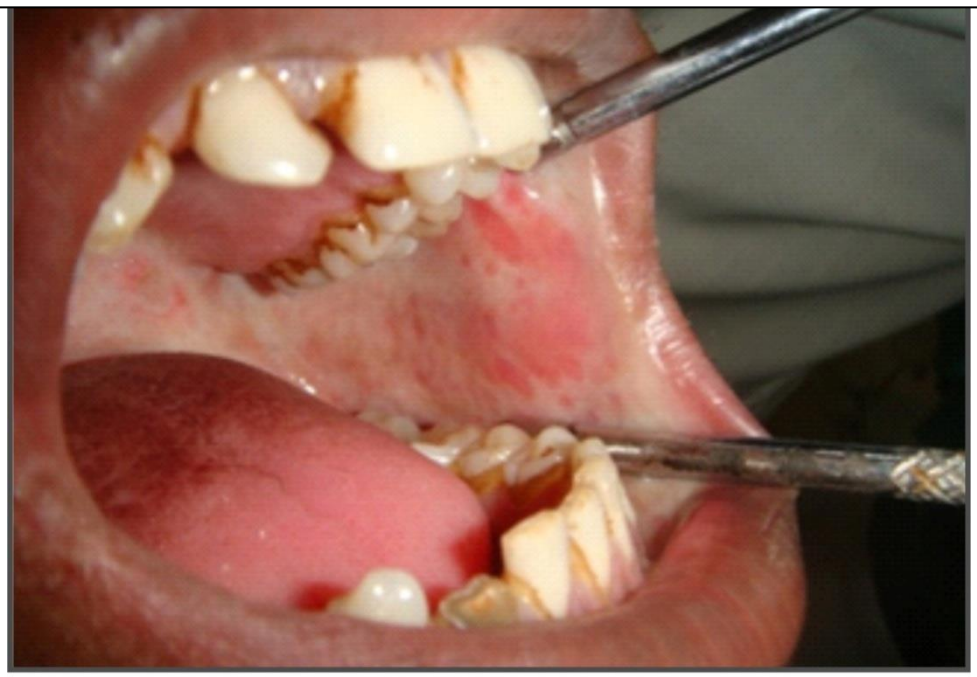
d) Negative predictive value=d/(c+d)X100



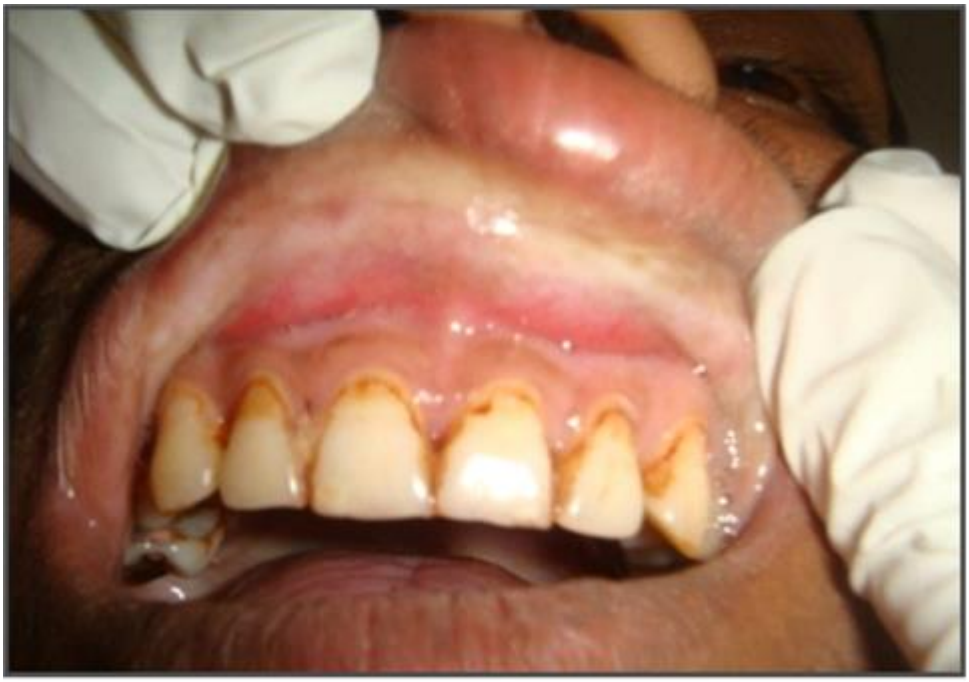
Photograph 5 : Armamentarium



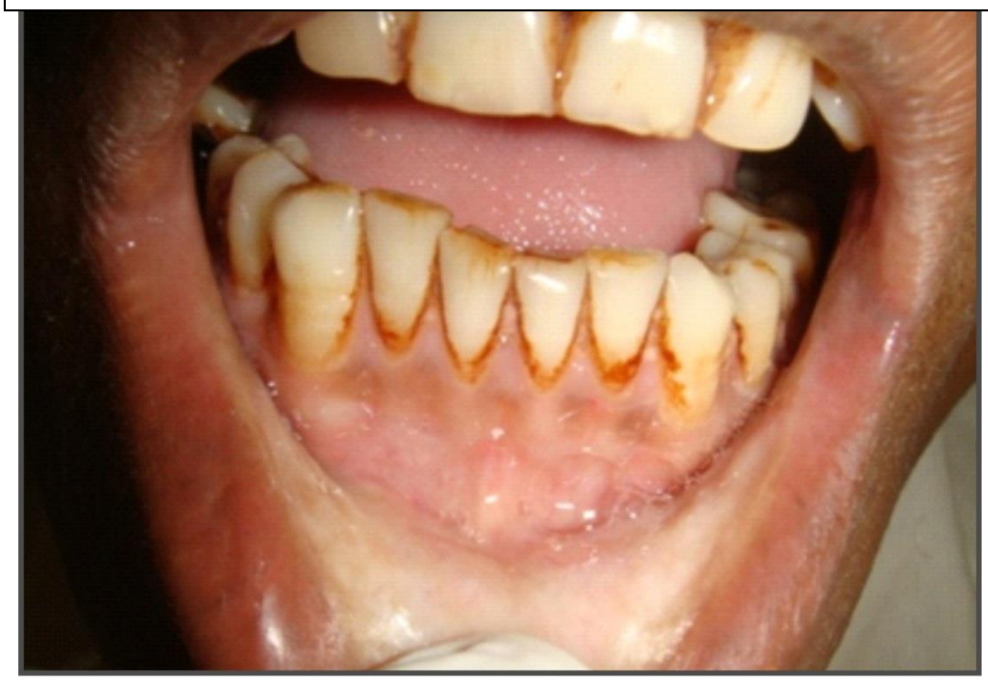
Photograph - 6: Blanching of right buccal mucosa



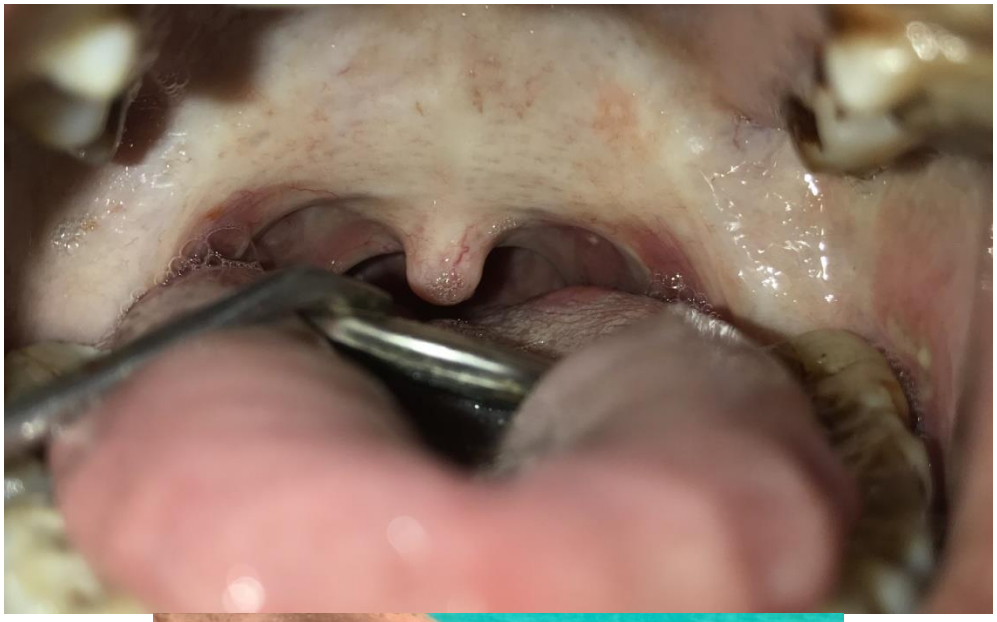
Photograph -7 : Blanching of leftbuccal mucosa



Photograph -8 : Blanching of upper labial mucosa

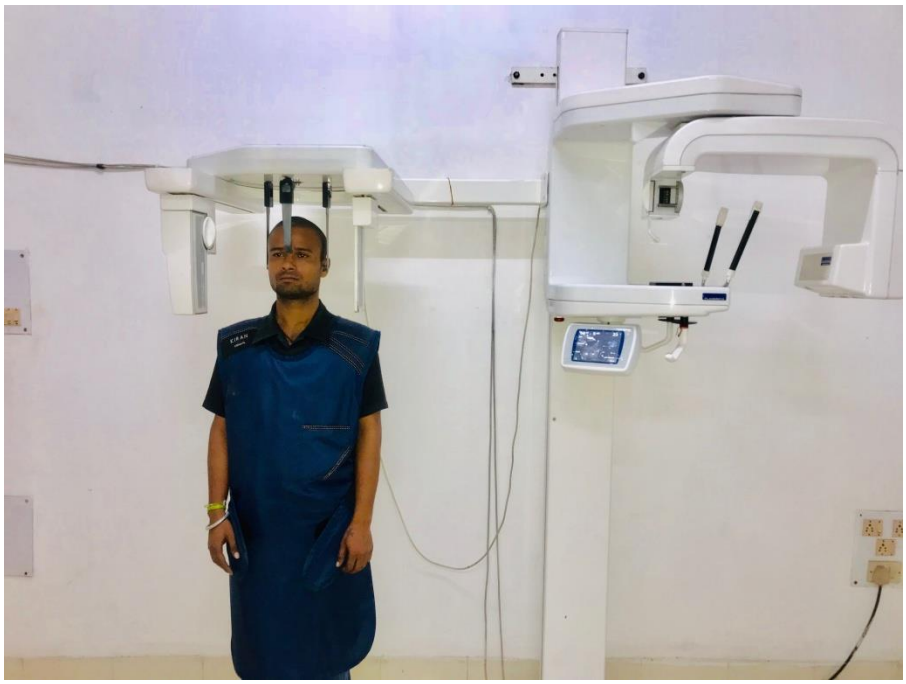


Photograph -9: Blanching of lower labial mucosa

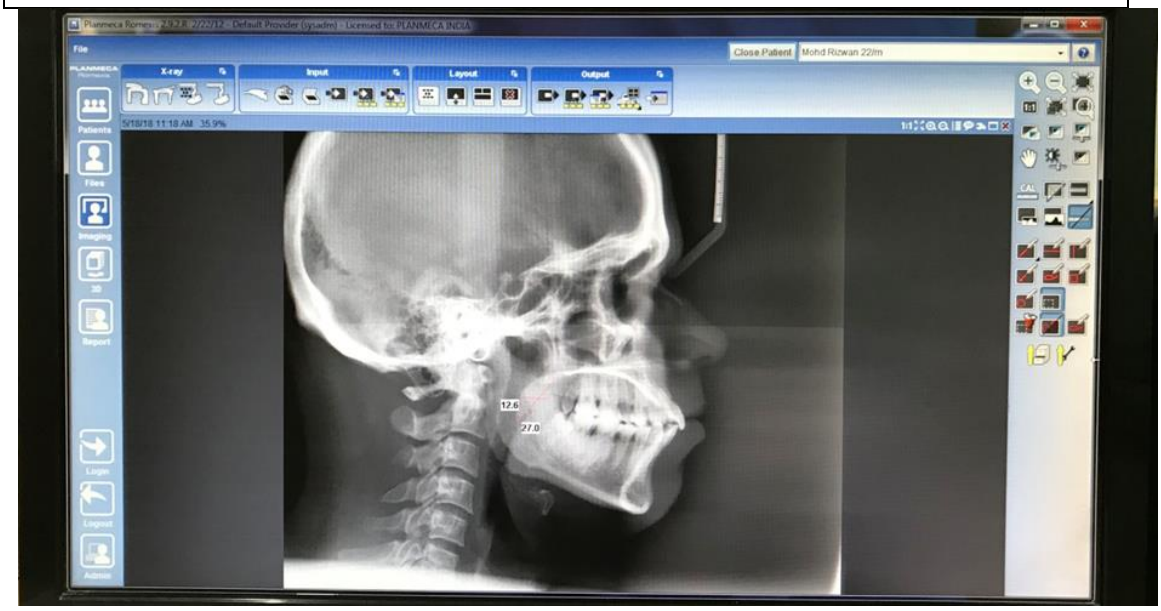


Photograph -10 : Shrunken Uvula

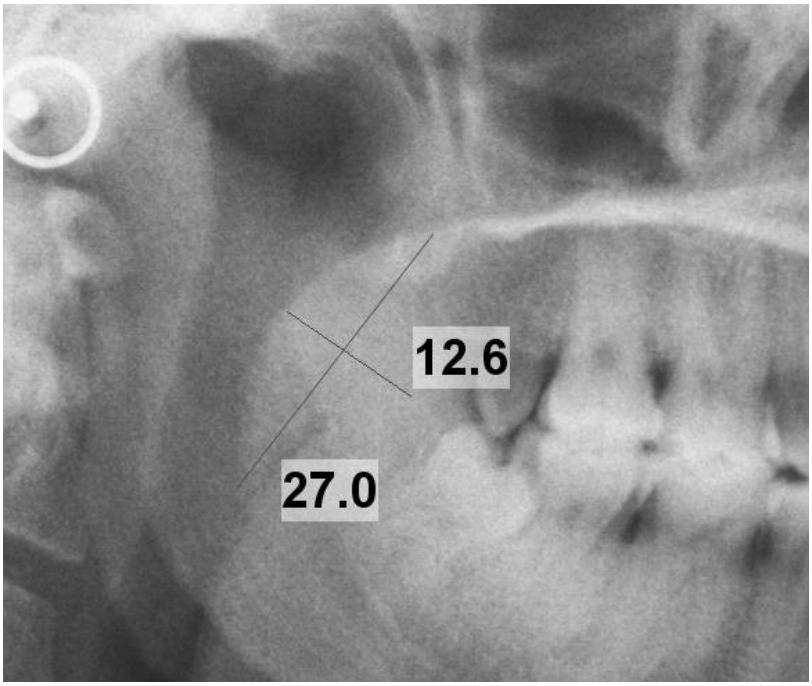
Photograph 11 : Reduced Mouth Opening



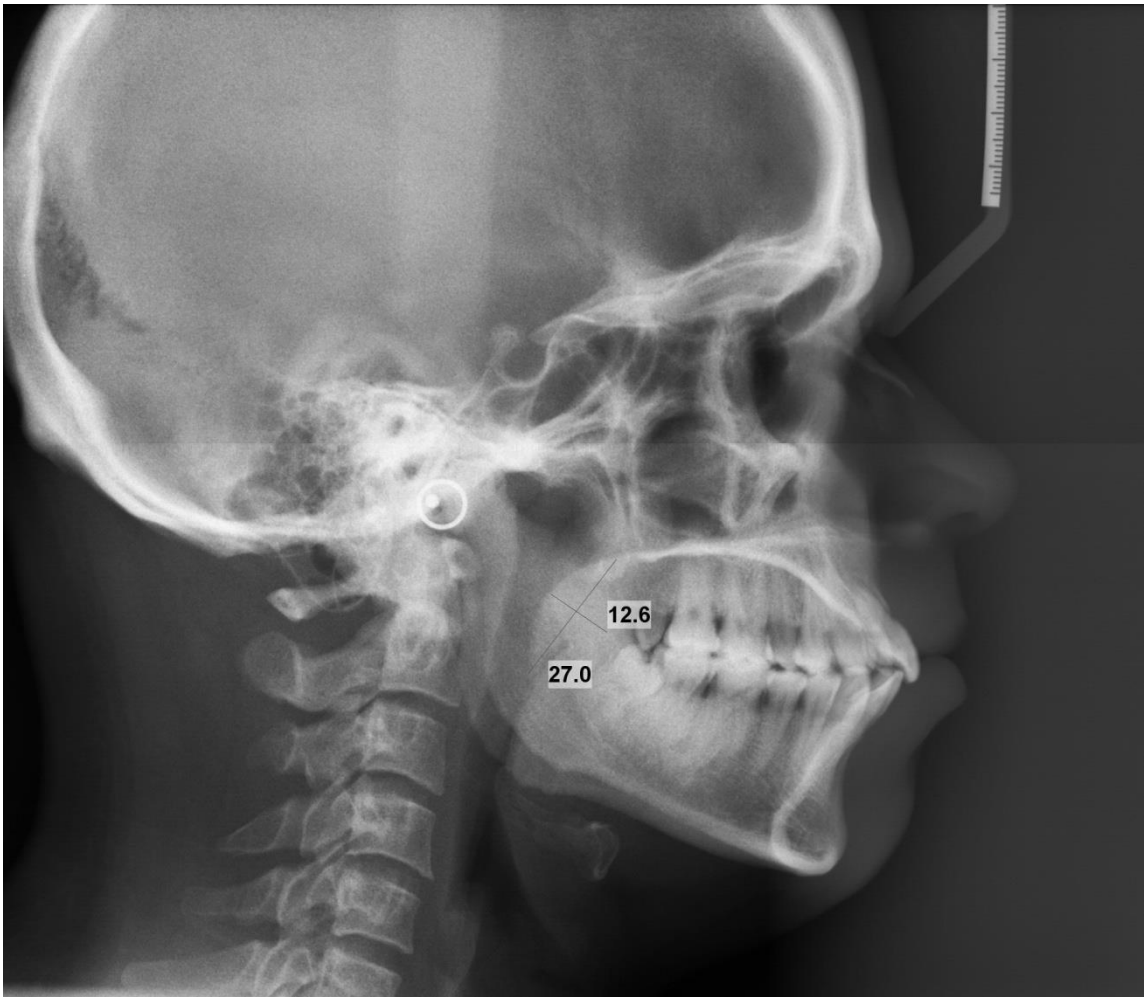
Photograph 12 : Patient along with the lateral cephalometric machine



Photograph 13 :Romex software used in lateral cephalometric radiograph



Photograph 14 : Measurement of soft palate (antero-posterior and supero-inferior dimensions, Type-1 Leaf Shape)



Photograph 15 : Lateral cephalometric radiograph for measurement of soft palate

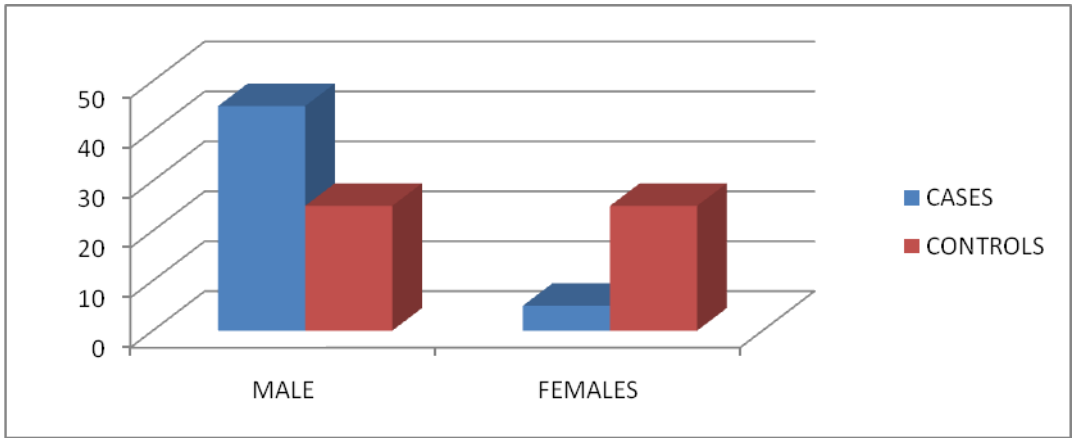
RESULTS

The present study was conducted in the Department of **Oral Medicine and Radiologyof BabuBanarasi Das College of Dental Sciences, Lucknow (UP)**with the aim to evaluate and correlate the morphology of soft palate in Oral submucous fibrosis patients and healthy control using lateral cephalogram.

A total of 100 subjects were included in the study with 50 clinically diagnosed OSMF cases and 50 healthy controls with age range 18-55 years.

Table 1: Gender distribution of cases and controls

GROUPS	CASES	CONTROLS
Male	45	25
Females	5	25



Graph 1: Gender distribution of patients

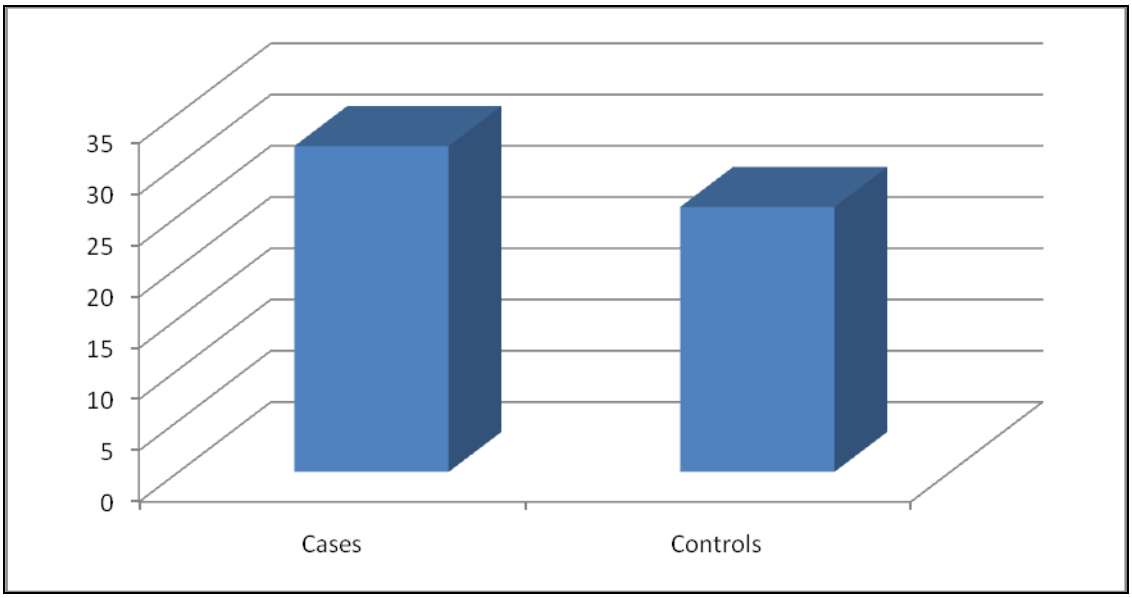
The observation showed that number of males in cases was 45 (90%) and in controls group was 25 (50%) and number of females in cases were 5 (10%) and in control were 25 (50%) (Table-1 & Graph-1).

Table 2: Distribution of age between cases and controls

Groups	Age in years (mean±SD)

Cases	31.8±9.75
Controls	25.86±6.01
t-value, df	3.66,0.78
p-value[1]	0.11

[1]Unpaired t-test

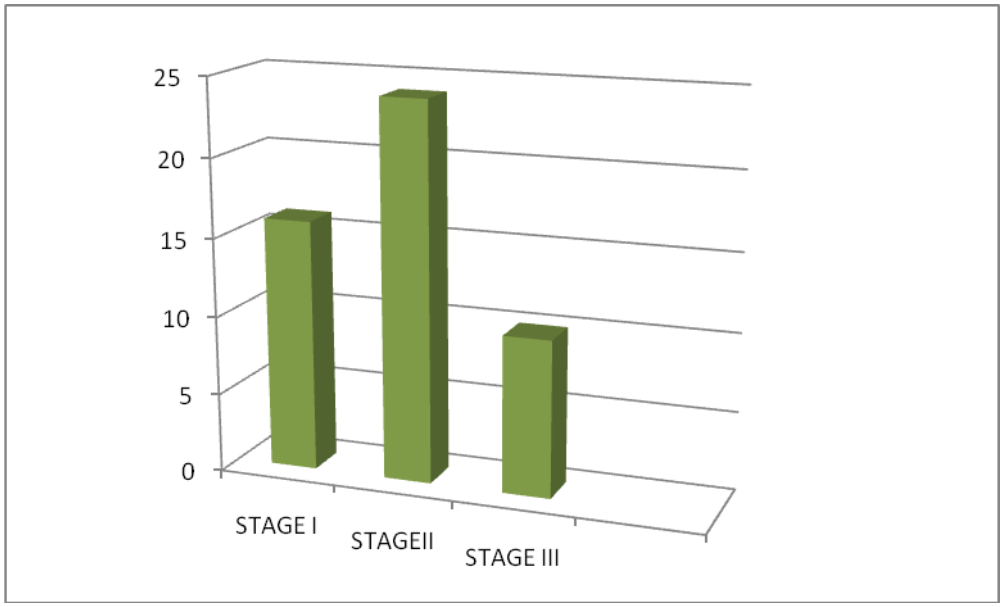


Graph 2: Distribution of age between cases and controls

The observation showed that mean age of cases and controls was 31.8±9.75 and 25.86±6.01 years respectively. There was no significant ($p>0.05$) difference between the two groups (Table- 2 & Graph-2).

Table 3: Distribution of OSMF Patients as Per Clinical Stages

CLINICAL STAGE	NO. OF OSMF PATIENTS (TOTAL=50)
STAGE I	16 (32%)
STAGE II	24 (48%)
STAGE III	10 (20%)

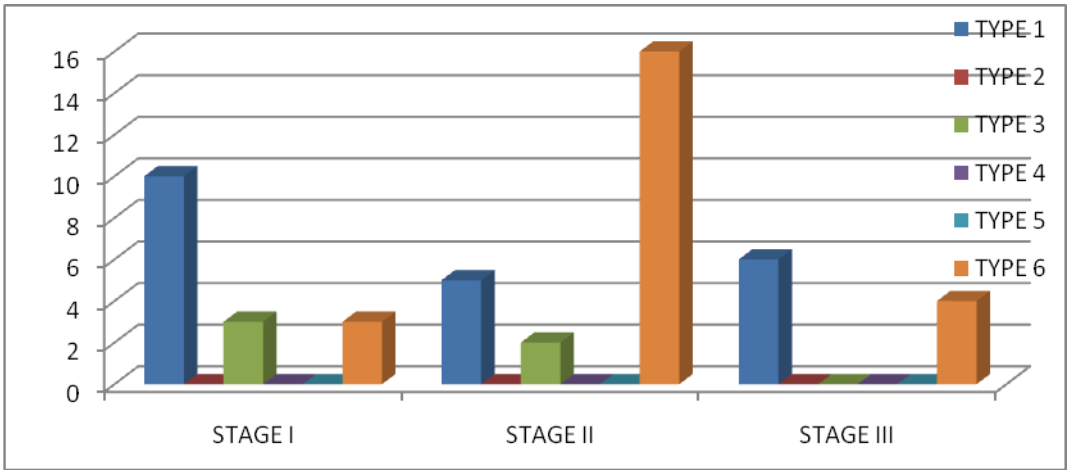


Graph 3:Distribution of OSMF Patients as Per Clinical Stages

The observation showed that in the OSMF group, 16 patients (32%) were classified as stage I, 24 patients (48%) belonged to stage II, while 10 patients(20%) belonged to clinical stage III clinically (Table 3 & Graph 3).

Table 4: Distribution of types of soft palateradiographicallyin Different Clinical Stages of OSMF

Type of soft palate	I	II	III	Grand Total
Type-1	10	5	7	22 (44%)
Type-2	0	0	0	0
Type-3	3	2	0	5(10%)
Type-4	0	0	0	0
Type-5	0	0	0	0
Type-6	3	16	4	23 (46%)
Grand Total	**16 (32%)**	**24 (48%)**	**10 (20%)**	**50**

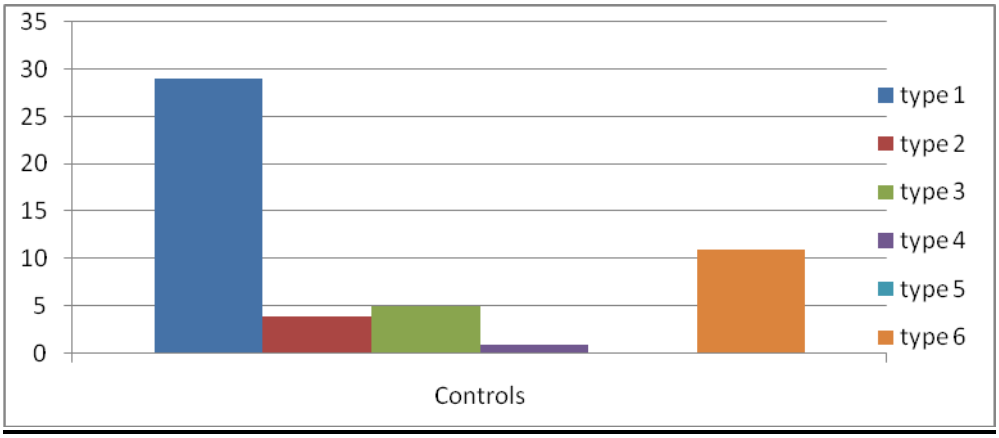


Graph 4: Distribution of Type of Soft Palateradiographically in Different Clinical Stages of OSMF

Observation showed that in the OSMF group, 22 patients (44%) had Type 1 soft palate, 5 patients (10%) had Type 3 while 23 patients (46%) had Type 6 soft palate (Table 4 & Graph 4).

Table 5: Distribution of Type of Soft Palateradiographically in healthy controls

Type of soft palate	Controls
Type-1	29 (58%)
Type-2	4 (8%)
Type-3	5 (10%)
Type-4	1 (2%)
Type-5	0
Type-6	11 (22%)
Grand Total	**50**



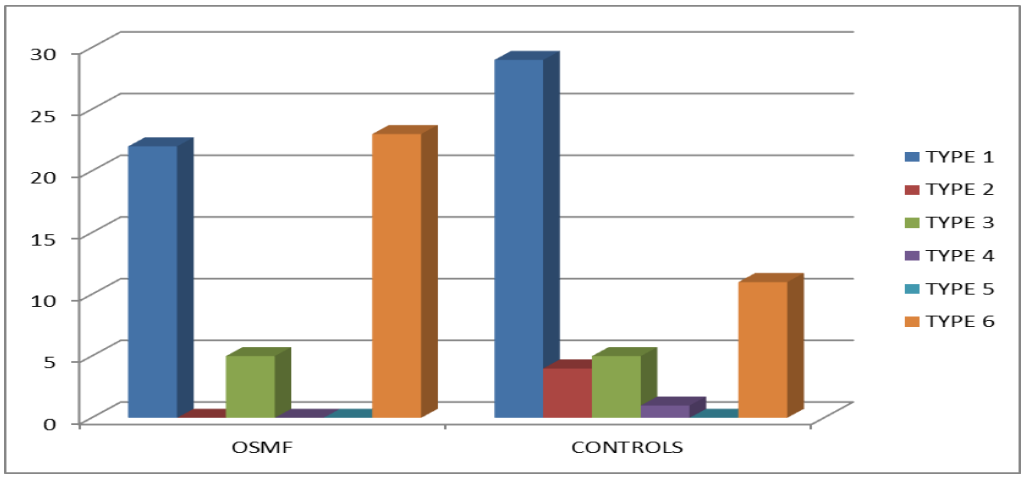
Graph 5: Distribution of Type of Soft Palateradiographically in healthy controls

Observation showed that in the control group, 29 patients (58%) had Type 1 soft palate, 4 patients (8%) had type 2 soft palate, 5 patients (10%) had type 3 soft

palate, 1 patient (2%) had type 4 soft palate and 11 patients (22%) had type 6 soft palate (Table 5 & Graph 5).

Table 6: Distribution of types of soft palateradiographically among the two groups

Groups	Type-1	Type-2	Type-3	Type-4	Type-5	Type-6	Grand Total
OSMF group	22	0	5	0	0	23	50
Control Group	29	4	5	1	0	11	50
Grand Total	51 (51%)	4 (4%)	10 (10%)	1 (1%)	0	34 (34%)	100



Graph 6: Distribution of type of soft palate radiographicallyamong the two groups

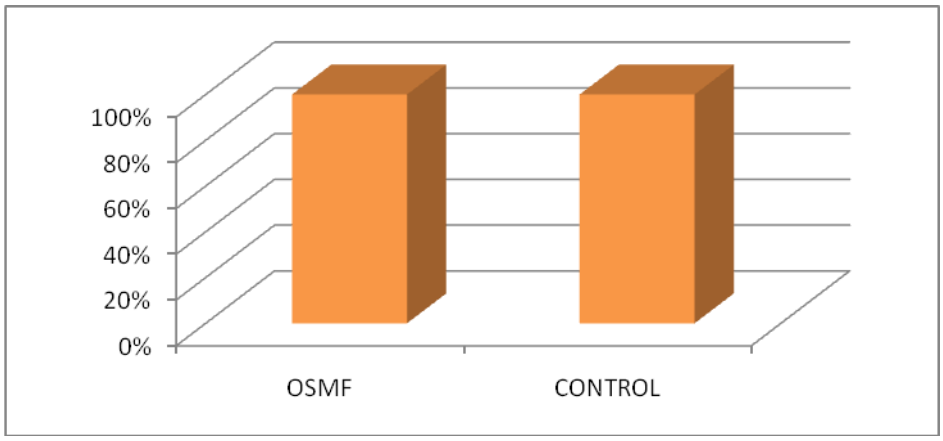
The observation showed that among both the groups 51 patients (51%) had Type 1 soft palate, 4 patients (4%) had Type 2 soft palate, 10 patients (10%) had Type 3 soft palate, 1 patient (1%) had Type 4 soft palate and 34 patients (34%) had Type 6 soft palate. Considering both the groups Type 1 was the most common type of soft palate among healthy individuals while Type 6 was more common type of soft palate in OSMF individuals (Table 6 & Graph 6)

Table 7: Comparison of length, which is anteroposterior dimension of soft palate among the two groups

Groups	Mean±SD
OSMF group	27.05±3.09
Control group	31.67±3.1
t-statistic	7.464

Significance level	< 0.0001
r value	0.0683

P< 0.05: Stastistically significant, SD: Standard deviation



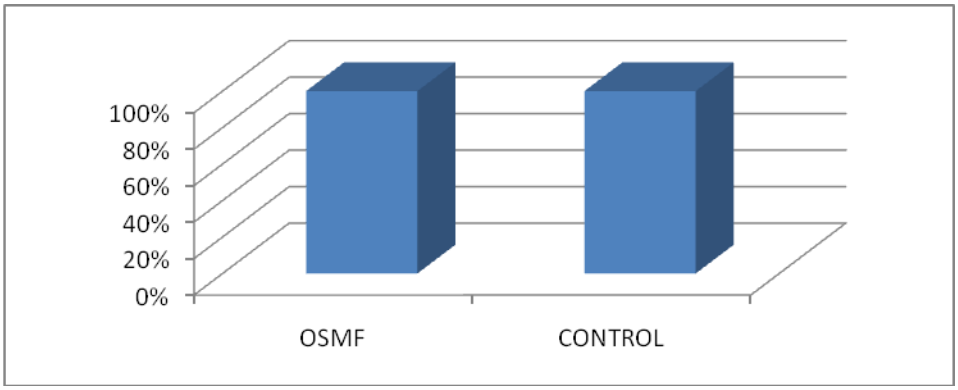
Graph 7: Comparison of length, which is anteroposterior dimension of soft palate among the two groups

The observation showed that the anteroposterior dimension of soft palate in the OSMF group was 27.05±3.09 and in control group was 31.67±3.1. The results showed that the anteroposterior dimension of soft palate decreased in the OSMF group as compared to the normal individuals. Anteroposterior dimension of soft palate was statistically significant (p=0.0001) among the normal and OSMF groups(Table 7 & Graph 7)

Table 8: Comparison of thickness, which is superoinferior dimension of soft palate among the two groups

Groups	Mean±SD
OSMF group	11.08±1.86
Control Group	9.26±1.5
t-statistic	-5.386
Significance level	< 0.0001
r	-0.0605

P< 0.05: Stastistically significant, SD: Standard deviation, OSMF: Oral submucous fibrosis

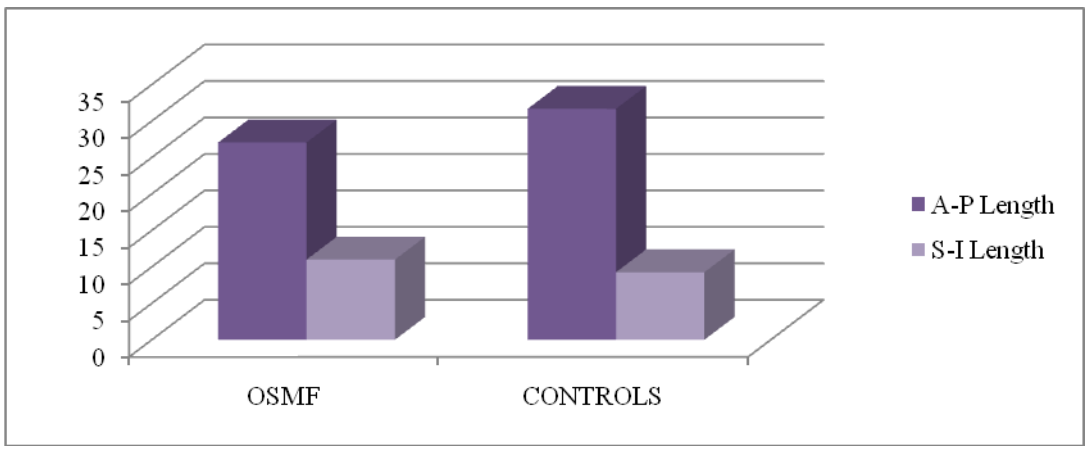


Graph8: Comparison of thickness, which is superoinferior dimension of soft palate among the two groups

The observation showed that the superoinferior dimension of soft palate in the OSMF group was 11.08±1.86 and in control group was 9.26±1.5.The results showed that the superoinferior dimension of soft palate decreased in the normal individuals as compared to OSMF group. Superoinferior dimension of soft palate was statistically significant (p=0.0001) among cases and controls (Table 8& Graph 8).

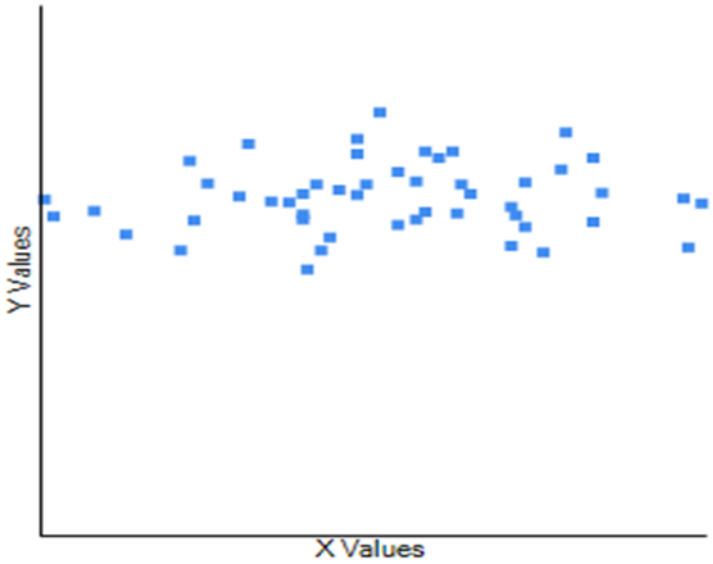
Table 9: Correlation of Radiographic Length in Study Group and Control Group

Parameter	Study	Mean (In Mm)	Median	P Value	Statistical Significance
A-P Length (unpaired t Test)	OSMF	27.05	27.65		
	CONTROL	31.67	31.85	< 0.0001	Significant
S-I Length (unpaired t Test	OSMF	10.99	10.8		
	CONTROL	9.26	9	< 0.0001	Significant



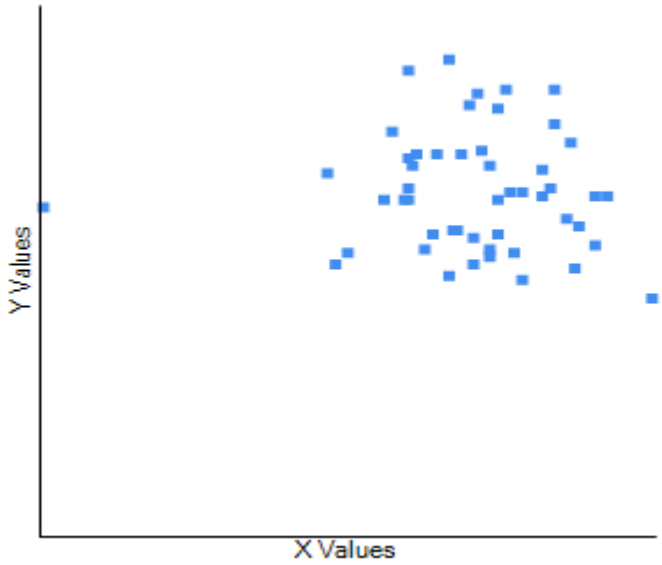
Graph9: Correlation of Radiographic Length and Type of Soft Palate in Study Group and Control Group

The observation showed that the anteroposterior dimension of soft palate among cases and controls was 27.05mm and 31.67mm respectively. The results showed that correlation of anteroposterior dimension among cases and control was found to be significant (p=0.0001). Superoinferiordimension of soft palate among cases andcontrols was 10.99 and 9.26 respectively. The correlation of superoinferior dimension among cases and control was found to be significant (p=0.0001) (Table 9 & Graph 9)



Graph 10: Correlation between length, which is anteroposterior dimension of soft palate among the two groups

The observation showed that the correlation between cases (X-axis) and control (Y-axis) which was found to be significant positive correlation (r=0.0683, p<0.05) in anteroposterior dimension of soft palate(Graph 10).



Graph 11: Correlation of thickness, which is superoinferior dimension of soft palate among the two groups

The observation showed that the correlation between cases (X-axis) and control (Y-axis) which was found to be significant negative correlation ($r=-0.0605$, $p<0.05$) in superoinferior dimension (Graph 11).

DISCUSSION

Oral submucous fibrosis is a chronic, complex, highly potent pre-cancerous condition characterized by juxta epithelial inflammatory reaction and progressive fibrosis of the submucosal tissues such as lamina propria and deeper connective tissue. The main etiological factor is areca nut chewing which consist of arecoline, arecaidine, guvacine, guvacoline of which arecoline is the main agent. Other causative factor include red chillies, prolonged deficiency of iron & vitamin in diet, extreme climatic conditions, immunological diseases.[13]

The disease is multifactorial but the exact pathogenesis is not well established.The mechanisms responsible for the pathogenesis are increased collagen accumulation, increased expression of fibrogenic cytokines, genetic polymorphisms and autoimmunity. The increased collagen accumulation results from increased collagen production and stabilization or decreased breakdown of collagen. Fibroblasts are changed into different phenotypes under the influence of areca nut alkaloids which secrete more amount of collagen. Increased fibrosis is also thought to be due to increased cross-linking of collagen through up-regulating of lysyl oxidase (present in copper which is present in betel nut) activity in OSMF fibroblasts. Thus OSMF is now considered a collagen metabolic disorder. Stabilization of collagen structure is produced by catechin and tannins from areca nut.[30]

The disease is characterized by blanching and stiffness of oral mucosa, trismus and burning sensation in the mouth. It also produces hypomobility of the soft palate and tongue and loss of gustatory sensation.[58]

The diagnosis in most of the cases is made from the history of repetitive exposure to causative agents, clinical appearance. Histopathological examination confirms the diagnosis, as biopsy is invasive process various other investigatory processes may be used for diagnosing precancerous and cancerous disorders.[58]

No successful treatment has been advocated till date, however specific treatment includes administration of steroids, placental extracts, IFN gamma, pentoxifylline, lycopene, surgical excision, curcumin, lycopene, carbon dioxide laser, chymotrypsin, collagenase, and vigorous physiotherapy.[86]

The soft palate is the posterior fibrovascular part of the palate that is attached to the posterior edge of hard palate. It participates in most of the oral functions like speech, swallowing and respiration. Soft palate plays a very crucial role in velopharyngeal closure, that is, approximation of soft palate with pharyngeal walls. This sphincteric mechanism separates nasal and oral cavity during speech and deglutition.[81]

The assessment of the soft tissue elements like soft palate and surrounding structures by usingcephalometry is comparatively economical method. The dimensional analysis of the soft palate and its surrounding structures, especially the velar length and width, which has been overlooked in the past, is reasonably responsible for the different dimensions of the soft palate.[81]

The lateral cephalometric analysis on the morphology of the soft palate was done which revealed the variable radiographic appearance of the soft palate.By observing the soft palate the radiographic appearances of the velum into six type as:[7]

Type 1: “Leaf-shape,” which was lanceolate, indicating that the middle portion of the soft palate elevated to both the naso-and the oro-side.

Type 2: “rat-tail shape,” When the soft palate showed that the anterior portion was inflated and the free margin had an obviouscoarctation.

Type 3: “butt-like”, soft palate showed a shorter and fatter velum appearance, and the width had almost no distinct difference from the anterior portion to the free margin.

Type 4:“straight line shape,” which indicated that the image of the soft palate presented a “straight line shape.

Type 5: S-shape, the distorted soft palate presented the S-shape.

Type 6: “crook” appearance, which revealed a “crook” appearance of the soft palate, in which the posterior portion of the soft palate crooks anterosuperiorly.

Knowledge about the varied morphological pattern of soft palate in OSMF patients can give us a clear understanding about disease progress in oropharyngeal region. Thorough understanding and knowledge of associated changes will help the

maxillofacial surgeon in successful structural and functional corrections associated with this disorder.[78]

Only few researches have reported on morphology of soft palate in OSMF patients, hence the present study was performed to evaluate morphological changes of soft palate in OSMF patients and comparison was done with normal individuals.[81]This study can aid to observe the extent of disease progress, to devise a comprehensive treatment plan with regards to the morphological corrections of the soft palate, post-surgical speech therapy and treatment of associated dysphagia.

The present study was conducted on 100 subjects who visited the department of Oral Medicine and Radiology, BabuBanarasi Das College of Dental Sciences, Lucknow. The patients were divided into two groups, Group A and Group B.

Group A- had 50 clinically diagnosed OSMF

Group B-had 50 healthy controls

OSMF patients were evaluated for burning sensation and mouth opening. Both the groups were then subjected for digital cephalometric radiographs.

1. Distribution of gender among cases and controls (Table-1)

Among50 OSMF patients 90% were male and 10% were female patients, showing male predominance over female with the ratio 9:1. A similar male predominance was reported by **Pindborg J.J**[16](81 out of 118 were male 2.2:1),**Hazarey V.K.et al.**[41] (male to female ratio was 4.9:1)

Male predominance was observed due to easy accessibility for males to use these products more frequently than females in our society.

2. Distribution of age between cases and controls (Table-2)

In the present study 50 cases and 50 healthy controls were in the age range 18-55 years of age. The mean age of the patients of Group A and Group B was 31.8±9.75 and 25.86±6.01 years respectively. This is comparable to mean age28.8±4.62 years by **Hazarey V.K. et al**[41] and 32.33±9.01 by **Gurudath et al**[45]

3. Distribution of OSMF Patients as Per Clinical Stages(Table 3)

In our study it was observed different OSMF group, 16 patients (32%) were classified as stage I, 24 patients (48%) belonged to stage II, while 10 patients (20%)

belonged to clinical stage III clinically. There were maximum participants of stage II OSMF seen in our study followed by stage I and stage III OSMF.

Similar distributions wasreported by **Patil et al[60](2017)** on 150 participants each in study and control group in which 34 participants (22.7%) had stage I OSMF, 90 participants (60%) had stage II OSMF, and 26 participants (17.3%) had stage III OSMF.

Shankar et al[79](2014) studied on 70 patients having 35 OSMF patients and 35 control and concluded that maximum participants of stage II (62.9%) followed by stage III (34.3%)and stage I (2.9%) clinically were present.

Mohan et al[78](2014)concluded on 50 OSMF patients and 50 control that there were 34 (68%) patients of stage II, 11 (22%) patients of stage III and 4 (8%) patients of stage IV.

Another study by **Chintamaneniet al[82](2016)**observed on 50 OSMF and 50 control that maximum participants of stage II (29 cases) followed by stage III (14 cases) and stage I (7 cases) were present clinically.

4. Distribution of types of soft palate radiographicallyamong the two groups (Table 4,5,6)

In the current study, the OSMF group revealed 22 patients (44%) with type-1 (Leaf-shaped) soft palate, 5 patients (10%) showed type-3 (Butt-like) soft palate, 23patients(46%) had type-6 (Crook-shaped) soft palate. No patients having type-2, type-4 and type-5 soft palatal morphology were observed in the study group.

Among the control group, 29 (58%) had type-1 (Leaf-shaped) soft palate, 4 patients (8%) had type-2 (Rat-tail shaped), 5 patients (10%) had type-3 (Butt-like), 11 patients (22%) had type-6 (Crook-shaped) while 1 patient had type-4 (Straight line) soft palatal morphology. No patients having type-5 soft palatal morphology were observed in the control group.

In our study results showed Type-6 (Crook-shaped) soft palate was most common with 23 patients (46%)in our OSMF group whereas in the control group the leaf-shaped (Type-1) soft palate was the most frequent type which was an expected finding, since this type was previously described as a classic velar morphology.[77]

Similar results were reported by**Patil et al[60](2017)**among 150 OSMF individuals in which 60 patients had type-6 soft palate, 38 patients had type-1 soft palate while 26 patients had type-3 soft palatal morphology.

Results of our study were contradicted to **Mohan etal**[78] **(2014)** study. They found that out of 50 OSMF patients 56% had type-1 soft palate, 20% had type-2 soft palate and 14% had type-3 soft palate morphology.

Whereas study doneby **Deshmukhet al[61] (2015)** conflicted with our results. They concluded that among 20 OSMF patients , 12 individuals had type-1 soft palate. 5 individuals of type-3 and 3 individuals of type-6 soft palate morphology were present.

Another study done by **Tekchandaniet al**[80] **(2015)** on 40 OSMF patients concluded that 22 patients had type-1 soft palate, 9 patients had type-6 and 7 patients had type-3 soft palatal morphology.

In the study conducted by **Ashwini et al**[84]**(2017)**on 40 OSMF patients found that16% had type-1 which is followed by 12.5% with type-6, 11.25% with type-2, 8.75% with type-3 and 1.25% with type-5 soft palate morphology.

The above variations may be due to disparity in the distribution of sample size and staging systems of OSMF.

5. Comparison of length, which is anteroposterior dimension of soft palate among the two groups(Table 7)

In the present study the anteroposterior dimension of soft palate in the OSMF group was 27.05±3.09 and in control group was 31.67±3.1. The anteroposterior dimension of soft palate decreased in the OSMF group as compared to the normal individuals. Statistically significant difference in the anteroposterior dimension of soft palate was noted among the normal and OSMF groups, indicating the severity of fibrotic changes involving soft palate observed in this disease.

Similar results were reported in the following studies:

Shankar et al[79]**(2014)** observed in 35 OSMF patients that there was gradual reduction in the length of soft palate in anterior-posterior direction.

Deshmukh et al[61]**(2015)** concluded on 20 individuals of habit group, 20 OSMF individuals and 20 healthy individualsthat the anteroposterior dimension was reduced in the habit group (37.6±4.53) as compared to normal individuals (34.4±4.65), with statistically significant difference in the OSMF group (32.7±4.02).

Another study done by **Chintamaneniet al**[82]**(2016)** on 100 subjects found that the mean value of anteroposterior length was 32.09 in study group and 35.29 in control group. This indicates that anteroposteriorlength was significantly greater in the control group and soft palate becomes short in OSMF.

The similar findings were reported by **Ashwiniet al**[84]**(2017)** on 40 OSMF individuals which showed that with OSMF staging advancement, length of soft palate decreases.

Similar study done by **Patilet al**[60]**(2017)** on 150 OSMF patients observed that there was diminution in anteroposterior length as the disease progressed.

The soft palate shows morphological changes with the progression of the disease, that is, long narrow type getting transformed into short thick pattern.[83]Decrease in anteroposterior dimension is due to the fibrosis of the mucosa over and around the uvula and velar in OSMF leads to characteristic abnormalities in the uvula such as forward pointing uvula or a vanishing uvula.[85] Thusdecrease in anteroposterior dimension indicates the severity of fibrotic changes in OSMF disease.[80]

6. Comparison of thickness, which is superoinferior dimension of soft palate among the two groups(Table 8)

In the present study the superoinferior dimension of soft palate in the OSMF group was 11.08±1.86 and in control group was 9.26±1.5. The results showed that the superoinferior dimension of soft palate decreased in the normal individuals as compared to OSMF group.

Similar results were reported in the following studies:

Shankar et al[79] **(2014)** observed in the study of 35 OSMF patients and 35 controlthat there was decrease in superoinferior dimension of soft palate in the control group as compared to OSMF group.

Deshmukh et al[61] **(2015)** concluded that among the three groups (20 individuals with habit, 20 OSMF individuals and 20 healthy individuals) the

superoinferior dimension of soft palate was decreased in the tobacco group (9.8±1.68) as compared to normal individuals (8±0.96) and in the OSMF group (10.9±1.54) as compared to both the habit group and the normal individuals. Statistically significant difference in the superoinferior dimension of soft palate was noted among individuals of all the three groups respectively.

Another study done by **Chintamaneni et al**[82] **(2016)** on 100 subjects found that the mean value of superoinferior width was 10.19 in study group and 9.23 in control group with statistically significant p value of 0.001. This indicates that superoinferior width was significantly greater in the study group and soft palate becomes stout/bulky in OSMF.

The similar findings were reported by **Ashwiniet al**[84] **(2017)**on 40 OSMF and 40 controlthat with OSMF staging advancement, width of soft palate increases.

Similar study done by **Patilet al**[60] **(2017)** on 150 participants each in OSMF and control group observed that there was increase in superoinferior measurement as the OSMF disease progressed.

The fibrosis of mucosa overlying the soft palate and the surface of uvula pulls the tip of the uvula in the forward direction. The uvula in such patients is less mobile and in extreme cases may be completely disappear. Disappearance of the uvula can be attributed to extensive fibrosis leading to retraction. Thus there is increase in superoinferior dimension.[85]

7. Correlation of Radiographic Length in Study Group and Control Group(Table 9)

In our study the anteroposterior dimension of soft palate among cases and controls was 27.05mm and 31.67mm respectively.The results showed that correlation of anteroposterior dimension among cases and control was found to be statistically significant (p=0.0001). Superoinferior dimension of soft palate among cases and controls was 10.99 and 9.26 respectively. The correlation of superoinferior dimension among cases and control was also found to be statistically significant (p=0.0001)

Chintamaneni et al[82] **(2016)** study on 100 subjects found thatthe correlation of radiographic anteroposterior length between cases and control was found to be 26.375mm and 35.150mm which was statistically significant (p<0.0001). The correlation of radiographic superoinferior length between cases and control were 11.600mm and 10.813mm which was statistically significant (p<0.0138).

In our study the correlation between cases and control was found to be significant positive correlation (r=0.0683) in anteroposterior dimension of soft palate.Positivecorrelation of anteroposterior dimension shows stronger relationship between OSMF and controls.

In the present study the correlation between cases and controlwas found to be significant negative correlation (r=-0.0605) in superoinferior dimension. Negative correlation shows weaker correlation between OSMF and controls superoinferioly.

In the present study we observed that a Gradual reduction in anterioposterior dimension and increase in superioinferior dimension suggesting that soft palate becomes shorter and thicker in OSMF individuals.

Gaining meticulous knowledge regarding changes in soft palate morphology due to OSMF will be helpful for proper diagnosis and successful structural and functional outcome.[84]Although histological analysis of the tissue sections remains the mainstay in the diagnosis of OSMF, radiographic evaluation can considered a powerful tool for the same. Lateral cephalograms can be used as an adjunct to conventional biopsy, and may eliminate the need for biopsy in cases of mass screening camps, medically compromised patients, cross-sectional community studies and patients with drastically reduced mouth opening.[79]

CONCLUSION

Oral Submucous Fibrosisis a insidious chronic disease affecting any part of oral cavity sometimes pharynx, although occasionally preceded by or associated with vesicle formation. It is always associated with juxtaepithelial inflammatory reaction followed by fibroelastic change in the lamina propria with epithelial atrophy leading to stiffness of the oral mucosa and causing trismus and inability to eat.

The diagnosis and prognosis of OSMF can be established by means of biopsy, which is an invasive, time-consuming procedure and causes psychological trauma to some patients. Apart from routine histopathology other diagnostic and prognostic methods such as cephalometric analysis is one of the most commonly accepted techniques for evaluating the morphology of soft palate in OSMF patients.

Only few researches have reported on morphology of soft palate in OSMF patients, hence the need was felt to conduct a study to evaluate changes in soft palate using digital lateral cephalogram.

So the present study was designed with the aim to evaluate and correlate the morphology of soft palate inOral submucous fibrosis patients andhealthy controls using lateral cephalograms in Department of Oral Medicine and Radiology, Babu Banarasi Das College of Dental Sciences, Lucknow. The patients were divided into two groups, Group A and Group B. Group A- had 50 OSMF patients while Group B- had 50 healthy controls.

In the present study among the OSMF group Type-6 (Crook-shaped) soft palate was most common(46%) whereas in the control group the leaf-shaped (Type-1) soft palate was the most frequent type.

Results of this present study also revealed that the anteroposterior dimension of soft palate in the OSMF group was 27.05±3.09 and in control group was 31.67±3.1. whereas the superoinferior dimension of soft palate in the OSMF group was 11.08±1.86 and in control group was 9.26±1.5. In the above parameters difference result was statistically significant.

The anteroposterior dimension of soft palate decreased in the OSMF group as compared to the normal individualsdue to the fibrosis of the mucosa over and around the uvula and velar in OSMF leads to characteristic abnormalities in the uvula such as forward pointing uvula or a vanishing uvula. Whilethe superoinferior dimension of soft palate was increased in OSMF individuals as the fibrosis of mucosa overlying the soft palate and the surface of uvula pulls the tip of the uvula in the forward direction. The uvula in such patients is less mobile and in extreme cases may be completely disappear. Disappearance of the uvula can be attributed to extensive fibrosis leading to retraction.

The result of our study is statistically significant in correlation to anteroposterior and superoinferior dimension among OSMF group hence it can be used as diagnostic tool to detect severity of OSMF disease.

Knowledge about the varied morphological pattern of soft palate in OSMF patients can give us a clear understanding about disease in oropharyngeal region.Although histological analysis of the tissue sections remains the mainstay in the diagnosis of OSMF, radiographic evaluation can considered a powerful tool for the same. Lateral cephalograms can be used as an adjunct to conventional biopsy,

and may eliminate the need for biopsy in cases of mass screening camps, medically compromised patients, cross-sectional community studies and patients with drastically reduced mouth opening.

Radiographic morphology can also help in proper diagnosis of conditionssuch as obstructive Sleep Apnoea due to increased airway resistance and other disorder of soft palate.

An adequate knowledge of velar variants with OSMF will help the maxillofacial surgeon in successful structural and functional corrections associated with this disorder.

For the betterment of our study CT & MRI gives more accurate values than radiographical methods as 3D imaging gives more precise and accurate values than 2D imaging.

Thus further study with larger population and different staging of OSMF have scope for validation of our study.

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ANNEXURES

ANNEXURE 1

DISSERTATION PROFORMA

MORPHOLOGICAL EVALUATION OF SOFT PALATE IN ORAL SUBMUCOUS FIBROSIS PATIENTS: A DIGITAL CEPHALOMETRIC STUDY

DEPARTMENT OF ORAL MEDICINE & RADIOLOGY

BabuBanarasi Das College of Dental Sciences, Lucknow(U.P.)

OPD NO: Case No:

Name: Age: Sex:

Marital status: Occupation:

Address:

Contact No:

Chief Complaint:

History of present illness:

Restricted mouth opening	Duration	Burning sensation(VAS)	Duration

Past Medical History:
Dental History:
Drug History and Allergy:
Family History:
Personal History:
Oral Hygiene Habits:
Abusive Habits:

GENERAL PHYSICAL EXAMINATION:

Built: Gait:
Nourishment: Palor:
Mental state: Cynosis:
Icterus: Clubbing:

Vital Sign:

Blood Pressure: Temperature:
Pulse: Respiratory rate:

EXTRAORAL EXAMINATION:

Mouth Opening:
Facial Symmetry:
Lymph Node:
Temporomandibular Joint:

INTRAORAL EXAMINATION (Hard Tissue Examination):

Teeth Present:
Missing:
Dental Caries:
Attrition, Abrasion, Erosion:
Mobility:

SOFT TISSUE EXAMINATION:

SITE	BLANCHED	STIFFNESS AND FIBROUS BAND	ANY WHITE LESION
Labial Mucosa			
Buccal Mucosa			
Vestibule			
Palate			
Floor of Mouth			
Retromolarpad area			

UVULA	INFLAMATION	BLANCHED	SHRUNKEN

TONGUE	PROTRUSION	STIFFNESS

Gingival & Periodontal Status:

Provisional Diagnosis:
Investigations (Digital Lateral Cephalogram):

Antero-posterior Dimensions	
Supero-inferior Dimensions	
Morphology of Soft Palate	

SIGNATURE OF STUDENT **SIGNATURE OF GUIDE**

ANNEXURE 2
CONSENT FORM

Title of the study…….

Study Number…….

Subject's Full Name……

Date of Birth/Age……

Address of the Subject……

Phone No. and email address……..

Qualification……

Occupation: Student/Self employed/Service/Housewife/Other

1. I confirm that I have read and understood the Participant Information Document dated ……. for the above study and have had the opportunity to ask questions

   OR

   I have been explained the nature of the study by the investigator and had the opportunity to ask questions.
2. I understand that my participation in the study is voluntary and given with the free will without any duress and that I am free to withdraw at any time, without given any reason and without my medical care or legal rights being affected.
3. I understand that the sponsor of the project, others working on the sponsor's behalf, the Ethics Committee and the regulatory authorities will not need my permission to look at my health records both in respect of the current study and any further research that may be conducted in relation to it, even if I

withdraw from the trail. However, I understand that my identity will not be revealed in any information released to third parties or published.

4. I agree not to restrict the use any data or results that arise from this study provided such a use is only for scientific purpose(s).
5. I agree to participate in the above study for the future research

   Yes [ ] No [ ] Not Applicable [ ]
6. I have been explained about the study, and have fully understood them. I have also read and understand the participant/volunteer's information document given to me.

Signature/Thumb impression of the subject/Legally acceptable Representative……....

Signatory's Name…….....Date…….....

Signature of Investigator's Name……..……..…

Study Investigator's Name……...Date……..

Signature of the witness…….…

Name of witness……...Date……..

Received a signed copy of the duly filled consent form

Signature/Thump Impression of the subject/Legally acceptable representative…….Date……

सहमति पत्र

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ANNEXURE 3

BABU BANARASI DAS COLLEGE OF DENTAL SCIENCES
(FACULTY OF BBD UNIVERSITY), LUCKNOW

INSTITUTIONAL RESEARCH COMMITTEE APPROVAL

The project titled **Morphological Evaluation of Soft palate in Oral Submucous Fibrosis Patients: A Digital Cephalometric Study** submitted by **Dr. Sakshi Verma** Post graduate student from the Department of **Oral Medicine and Radiology** as part of MDS Curriculum for the academic year 2016-2019 with the Accompanying proforma was reviewed by the institutional research committee present on **7th and 8th December 2016** at BBDCODS. The Committee has granted approval on the scientific content of the project. The proposal may now be reviewed by the institutional ethics committee for granting ethical approval.

Prof. (Dr).Vivek Govila

Principal

PRINCIPAL
Babu Banarasi Das College of Dental Sciences
(Babu Banarasi Das University)

Chairperson Institutional Research Committee

ANNEXURE 4

Babu Banarasi Das University
Babu Banarasi Das College of Dental Sciences,
BBD City, Faizabad Road, Lucknow – 226028 (INDIA)

Dr. Lakshmi Bala
Professor and Head Biochemistry and
Member-Secretary, Institutional Ethics Committee

Communication of the Decision of the Vth Institutional Ethics Sub-Committee

IEC Code: 28 **BBDCODS/03/2017**

Title of the Project: Morphological Evaluation of Soft Palate in Oral Submucous Fibrosis Patients: A Digital Cephalometric Study.

Principal Investigator: Dr. Sakshi Verma **Department:** Oral Medicine & Radiology

Name and Address of the Institution: BBD College of Dental Sciences Lucknow.

Type of Submission: New, MDS Project Protocol

Dear Dr. Sakshi Verma

The Institutional Ethics Sub-Committee meeting comprising following four members was held on 02nd March, 2017.

1.	Dr. Lakshmi Bala Member Secretary	Prof. and Head, Department of Biochemistry, BBDCODS, Lucknow
2.	Dr. Neerja Singh Member	Prof. & Head, Department of Pedodontics, BBDCODS, Lucknow
3.	Dr. Rana Pratap Maurya Member	Reader, Department of Orthodontics, BBDCODS, Lucknow
4.	Dr. Manu Narayan Member	Reader, Department of Public Health Dentistry, BBDCODS, Lucknow

The committee reviewed and discussed your submitted documents of the current MDS Project Protocol in the meeting.
The proposal was reviewed, comments were communicated to PI thereafter it was revised.

Decisions: The committee approved the above protocol from ethics point of view.

Forwarded by:

Lakshmi Bala 29/4/17

(Dr. Lakshmi Bala)
Member-Secretary
IEC

Member-Secretary
Institutional Ethic Committee
BBD College of Dental Sciences
BBD University
Faizabad Road, Lucknow-226028

(Dr. Vivek Govila)
Principal
BBDCODS

PRINCIPAL
Babu Banarasi Das College of Dental Sciences
(Babu Banarasi Das University)
BBD City, Faizabad Road, Lucknow

ANNEXURE 5

CASE GROUP							
S.NO	**OPD NO**	**PATIENT NAME**	**AGE/SEX**	**ANTERIOPOSTERIOR DIMENSION**	**SUPERIOINFERIOR DIMENSION**	**SHAPE OF UVULA**	**STAGE OF OSMF**
1	32580	MohdRizwan	22/M	27.0mm	12.6mm	Type-6	III
2	24245	Sachin	32/M	29.5mm	12.5mm	Type-6	II
3	40015	PawanPandey	35/M	28.5mm	11.5mm	Type-6	II
4	40830	Ramu	32/M	26.6mm	10.1mm	Type-1	III

5	35490	Chaitanya Gupta	22/M	34.2mm	11.0mm	Type-1	I
6	30472	Vinod Kumar	25/M	21.2mm	10.6mm	Type-1	II
7	10849	Uttam Kumar	20/M	25.9mm	11.2mm	Type-6	II
8	42150	Pradeep	26/M	27.4mm	10.2mm	Type-3	II
9	36515	Sharif	24/M	31.1mm	9.4mm	Type-1	I
10	43005	Vijay	24/M	25.8mm	9.2mm	Type-1	II
11	45660	Rahul Singh	20/M	34.3mm	7.0mm	Type-1	I
12	16522	Sundari	30/F	20.3mm	7.5mm	Type-3	II
13	44880	Raj Kishore	18/M	26.1mm	8.9mm	Type-6	II
14	53835	Sushil	35/M	28.3mm	11.2mm	Type-1	II
15	19195	Suresh	32/M	27.2mm	15.0mm	Type-6	II
16	54010	Pramod	28/M	32.4mm	9.0mm	Type-1	I
17	18840	Mithlesh	27/M	28.5mm	12.3mm	Type-1	III
18	13546	Udit Singh	20/M	32.2mm	11.8mm	Type-1	I
19	54360	Deep Chand	31/M	30.7mm	13.9mm	Type-6	II
20	54365	Pankaj Kumar	25/M	31.5mm	13.1mm	Type-1	I
21	14124	Aziz Khan	21/M	21.9mm	10.6mm	Type-1	I
22	38210	AbhishekAgraharri	25/M	29.1mm	11.0mm	Type-6	I
23	19786	Kailashwati	33/F	23.7mm	10.3mm	Type-1	I
24	55260	Manoj Singh	32/M	31.6mm	10.7mm	Type-6	II
25	33880	Renu	45/F	25.8mm	8.6mm	Type-1	III
26	20356	K.K.Srivastava	50/M	25.1mm	11mm	Type-6	III
27	37280	Shambhu	44/M	34.6mm	9.0mm	Type-6	II
28	39935	RamveerYadav	43/M	27mm	9.7mm	Type-6	II
29	41130	Sunita	40/F	20.1mm	9.6mm	Type-6	III
30	14602	Sunil kumarVerma	54/M	28.8mm	12.9mm	Type-1	II
31	52000	Ganesh Dutt	42/M	24.4mm	10.8mm	Type-1	III
32	18621	Harish Agarwal	40/M	30.4mm	7.2mm	Type-1	III
33	18622	Rajesh Pandey	38/M	27.9mm	13.0mm	Type-3	I
34	19333	RajuMaurya	40/M	24.6mm	10.0mm	Type-6	II
35	54945	AnuragShukla	18/M	23.1mm	9.0mm	Type-6	II
36	28860	Mohd Ahmad	24/M	30.5mm	11.4mm	Type-3	I
37	29623	Vinay	21/M	32.2mm	11.8mm	Type-6	I
38	52895	Azra	55/F	26.2mm	9.1mm	Type-1	III
39	56065	Vidhya Prasad	40/M	25.5mm	13.6mm	Type-6	II
40	56025	SurajTiwari	27/M	27.0mm	12.6mm	Type-6	III
41	41570	Siddh	35/M	23.3mm	8.4mm	Type-6	I
42	57700	Suraj Kumar Singh	27/M	26.4mm	12.3mm	Type-6	II
43	42080	Mayank	22/M	29.2mm	10.5mm	Type-1	I
44	20839	Bablu Prasad	28/M	25.5mm	11.6mm	Type-1	II
45	25731	Pradeep Kumar	53/M	30.4mm	13.2mm	Type-6	II
46	25730	Rahul	25/M	30.7mm	9.0mm	Type-1	I
47	18600	Rajesh	38/M	27.9mm	13.omm	Type-3	I

48	53818	Sushil	35/M	28.3mm	11.2mm	Type-1	II
49	57760	Suraj Kumar	27/M	29.3mm	13.6mm	Type-6	II
50	19333	Raju	40/M	23.4mm	10.0mm	Type-6	II

CONTROL GROUP						
S.NO.	**OPD NO**	**PATIENT NAME**	**AGE/SEX**	**ANTEROPOSTERIOR DIMENSION(mm)**	**SUPEROINFERIOR DIMENSION(mm)**	**SHAPE OF SOFT PALATE**
1	29623	Vinay	21/M	32.2	11.8	Type-6
2	81105	Bansilal	32/M	32.3	9.2	Type-1
3	12280	Kailash Kr Gautam	30/M	36.3	9.1	Type-2
4	59375	KadambaniLal	35/F	32.7	8.1	Type-1
5	46215	Aisha Ansari	33/F	31.9	9.8	Type-2
6	48920	Sachin Gupta	21/M	30.7	7.9	Type-1
7	10340	Shailendra	27/M	40	11.3	Type-1
8	16285	LaxmiPathak	22/F	26.8	8.1	Type-3
9	54055	SakshiDeorah	21/F	29.9	7.6	Type-1
10	45625	PreetiYadav	20/F	27.3	10.1	Type-1
11	39005	Dheeraj	18/M	30.2	9.6	Type-6
12	48928	Sachin	21/M	33.2	7.5	Type-1
13	32930	Nidhi	23/F	25.2	8.9	Type-1
14	70230	Neha Gupta	22/F	29.9	8	Type-1
15	28310	RochakAgarwal	19/M	33.2	6.3	Type-4
16	51110	AkshitaTripathi	18/F	32.4	8.9	Type-1
17	50935	PankajRawat	21/M	30.6	9.7	Type-1
18	49805	SanafZaman	25/F	29.7	6.8	Type-1
19	49800	Shipra Sharma	25/F	33.4	9	Type-2
20	49795	P.Renuka	26/F	34.6	7.1	Type-1
21	41710	MeeraKumari	20/F	28.5	7.2	Type-1
22	53395	ChahatJaiswal	20/M	36.3	7.4	Type-1
23	895	Rajneesh Kumar	20/M	33.3	10.1	Type-6
24	56655	VivekPandey	28/M	38.1	11.7	Type-1
25	78130	Sushil	28/M	32.3	10.7	Type-6
26	26965	SangeetaPandey	40/F	31.6	7.6	Type-1
27	19382	Ramawati	46/F	31.4	12.3	Type-6
28	24690	GireeshTripathi	37/M	37.5	10.1	Type-1
29	64850	LataVerma	36/F	31.8	8	Type-2
30	10605	Tej Kumar	38/M	35.7	8.4	Type-6
31	62300	MohdSafiq	29/M	32.1	10.2	Type-3
32	28600	PallavVerma	27/M	27.4	7.2	Type-1
33	56630	AmitSahu	27/M	34.4	10.4	Type-1
34	56025	SurajTiwari	27/M	37	12.6	Type-6
35	56555	Nisha	26/F	27	9.2	Type-1
36	920	Rajesh Verma	26/M	30.3	11.8	Type-3
37	28002	Jai Shankar	25/M	35.7	9.1	Type-1
38	56960	Seeba	25/M	27	9.8	Type-6
39	1805	Devendra Kumar	25/M	31.5	9	Type-1

40	35025	Vikrant Singh	24/M	36.1	10.9	Type-6
41	21188	Ram Milan Gupta	24/M	35.4	8.9	Type-1
42	40846	Kansa	25/F	28.2	9	Type-6
43	28860	Mohd Ahmad	24/M	30.5	11.4	Type-3
44	30735	Deepti	28/F	30.4	7.5	Type-1
45	31590	Reena	22/F	31.1	8.2	Type-1
46	40630	Pushpa	28/F	29.2	10	Type-6
47	19960	ShahibaKhatoon	21/F	33.5	8.7	Type-1
48	53985	RafatAnjum	20/F	29.4	8.9	Type-3
49	39030	Arti	22/F	33.2	7.7	Type-1
50	40305	Sunita	25/F	29.8	6.9	Type-1