Evaluation of Haemoglobin and Iron Levels in Serum of Patients with Oral Sub Mucous Fibrosis: A Clinical Study

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Abstracts: Background: Oral sub mucous fibrosis (OSMF) is a chronic, insidious oral mucosal condition affecting the most parts of the oral cavity with high malignant transformation rate triggered by areca nut chewing, nutritional deficiencies, immunologic processes, and genetic predisposition. OSMF causes significant haematological abnormalities resulting in change in levels of various elements. **Aim and Objectives:** The aim of this study was to estimate the haemoglobin and iron levels in serum among patients with oral sub mucous fibrosis and to compare the values with healthy subjects. Materials and Methods: In this clinical study 50 patients who were diagnosed histopathologically with OSMF and 50 healthy individuals will be included, and the values of haemoglobin levels will be estimated using Sahli's serum iron by Ferrene methods. **Results:** OSMF patients showed significantly lower levels of haemoglobin and serum iron when compared with the healthy subjects. **Conclusion:** The present study shows the serum iron assessment for patients with oral sub mucous fibrosis. Determining iron status is a part of biochemical assessment, which may be of proactive intervention for high-risk groups. It is suggested that the biochemical assessment of oral precancerous conditions may help in early diagnosis and prognosis. It is also of key importance that iron therapy should be instituted parallel with the initial diagnosis along with a proper balanced diet, as a part of the overall treatment of oral sub mucous fibrosis with other modes of treatment. This helps to stop the further progression of the condition. [Pathak D NJIRM 2014; 5(5):30-34]

Key Words: Haemoglobin, Iron Levels, Oral Sub Mucous Fibrosis

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Introduction: Oral submucous fibrosis (OSMF), first described in the early 1950s, is a potentially malignant disease predominantly seen in people of Asian descent. It is a chronic progressive disorder, and its clinical presentation depends on the stage of the disease at detection. The majority of patients present with an intolerance to spicy food and rigidity of lip, tongue, and palate leading to varying degrees of limitation of opening of the mouth and tongue movement. The hallmark of the disease is submucosal fibrosis that affects most parts of the oral cavity, pharynx, and upper third of the esophagus. Etiological factors hypothesized to trigger the disease process include areca nut chewing, nutritional deficiencies, immunologic processes, and genetic predisposition Nutritional deficiencies, primarily of iron and vitamins, are implicated in the etiology of OSMF.[1,2,3]

Iron is essential for the overall integrity and health of epithelia of digestive tract and its contribution to normal enzymatic functions. OSMF is also considered as an Asian version of sideropenic dysphagia, wherein chronic iron deficiency leads to mucosal susceptibility to irritants, such as chilies and areca nut products.[4,5]

Hemoglobin levels, in particular serum iron levels, are considered as biochemical indicators for nutritional assessment. Deficiency of iron, Vitamin B-12, and folate can affect the integrity of the oral mucosa. Significant haematological abnormalities have been reported in OSMF, including an increased blood sedimentation rate, and a decrease in serum iron and an increase in total iron binding capacity. [4,6,7]

Copper is essential for numerous enzymes and therefore variation in serum levels may be associated with pathogenesis of oral cancer.

Thus, the present study is conducted to assess the level of haemoglobin and serum iron binding capacity among clinically and histopathologically diagnosed patients with oral submucous fibrosis and comparing the values with that of healthy subjects.

Material and Methods: A clinical study was conducted in 50 clinically diagnosed and

histopathologically proven patients of OSMF (OSMF group) in Ahmedabad, Gujarat population. Patients with habit of chewing areca nut or one of its commercial preparations, with the presence of burning sensation, inability to consume spices, stiffness of buccal mucosa, vesicle formation, ulceration, and blanching of oral mucosa were undergone histopathological examination of biopsy taken from buccal mucosa and included in the OSMF group. Patients with any systemic complications, suffering from any major illness, and habit of chewing only tobacco and patients with habit chewing areca nut or one of its commercial preparations but without OSMF will be excluded. The OSMF group were clinically staged into stage I and stage II as per the staging given by Pindborg. 50 healthy individuals were matched for gender and age, without any history of habit of chewing areca and tobacco and any major illness in recent past were included as controls. Subjects with any habits and suffering from any systemic disease in the recent past will be excluded from the control group. Ethical clearance and informed consent were obtained from the individuals who were participating in the study.

Method: 5 mL of fasting venous blood were collected and submitted for the estimation of hemoglobin levels by using Sahli's method and serum sample for serum levels of iron by using Ferrene method.

Statistical Analysis: The values obtained were statistically analysed using Student's t-test to find the significance of study parameters on a continuous scale for intergroup analysis.

Result: The study group (OSMF group) comprised of 50 cases with age between 18 and 60 years with a mean age of years. The maximum numbers of cases were between 21 and 28 years. The OSMF group showed male predominance with 38 males and 12 female. (Chart 1 and Chart 2)

Mean values of hemoglobin and serum iron levels of Control group were 14 mg/dL and 138.20 mcg/dL, where as those of OSMF group were 09.73 mg/dL and 60.83 mcg/dL respectively. On comparison of OSMF group with the Control group, OSMF group showed significantly lower levels of hemoglobin and serum iron with $P < 0.0001$.(chart 3)

Mean values of hemoglobin levels of OSMF stage II group were 9.07 mg/dL and serum iron levels were 53.23 mcg/dL respectively. Inter stage comparison of OSMF stage II group with the Control group, and OSMF stage II group showed significantly lower levels of hemoglobin and serum iron with $P < 0.0001$. (Chart 4)

Discussion: Oral submucous fibrosis (OSMF) is a chronic, insidious oral mucosal condition that occurs predominantly among Indians and occasionally in other Asians. In the Indian continent alone, the statistics for OSMF is about 5 million people (0.5%) of the population. Several factors such as chillies consumption, nutritional deficiency, areca nut chewing, [8,9]

Genetic susceptibility, autoimmunity and collagen disorders have suggested to be involved in the pathogenesis of this condition. Currently, areca nut chewing is considered to be most important etiologic factor of oral submucous fibrosis The reasons for the rapid increase of the disease are reported to be due to an upsurge in the popularity of commercially prepared areca nut preparations (pan masala) in India and an increased uptake of this habit by young people due to easy access, effective price changes, and marketing strategies.[10,11]

It manifests as blanching and stiffness of the oral mucosa, trismus, burning sensation in the mouth, reduced mobility of the soft palate and tongue, loss of gustatory sensation, intolerance to eating hot and spicy foods and occasionally, mild hearing loss due to blockage of Eustachian tube.[6] The hallmark of the disease is submucosal fibrosis that affects the oral cavity and progressively involves the pharynx and the upper esophagus. This leads to burning sensation in the oral cavity, blanching, and stiffening of oral mucosa, and oropharynx, resulting in restricted mouth opening and reduction in tongue movement which in turn causes limited food consumption, and difficulty in maintaining oral hyagine and impairs the ability to speak. The mean age of the OSMF group in our study was 28.34 years, which is consistent with

findings of 29.04 years by Katharia et al.[12] and 30 years by Maher et al.[13]

Alkaloids of areca nut such as arecoline act as initiating factors causing a juxta-epithelial inflammatory reaction and soluble irritants, such as capsaicin in chilies and spices, were observed as one of the predisposing factors of OSMF. One of the mechanisms that can lead to increased fibrosis is by reduced degradation of collagen by forming a more stable collagen structure. The large quantities of tannin present in areca nut reduce collagen

Degradation by inhibiting collagenases and result in fibrosis, as the combined effect of tannin and arecoline by reducing degradation and increased production of collagen, respectively .[10,11.14]

A male predominance was seen in the OSMF group with 12 female and 38 males , which is consistent with Ranganathan et al.[8] that Males were found to be dominating, as they were using Gutkha , Paan (containing betel nut) , Mawa (betel nut , tobacco and lime) preparation and other related products more because of easy availability in all the places whereas females were more conscious about their health and esthetic value and probably felt uncomfortable to ask the vendors in getting this commercial products. This may be one of the reasons, which may be responsible for a high male-to female ratio. A female predominance was seen in the anemia group with 9 females and 5 males, as iron deficiency anemia is very common in females because of malabsorption, poor dietary intake, folate deficiency, chronic blood loss due to menstruation or menorrhagia, at the time of child birth, excessive demands as in pregnancy and breast feeding.

Burning sensation, vesiculation, and ulceration of the oral mucosa render a phase for difficulty in consumption of the normal diet leading to poor nutrition. Deficiency of iron and

vitamin B complex other trace elements due to nutritional depletion could possibly initiate anemia and altered cell-mediated immunity, which in turn acts as a promoting factor to this preexisting pathologic response of the lamina propria . After a frank establishment of the lesion, anemia may further perpetuate by inadequate intake of food due to fibrosis and trismus .[6]

Low levels of hemoglobin and serum iron are suggestive of iron deficiency anemia .[16] Iron deficiency anemia in patients with OSMF could be related to the precancerous nature of this condition. Anuradha and Devi [17] have suggested that decreased iron levels in oral submucous fibrosis patients might be due to utilization of iron in collagen synthesis. In the present study, OSMF group shows significant lower levels of hemoglobin and serum iron on comparison with the values of the control group, which is consistent with results reported by Anuradha and Devi 17, and Khanna and Karjodkar 18and Hegde et al . Cytochrome oxidase is an iron-dependent enzyme which is required for the normal maturation of the epithelium. In iron deficiency state, the levels of cytochrome oxidase are low, consequently leading to epithelial atrophy. An atrophic epithelium makes the oral mucosa vulnerable to the soluble irritants.19 Fibrosis dictates that OSMF is basically a disorder of collagen metabolism. Hydroxyproline is an amino acid found only in collagen, which is incorporated in the hydroxylated form. This hydroxylation reaction requires ferrous iron and ascorbic acid. Utilization of iron, for the hydroxylation of proline and lysine, leads to decreased serum iron level.18 In OSMF patients, there is an increase in the production of highly cross-linked

Insoluble collagen type I, loss of more soluble procollagen type III and collagen type VI. The cross-linking of collagen due to the upregulation of lysyl oxidase plays a crucial role in the development and progression of the condition .[20]

From the above discussion, it is evident that a suggestively significant lower level of hemoglobin and serum iron can be accepted in stage II OSMF patients than in stage I, concluding that serum iron levels also deplete as disease progresses. Serum iron content can be a predictor for the progression of the condition. There appears an association between serum iron content and oral carcinogenesis.

It is documented that patients with severe iron deficiency condition, known as sideropenic dysphagia, are at a higher risk of developing oral carcinoma, post cricoid carcinoma and esophageal carcinoma. Though OSMF is a clinically benign condition, it is a potentially malignant disorder. Malignant transformation rate of OSMF has been reported to be around 7.6% over a 17-year period.

Although OSMF and iron deficiency anemia exist as separate conditions, the clinical findings of OSMF mimic those of iron deficiency anemia, which includes blanching, burning sensation, and dysphagia. Due to a qualitative and quantitative defect in the oxygen and nutrient perfusion of the lamina propria and the overlying mucous membrane histologically, epithelial atrophy occurs. The effect of soluble irritants on the atrophic epithelium, which ensues in due course, leads to malignancy. Thus, this unclear line of demarcation still persists, which calls upon for further extensive studies to understand the correlation between

OSMF and iron deficiency as well as the validation of serum iron levels in various stages of OSMF, as an indicator of malignant transformation.

Conclusion: The present study shows the serum iron assessment for patients with oral submucous fibrosis. Determining iron status is a part of biochemical assessment, which may be of proactive intervention for high-risk groups. It is suggested that the biochemical assessment of oral precancerous conditions may help in early diagnosis and prognosis. It is also of key importance that iron therapy should be instituted parallel with the initial diagnosis along with a proper balanced diet, as a part of the overall treatment of oral submucous fibrosis with other modes of treatment. This helps to stop the further progression of the condition.

Chart 1:

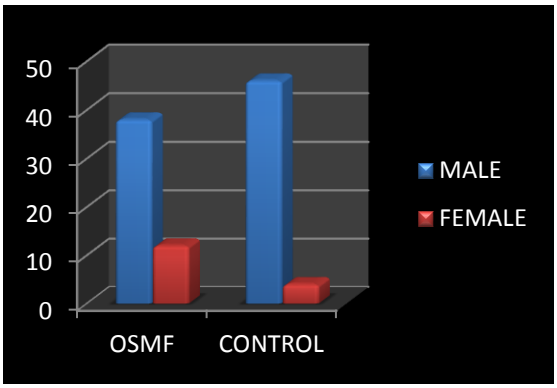


Chart 2:

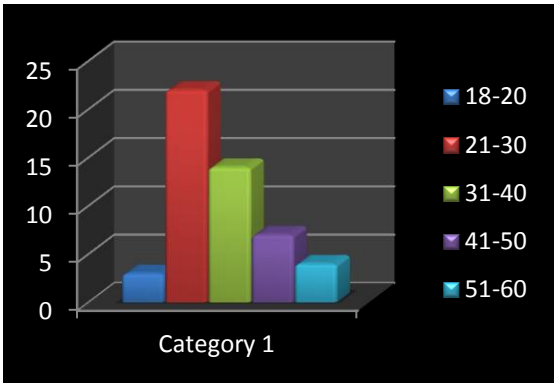


Chart 3:

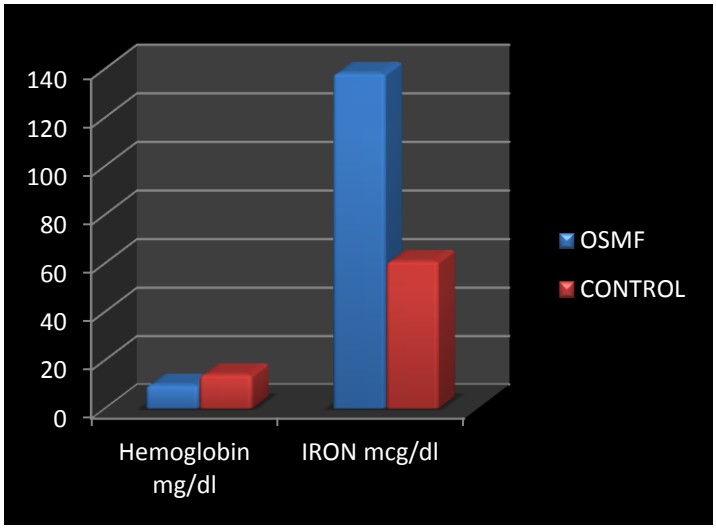
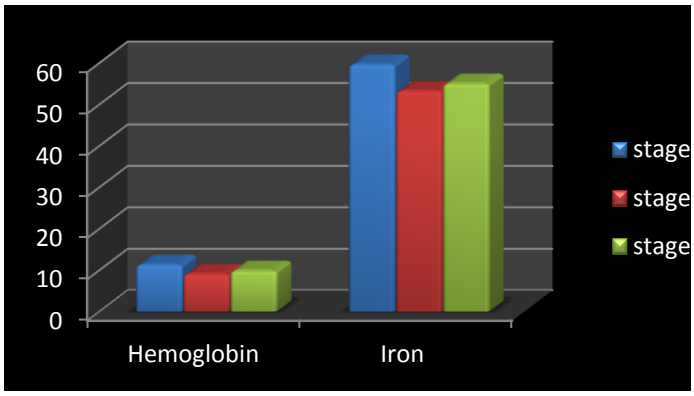


Chart 4:



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