

Oral submucous fibrosis and iron deficiency anemia: A clinical study

¹Dr. Anjana, PG Student, Department of Oral Medicine and Radiology, Rama Dental College, Hospital and Research Centre

²Dr. Rahul Srivastava, Professor, Department of Oral Medicine and Radiology, Rama Dental College, Hospital and Research Centre

³Dr. Vishal Mehrotra, Prof & HOD, Department of Oral Medicine and Radiology, Rama Dental College, Hospital and Research Centre

⁴Dr. Kriti Garg, Reader, Department of Oral Medicine and Radiology, Rama Dental College, Hospital and Research Centre

⁵Dr. Shivi Rajput, PG Student, Department of Oral Medicine and Radiology, Rama Dental College, Hospital and Research Centre

⁶Dr. Swati Dixit, PG Student, Department of Oral Medicine and Radiology, K.D. Dental College & Hospital Mathura

Corresponding Author: Dr. Anjana, PG Student, Department of Oral Medicine and Radiology, Rama Dental College, Hospital and Research Centre.

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Abstract

Background: Oral submucous fibrosis (OSMF) is a potentially malignant disorder and crippling condition of oral mucosa. It is a well-known chronic disease that is sneaky, precancerous, autoimmune, collagen-related, and multifactorial in origin. It is characterised by gradual hyalinization of the lamina propria and is linked to eating betel nut. Substantial haematological abnormalities are brought on by it, which lead to anemia and a drop in blood iron levels.

Methods: The total number of participant in study were 100 and age ranging from 20 to 50 years old either sex. 50 patients clinically diagnosed with OSMF and without any other systemic disease constituted the study group , 50 healthy subjects constituted the control group. Hemoglobin and serum iron levels were estimated by Sahli’s and Ferrene methods respectively.

Results: The OSMF group showed significantly lower levels of Hemoglobin and serum iron in comparison with the healthy control group. The above results establish the fact that serum iron level is an important marker for

OSMF and the levels of which could be used to predict the prognosis and progression of the condition to malignancy with greater accuracy.

Conclusion: The finding of the present study focusses on the assessment of hemoglobin and serum iron for patients with oral submucous fibrosis. Also iron therapy should be instituted concomitantly with the initial diagnosis which helps to cease the further progression of the condition. Further extensive studies are indicated to understand the correlation between Oral submucous fibrosis and iron deficiency anemia.

Keywords: Oral Submucous Fibrosis, Iron Deficiency Anemia, Serum Hemoglobin, Serum Iron.

Introduction

Oral submucous fibrosis (OSMF), also known as atropica idiopathica (tropica) mucosae oris, was initially identified by Schwartz in 1952 in five East African women of Indian descent. It is a chronic, progressive, debilitating, scarring, and precancerous disorder of the oral mucosa. Other names for it include diffuse oral submucous fibrosis, idiopathic palatal fibrosis, sclerosing stomatitis, and submucous fibrosis of the palate and pillars.¹ OSMF has been documented in the Indian population since the time of Sushruta- a renowned Indian physician (circa sixth century BCE) as Vidari, the features of which simulate.²

Submucous fibrosis is an insidious, chronic disease affecting any part of the oral cavity and sometimes the pharynx. Occasionally it is preceded by and/or associated with vesicle formation and is always associated with a juxta-epithelial inflammatory reaction followed by progressive hyalinization of the lamina propria. The later subepithelial and submucosal myofibrosis leads to stiffness of the oral mucosa and deeper tissues with progressive limitation in opening of the mouth and protrusion of the tongue, thus causing

difficulty in eating, swallowing and phonation. Epithelial atrophy is marked in advanced stages of the disease.³

Apparent divergencies in these characteristics between groups of patients in different studies raised the question whether OSMF should be considered as one, or more than one disease. Although the evidence that it predisposes to cancer is not yet absolutely conclusive, it is highly probable that this relationship exists. The WHO definition for an oral precancerous condition-a generalized pathological state of the oral mucosa associated with a significantly increased risk of cancer- accords well with the characteristics of OSMF.³ The condition known as OSMF is also referred to as an Asian form of sideropenic dysphagia, in which a persistent iron shortage makes the mucosa more sensitive to irritants like areca nut products.⁴

Hemoglobin levels as well as serum iron levels, are considered as biochemical indicators for nutritional assessment.^{5,6} The goal of the current study is to understand the relationship between OSMF and iron deficiency anaemia by measuring the haemoglobin and serum iron levels in patients with oral submucous fibrosis and comparing the results to those of healthy individuals.

Materials and Methods

This study was done at the outpatient Department of Oral Medicine and Radiology at Rama Dental College Hospital and Research Centre, Kanpur. The present study was approved by the Institutional Review Board of our college. The aim of the study was briefed to the participants, and thereafter, written informed consent was obtained from them. The total number of participants who agreed to take part in the study were 100 and age ranging from 20 to 50 years old either sex. 50 patients clinically diagnosed with OSMF and without any other systemic disease constituted the study

group, 50 healthy subjects constituted the control group. Hemoglobin and serum iron levels were estimated by Sahli's and Ferrene methods respectively. This study was conducted over a period of 2 years in clinically diagnosed patients of OSMF. 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 included in the OSMF group.

Exclusion criteria

Patients with any systemic complications, suffering from any major illness, Habit of chewing only tobacco, Patients with habit chewing areca nut or one of its commercial preparations but without OSMF. Fifteen healthy individuals, 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 were excluded from the control group. Institutional ethical clearance and informed consent was obtained from the individuals who participated in the study. Five mL of fasting venous blood was 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.

Results

The OSMF study group patients were comprised of 50 patients of age group ranging from 20 to 50 years with a mean age of 19.48 ± 9.81 years. The mean hemoglobin levels in control group were $14.2 \pm$ mg/dl, whereas those of OSMF group were $10.50 \pm$ mg/dl. Comparison of the hemoglobin levels between control group and the OSMF patients showed highly significant difference ($p < 0.001$, Student's t test). (Table 1)

Table 1: Comparison of the hemoglobin levels between control group and the OSMF patients using student's t test.

Group	Cases (n)	Hb levels (Mean \pm S D)	P value
Control group	50	$14.2 \pm$	$P < 0.001^*$
OSMF group	50	$10.50 \pm$	

* Significant

The serum iron levels in control group were $139.22 \pm$ and in OSMF patients were $66.29 \pm$. Comparison of the serum iron levels between control group and the OSMF patients also showed highly significant difference ($p < 0.001$, Student's t test). (Table 2)

Table 2: Comparison of the serum iron levels between control group and the OSMF patients using student's t test.

Group	Cases (n)	Serum iron levels (Mean \pm SD)	P value
Control group	50	$139.22 \pm$	$p < 0.001^*$
OSMF group	50	$66.29 \pm$	

* $P < 0.001$ = statistically highly significant. SD = Standard deviation.

Discussion

Oral submucous fibrosis is a chronic, insidious oral mucosal condition which occurs predominantly in younger individuals of Asia and India. In India alone, around 5 million people are suffering from OSMF.⁷ The incidence rate of OSMF is increasing in India due to the high demand of areca nut in the form of pan masala and increase in the uptake of this habit by young people due to easy access and good market strategies.⁸

When OSMF was first described in 1952, it was classified as an idiopathic disorder. Later on many researchers put forward various hypothesis suggesting that OSMF is multifactorial origin with possible etiological factors to date are areca nut, capsaicin in

chilies, micronutrient deficiencies of iron, zinc and essential vitamins. In addition, a possible autoimmune basis to the disease with demonstration of various autoantibodies and an association with specific HLA antigens has also been proposed.²

It has been suggested that oral submucous fibrosis is caused due to the action of arecoline. Arecoline not only stimulates fibroblast proliferation and collagen synthesis, but also decreases its breakdown by forming more stable collagen structure. So there is more collagen availability leading to OSMF.⁴

Soluble irritants, such as alkaloids present in areca nut act as initiating factors causing a juxta-epithelial inflammatory reaction thus leading to burning sensation, vesiculation and ulceration of the oral mucosa, which renders a phase for difficulty in consumption of the normal diet leading to poor nutrition. Deficiency of Vitamin B complex, iron and 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 pre-existing pathologic response of the lamina. After a frank establishment of the lesion, anemia may further perpetuate by inadequate intake of food due to fibrosis and trismus, thus becoming a vicious cycle.^{6,9}

Nutritional deficiencies, primarily of iron and vitamins, are implicated in the etiology of OSMF. 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.^{4,9} Hemoglobin levels, in particular serum iron levels, are considered as biochemical indicators for nutritional assessment.^{5,9,10} In the present study, OSMF group shows significant lower

levels of hemoglobin and serum iron on comparison with the values of the control group. Studies with similar results are reported by Rupak S et al⁶, Anuradha CD et al¹¹, Hegde K et al⁹, Ganapathy KS et al¹² and Khanna SS et al¹³.

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. 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. 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.^{6,9,10}

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. Epithelial atrophy occurs due to a qualitative and quantitative defect in the oxygen and nutrient perfusion of the lamina propria and the overlying mucous membrane. 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.^{6,9,10}

Conclusion

The measurement of haemoglobin and serum iron in OSMF patients is the primary focus of the current investigation. The biochemical evaluation of oral precancerous situations is said to aid in early detection and prognosis. Also, it aids in forecasting the likelihood of cancer, particularly in high-risk populations. As part of the overall management of oral submucous fibrosis with other types of treatment, it is crucial that iron therapy be started concurrent with the first diagnosis along with a good balanced diet. This aids in halting the condition's continued development.

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