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ORIGINAL ARTICLE

A clinical study on role of Haematological Parameters in Oral Sub Mucous Fibrosis

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ABSTRACT

Introduction: The most common presentations include intolerance to spicy food and rigidity of lip, tongue and palate leading to decreased mouth opening; restricted tongue movements; dysphagia and hearing impairment in the advanced stages. **Methods:** 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. **Results:** There was also a very high increase in the eosinophil count in early and advanced OSMF patients compared with the control group value. Similarly, there was a marked increase ($p<0.001$) in the ESR in both patient groups. **Conclusions:** The present study emphasizes on the assessment of the haematological status 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.

Keywords: haematological, oral sub mucous, fibrosis.

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INTRODUCTION:

Since the last decade, there has been constant rise in OSMF in India. This rise in OSMF in India has been attributed to the increased consumption of areca nut, containing detectable levels of trace elements like copper, zinc, iron and magnesium.[1] Various nutritional deficiencies, primarily of iron and vitamins, are also implicated in the etiology of OSMF. Iron plays a vitol role in the overall integrity of epithelia of digestive tract and is essential for normal enzymatic functions. OSMF is also regarded as an Asian version of sideropenic dysphagia, wherein chronic iron deficiency leads to mucosal susceptibility to various irritants.[2] Therefore, nutritional deficiencies like that of iron, Vitamin B-12, and folate can affect the integrity of the oral mucosa. Previous studies indicate significant hematological abnormalities associated with OSMF, including an increased blood sedimentation rate, and a decrease in serum iron and an increase in total iron binding capacity.[3]

The condition is progressive, and patients present with varied clinical presentation depending on the stage of the disease at the time of diagnosis. The most common presentations include intolerance to spicy food and rigidity of lip, tongue and palate leading to decreased mouth opening; restricted tongue movements; dysphagia and hearing impairment in the advanced stages. The trademark of the disease is submucosal fibrosis involving most parts of the oral cavity, pharynx and upper third of the esophagus.[4]

The role of nutritional deficiencies, principally of iron and vitamins, has been proposed in the etiology of OSMF.[5] Significant research has been carried out to emphasize their role in OSMF. Wahi *et al.*[6] reported a significantly higher prevalence of malnutrition in 104 OSMF patients than in 200 normal control participants. Iron has been studied as a diagnostic and prognostic marker in malignancies such as esophageal cancers (Plummer–Vinson syndrome) and postcricoidal carcinoma. Serum levels of iron were found to be significantly altered in oral cancer and PMDs.[7] Vitamin B12 deficiency can cause moderate-to-severe epithelial dysplasia that resolves after correction of the deficiency. Both the trace elements are required for maintaining the integrity of the oral mucosa.[8,9]

Hemoglobin levels, in particular serum iron levels, are considered as biochemical indicators for nutritional assessment.[10] Deficiency of iron, Vitamin B-12, and folate can affect the integrity of the oral mucosa. Significant hematological 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.[11]

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

MATERIALS AND METHODS:

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. Patients with any systemic disease or any major illness, and habit of chewing only tobacco were excluded. The OSMF group was clinically staged into stage I and stage II as per the staging given byPindborg. Twenty 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.

Estimation of iron, hemoglobin and red cell indices

Estimation of iron was done using Ferrene's method. The red cell indices (RCIs) and Hb level were analyzed by? the automated cell counter method. All the test tubes used for analysis were immersed overnight in deionized water and then washed the next day using deionized water. The serum sample used for the estimation was mixed with appropriate proportions of buffer and color reagents supplied in the iron estimation kit in clean, dry test tube as per the manufacturer's instructions. The absorbance of these samples was compared to that of the standard solution provided in the kits at 578 nm in a semi-autoanalyzer (Microlab – 200). Bucheon-si;Gyeonggi-do :South Korea.

Estimation of Vitamin B12 was done by the chemiluminescent microparticle intrinsic factor assay for the quantitative determination of Vitamin B12 in human serum method.

Statistical analysis

Statistical procedure was carried out using the IBM SPSS Statistics for Windows, version XX (IBM Corp., Armonk, N.Y., USA)'. The mean values and standard deviations for all the groups were calculated by Chi-square test. Normality of various parameters in the control and study groups was assessed by Kolmogorov–Smirnov test. Independent *t*-test was used to compare more than two means simultaneously, that is, whether there was a significant difference between the mean values of serum iron, Vitamin B12 and Hb among the two groups. Correlation analysis among various parameters in the control and study groups was done by Karl Pearson's correlation coefficient method. A logistic regression analysis was performed to predict which hematological variable was more significant for OSMF. The level of significance was fixed at $P < 0.05$.

RESULTS:

The data was subjected to a statistical analysis by using mean, standard deviation and the Student's unpaired 't'-test. There was no significant change in the RBC and WBC count in any stage of the disease between patients and controls. There was also a very high increase in the eosinophil count in early and advanced OSMF patients compared with the control group value. Similarly, there was a marked increase ($p<0.001$) in the ESR in both patient groups. There was a decrease in the hemoglobin level in early OSMF patients and a highly significant decrease advanced OSMF patients when their levels were compared to the control ones.

	Group I (Early OSMF)	**Group II (Advanced OSMF)**	**Normal control**
Red Cell Count ($X10^6$ /µl blood)	6.22±.6 (NS)	6.41±1.4 (NS)	6.21±1.8
White Cell Count ($X 10^3$ /µl blood)	7.21±3.0 (NS)	9.00±1.3 (NS)	8.91±4.0
ESR (mm/h)	8.0±1.3***	16±4.1***	3.1±.4
Hb (g/dl)	14.3±1.8***	14.2±1.9**	16.3±3.1
MCV (µm^3 cell) / red	81.4±5.3***	91.3±5.4	91.1±6.0
MCH (pg/RB C)	27.2±3.6***	25.8±3.8**	30.1±3.8
MCHC (g/dl RBC)	35.1±3.4***	28.1±1.4**	33.1±3.6
PCV (%)	42.1±5.2 (NS)	50.1±3.4 (NS)	50.3±3.8

Values are expressed as the mean ± SD for 20 patients in each group.Group I and Group II were compared with normal control group. NS: Non Significant. ***p<0.001

DISCUSSION:

In the Indian continent alone, the statistics for OSMF is about 5 million people (0.5%) of the population.[12] Examination of the blood picture is performed in almost all patients with illness because of the importance of determining alterations that may be present in it.[13] The Non significant change in normal red cell count and white cell count agree with those of earlier studies.[13,14] Since OSMF is characterized by juxtaepithelial inflammatory reaction, the increased level of eosinophils may be due to inflammatory reactions, which are evident in OSMF patients.[9] Decrease in hemoglobin levels indicate iron deficiency state. Our results were in correlation in previous studies with also recorded a decrease in Hb conc. in OSMF patients.[13,15]

The PCV in OSMF patients was normal. The PCV is the portion of blood occupied by erythrocytes and since the red cell count is normal in these patients, it explains the normal hematocrit value. The decrease in MCV suggests microcytic anemia. As the degree of iron deficiency increases, so is the Hb conc, and further MCV. Previous studies also indicate that most of the iron deficiency anemia cases are reported to display microcytosis.[13,16]

OSMF manifests early in gutkha chewers than betel quid chewers due to the presence of higher amount of dry weight tobacco content and absence of betel leaf (has beta carotene which acts as an antioxidant).[17,18] Areca nut induces mechanical abrasion, cytotoxicity and collagen cross-linking of the oral mucosa. The addition of nicotine amplifies the cytotoxicity induced by nicotine, leading to the production of damaged collagen.[19]

The trismus, fibrosis and malignant classification by Arakeri Thomas *et al*.[20] was used in the present study as it helps in classifying the information efficiently, recording the data, proper communication, obtaining prognostic information and also to make it easy to understand the disease characteristics, which can be easily applied by the trainees and clinicians. It is a three-tier staging system, differentiating between medical, surgical and malignant disease therapy.

From the aforementioned 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, postcricoid carcinoma and esophageal carcinoma. Though OSMF is a clinically benign condition, it is a potentially malignant disease. Malignant transformation rate of OSMF has been reported to be around 7.6% over a 17-year period.[21]

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 emphasizes on the assessment of the haematological status 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 analysis can be helpful in mass screening of the OSMF patients. Further research work is required in this field to find out the exact role which these parameters play in the pathogenesis of OSMF.

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