be given by serum ferritin, though this was not assessed in the current investigation. The TIBC was also reported to be a better index to assess the nutritional status of iron.[14]

Anemia and deficiencies of vitamin B complex have long been known to cause persistent glossitis and stomatitis.[20] In patients with OSMF the blood sedimentation rate is reported to be elevated,[21] and anemia is often present.[22] Ramanathan[11] has postulated that OSMF is caused by chronic iron deficiency. It is well known that the incidence of OSMF is high in developing countries where nutritional deficiency is common.[12] In the present study iron deficiency anemia was found not only in OSMF but also in OLKP. This cannot be due to malnourishment alone, since the controls were also from the same socio-economic group.

The serum protein values, which are normally taken as biochemical indicators for nutritional assessment,[23,24] showed a significant depression in OSMF even as compared to patients with OLKP. The percentage saturation of transferrin was found to be significantly low in the OSMF patients, but in OLKP the values were almost within the normal range. This highly unsaturated transferrin shows the severity of anemia in those patients. The hematological abnormalities noticed in OSMF patients may be a reflection of the hypoprotenemia observed in them. This study suggests that iron deficiency anemia may be a factor which predisposes an individual to OSMF.

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SERUM LEVELS OF IRON AND PROTEINS IN ORAL SUBMUCOUS FIBROSIS (OSMF)

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ABSTRACT

Serum proteins, serum iron and total iron binding capacity were estimated in 50 patients with oral submucous fibrosis and 50 patients with oral leukoplakia. The values were compared with that of 50 age- and sex-matched controls. A significant depression in hemoglobin and serum iron was observed in both groups of patients, whereas total iron binding capacity showed significant change only in the oral submucous fibrosis patients. Serum protein values were significantly lower in all the patients. The role of iron deficiency anemia in the causation of this premalignant lesion is discussed.

Abbreviations Used:

OLKP – Oral Leukoplakia; OC – Oral Cancer; OSMF – Oral Submucous Fibrosis; TIBC – Total Iron Binding Capacity.

Introduction

A major health problem in Southeast Asia is oral cancer, with more than a hundred thousand new cases each year.[1] A very high incidence of oral cancer (OC) has been reported from Kerala, India compared to other parts of the world.[2] Recently a highest site specific incidence rate for oral cancer (ICD 140-145) was observed in Kerala.[3] Similarly, the incidence of precancerous oral lesions such as oral leukoplakia (OLKP) and oral submucous fibrosis (OSMF) is also very high in this area.[4,5] The etiology of this high incidence is not fully known. Many factors have been implicated, such as chewing and smoking tobacco,[6] and viral infections.[7] According to WHO,[1] approximately 90% of oral cancers in this region are caused by tobacco chewing and/or smoking.

It has been speculated that OC arises more in people of low socio-economic strata and almost invariably in a pre-existing precancerous lesion, namely OLKP or OSMF.[8] No definite causative factors are known to date for the high prevalence of OSMF. Two factors in the etiology of OSMF have been already identified by Canniff et al.,[9] viz., a genetic predisposition and the use of betel nut. The high incidence of OSMF may be one of the reasons for the increased occurrence of OC noted in this area. An immunological derangement similar to that of OC was noted in OSMF by Rajendran et al.[10]

Ramanathan[11] had suggested that OSMF is the Asian version of sideropenic dysphagia (Patterson-Kelly syndrome). According to him prolonged iron and B complex deficiency alters the oral mucosa leading to changes similar to OSMF. The low nutritional status of people of this area lends further credence to this hypothesis.[12] Studies on the hematological and biochemical changes, especially iron and protein levels in OSMF, are scanty. Hence the present study was undertaken to evaluate the hematological changes, if any, in patients suffering from OSMF. Since proteins play an important role in the metabolism of iron, an attempt was also made to study the serum protein profile of these patients.

Materials and Methods

Fifty patients with OSMF and 50 patients with OLKP were selected for the study. There was an equal number of males and females in both groups of patients. Only histopathologically proved cases were selected. For comparison of the results, 50 age- and sex-matched controls were also included. None of the subjects was suffering from any systemic diseases, liver or renal diseases and/or infections, and none had

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blood was collected from all the subjects. 1 ml was collected in heparinized tubes for hemoglobin (Hb) estimation by Cyan-Meth hemoglobin method[13] and the remaining 9 ml was allowed to clot. Serum was separated and the following investigations were carried out:

1. Serum total protein by Biuret method.
2. Serum albumin using bromocresol green and
3. Serum iron and Total Iron Binding Capacity (TIBC) by Bathophenanthroline method.[14]

From these values serum globulins, albumin/globulin ratio and the percentage saturation of transferrin were calculated. The statistical evaluation of the results were carried out by the student's 't' test.

Results

There was an equal number of males and females in all the three groups, viz., normal control, OLKP and OSMF. The average age of the subjects varied from 36.2 – 41.5. The serum protein profile of all the subjects is given in Table 1. The total protein and albumin values of both OLKP and OSMF patients were significantly lower than that of the normal control ($P<0.05$). Even though the globulin values of OSMF patients were also lower than that of the normal control and OLKP patients, the difference was not significant. The total protein and serum albumin values of the OSMF patients were lower ($P<0.05$), even compared with OLKP. Sex had no influence in the serum protein profile of the patients.

The hemoglobin (Hb) and serum iron of the OSMF patients were significantly lower than those of the normal controls ($P<0.05$). The TIBC of the OSMF patients showed a significant elevation ($P<0.05$). The percentage saturation of transferrin of the OSMF patients was significantly lower ($P<0.001$). In the case of OLKP the reduction in Hb, serum iron and percentage saturation of transferrin was significant ($P<0.05$) from that of the normal controls. TIBC did not show much variation. These differences were observed in both male and female patients (*Table* 2). In the case of OSMF patients, except for the TIBC in males, all other factors were significantly altered compared to the corresponding values of the OLKP patients.

TABLE 1

Changes in serum proteins in patients and in control subjects.

Subjects	Total proteins gm/dl	Albumin gm/dl	Globulin gm/dl	A/G Ratio
1. Normal control (NC), n = 50	6.5 ± 0.06	3.9 ± 0.07	2.6 ± 0.05	1.5
2. Oral Leukoplakia (OLKP), n = 50	6.2 ± 0.09*	3.6 ± 0.07*	2.6 ± 0.05	1.4
3. Oral Submucous Fibrosis (OSMF), n = 50	5.8 ± 0.10*	3.4 ± 0.08*	2.4 ± 0.09	1.4

n = number of subjects. All values are Mean ± SE.
*P<0.05 (comparison was made with the values of NC) (values of OSMF were significant even compared to OLKP

TABLE 2

Hematological changes in patients with OSMF and OLKP.

Subjects	Hb gm/dl	Serum iron µgm/dl	TIBC µgm/dl	% saturation
1. NC				
M (n = 25)	13.5 ± 0.3	131 ± 2.2	370 ± 3.4	35.4 ± 1.5
F (n = 25)	12.1 ± 0.25	123 ± 2.2	361 ± 2.9	34.1 ± 1.7
2. OLKP				
M (n = 25)	11.4 ± 0.18*	105 ± 3.2*	377 ± 3.7	27.8 ± 1.9 †
F (n = 25)	10.3 ± 0.25*	98.5 ± 2.1*	363 ± 4.0	26.9 ± 1.3 †
3. OSMF				
M (n = 25)	10.0 ± 0.03*	64.6 ± 1.9*	382 ± 3.3*	16.9 ± 1.1 ‡
F (n = 25)	9.4 ± 0.06*	61.7 ± 2.1*	393 ± 2.9*	15.7 ± 0.09‡

n = number of subjects. All values are Mean ± SE. All comparisons were made with that of the control.
* = P<0.05 † = P<0.01 ‡ = P<0.001

Discussion

It has been established that anemia or deficiencies of vitamin B_{12}, folate and iron can all affect the oral mucosa.[15] The mean epithelial thickness is significantly reduced in iron deficient patients,[16] and such patients might be particularly susceptible to a variety of oral diseases. The accuracy of diagnosing hematological abnormalities in oral disease has recently been the subject of some controversy.[17] It is accepted that true iron deficiency is difficult to diagnose since the serum iron shows diurnal variation and the iron binding capacity is not a very accurate test;[18] thus the percentage saturation (which is a ratio of serum iron and TIBC) is rather variable. A low serum iron may be the sideropenia of chronic disease and certainly seems to be true in many ulcerative oral diseases.[19] This lends further credence to our hypothesis that iron deficiency anemia is the cause and not the effect of