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Assessment Of Hemoglobin Levels in Patients with Potentially Malignant Disorders and Oral Cancer

Research Article

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Abstract

Potentially malignant disorders (PMD) of the oral cavity are a group of lesions with risk of malignant transformation progressing to invasive cancer. Most common PMD's include leukoplakia, lichen planus, oral submucous fibrosis. Both oral cancer and PMDs remain a cause of serious concern despite intensive research and development. Micronutrients like iron plays a vital role and if not present in sufficient levels can `contribute to pathogenesis and progression of these lesions.The aim of the present study is to assess the hemoglobin levels in PMD and oral cancer patients of Saveetha dental College and hospitals, Chennai.The study was carried out from June 2019 to April 2020 on 33 patients (20 males and 13 females) who visited Saveetha dental College and Hospitals,Chennai. Data collection included age, gender, hemoglobin levels of PMD and Oral cancer patients and association between these were obtained using pearson's chi-square test . One-way ANOVA was done to compare between anemic and non anaemic groups between different potentially malignant disorders and oral cancer. In this study we observed that majority of males (59%) had reduced haemoglobin levels. 41% patients with oral cancer are anaemic compared to PMD. Among PMD, oral submucous fibrosis patients had decreased mean value of haemoglobin which was 9.8 ± 1.52 mg/dl, p-0.003($p<0.05$) was statistically significant, followed by oral lichen planus 10.7 ± 0.801mg/dl, p-0.004($p<0.05$).51 to 65 years(18.18 %) had majority of anaemic patients. p value=3.49, not statistically significant. Within the limitation of the study older patients and males are most anaemic. Majority of Oral cancer patients had reduced haemoglobin levels, among PMD, OSMF were most anaemic due to reduced mean hemoglobin level.

Keywords: Anaemic; Hemoglobin; Oral Cancer; Potentially Malignant Disorders; Oral Submucous fibrosis.

Introduction

According to the world health organisation (WHO) "the risk of malignancy being present in a lesion or condition either at the time of initial diagnosis or at a future date" are termed as potentially malignant disorders (PMD's) [1, 2, 3] Prevention and early detection of PMD's have the potential of not only decreasing incidence but also improves survival rate of oral cancer [4, 5].

Oral cancer is the sixth most common cancer worldwide. The development of PMDs and oral cancer is a multistep process with several modifying factors like diet and immunity [6]. Micronutrients like iron is an integral component in the subject of recent studies focused on eliciting their role in pathogenesis and progression of the lesions.

Oral Submucous Fibrosis (OSMF) is defined as "An insidious chronic disease affecting any part of the oral cavity and sometimes the pharynx. 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" [7]. According to pindborg classification, Stage 1 is Stomatitis includes ery-

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thematous mucosa, vesicles, mucosal ulcers, melanotic mucosal pigmentation and mucosal petechiae. Stage 2 is Fibrosis occurs in healing vesicles and ulcer, Early lesions demonstrate blanching of oral mucosa. Older lesions include vertical and circular palpable fibrous bands in the buccal mucosa and around the mouth opening or lips, resulting in a mottled marble-like appearance of the mucosa with shrunken bud like uvula. Stage 3 is Leukoplakia is found in more than 25% of individuals with OSMF and speech and hearing deficits may occur because of involvement of the Eustachian tubes [8]. It is characterised by blanching and stiffness of the oral mucosa leading to progressive limitation of mouth opening and intolerance to hot and spicy food [9, 10]. Haematological abnormalities have been reported in oral submucous fibrosis [11].

Oral leukoplakia definition given by WHO "white plaques of questionable risk having excluded (other) known diseases or disorders that carry no increased risk for cancer." Leukoplakia is the most common PMD.Tobacco,anatomical location and size of the lesion are indicators of high risk and contribute to the progression of oral leukoplakia into cancer [12]. Biopsy is essential to confirm the provisional clinical diagnosis, and timely referral to a specialist is indicated.

Oral lichen planus (OLP) is a chronic inflammatory mucocutaneous disease that frequently involves the oral mucosa. Lichen planus shows an imbalance of iron content which is important in pathogenesis of these disease [13]. Patients with Lichen planus may be at a greater risk of developing oral cancer,irondeficiency. The clinical findings often show inflammatory and atrophic changes in mucous membranes, as well as immunodeficiency states. Altered iron is detected in oral cancer and precancerous conditions [14]. It may cause significant abnormalities of blood such as anemia and a decline in serum iron levels [15, 16]. Diet low in micronutrients such as iron can be a risk factor in progression and pathogenesis of oral potentially malignant disorders and oral cancer [17]. Prognosis depends on investigation of haematological parameters such as haemoglobin in the earlier stage of disease, hence the present study aimed to assess the level of haemoglobin,its anemic status in oral potentially malignant disorders and oral cancer patients.

Materials and Methods

Study designs and Study setting

The present study was conducted in a university setting (Saveetha dental college and hospitals, Chennai, India). Thus the data available is of patients from the same geographic location and have similar ethnicity. The retrospective study was carried out with the help of digital case records of 33 patients who reported to the hospital. Ethical clearance to conduct this study was obtained from the Scientific Review Board of the hospital. The ethical approval number for the present study is SDC/SIHEC/2020/DIASDATA/0619-0320.

Sampling

Data of 33 patients (20 males and 13 females) were reviewed and then extracted. All patients with lichen planus, leukoplakia, OSMF and oral cancer in the given duration of time period were evaluated for hemoglobin levels. Only relevant data was included to minimize sampling bias. Simple random sampling method was carried out. Cross verification of data for error was done by presence of additional reviewer and by photographic evaluation. Incomplete data collection was excluded from the study.

Data Collection

A single calibrated examiner evaluated the digital case records of patients who reported to Saveetha Dental College from June 2019 to March 2020. For the present study, inclusion criteria was data of patients with Potentially malignant disorders and oral cancer. Data obtained were age, gender, types of PMD and oral cancer, hemoglobin values. All obtained data were tabulated into Microsoft excel documents.

Statistical analysis

The collected data was tabulated and analysed with Statistical Package for Social Sciences for Windows, version 20.0 (SPSS Inc., Vancouver style) and results were obtained. Categorical variables were expressed in frequency and percentage. Chi square test was used to test association between categorical variables. Chi square tests were carried out using age, gender and as independent variables and dependent variable. The statistical analysis was done by pearson chi square test. P value < 0.05 was considered statistically significant.

Results and Discussion

Descriptive study done on study population shows distribution of type of PMDs and oral cancer in Figure 1. Patients with lichen planus were 30.30 %, leukoplakia were 15.15 % OSMF were 30.30 % and oral cancer were 24.24%. Distribution of males and females is shown in Figure -2. Patients with PMDs and oral cancer were predominantly higher in 50.61% males compared to 39.09 % females. Association of Type of PMDs and oral cancer based on gender is shown in figure-3. 9.09% males and 21.21 % females in lichen planus,12.12% males and 3.03 % females in leukoplakia, 21.21% males and 9.09% females in OSMF and 18.18 % males and 6.06 % females in oral cancer. (Chi-square value=1.034; p value=2.385) Association of age and hemoglobin levels of PMDs and oral cancer patients is shown in Figure -4. 6.06% anaemic and 6.06 % non-anaemic patients were in the age group between 20-35 years. 15.15 % anaemic and 12.12 % non-anaemic patients were in the age group between 36-50 years. 18.18 % anaemic and 24.24 % non-anaemic were in the age group between 51-65 years.12.12 % anaemic and 6.06 % non-anaemic in the age group between 66-80 years. (Chi--square value = 1.034; p value=2.385).

Association of gender and Anaemic patients is shown in Figure-5. 30.30% anaemic and non-anaemic among males and 21.21 % anaemic and 18.18 % non-anaemic among females. (Chi--square value=5.475; p value=0.30).

Association of type of PMDs and oral cancer based on anaemia is shown in Figure- 6. 12.12 % anaemic and 18.18 % non-anaemic patients were among Lichen planus. 6.06 % anaemic and 9.09 % non-anaemic patients were among Leukoplakia,12.12 % anaemic and 18.18% non-anaemic in OSMF and 21.21 % anaemic and 3.03% non-anaemic in oral cancer (Chi- square value=0.047; p value=3.49). Mean hemoglobin value of anaemic patients with

Figure 1. Bar graph shows frequency distribution of potentially malignant disorders (PMDs) and oral cancer. X-axis denotes type of PMDs and oral cancer. Y-axis denotes the number of patients with PMDs and oral cancer. Highest prevalence among the PMDs were lichen planus (yellow) and OSMF (peach)30.3% each followed by oral cancer (green) 24.24%.

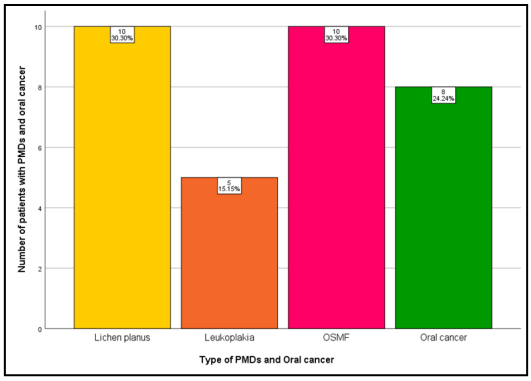


Figure 2. Pie-chart shows distribution of gender variation with PMDs and oral cancer.Grey denotes males and Purple denotes females.Majority of the patients affected with PMD and oral cancer were males compared to females.

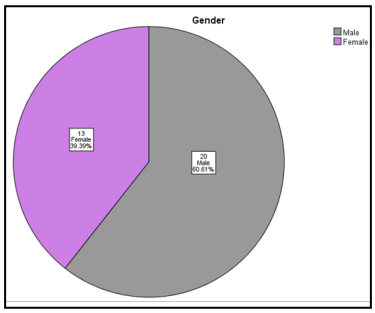


Figure 3. Bar graph shows the association of Type of PMDs and oral cancer based on gender The x-axis denotes Type of PMDs, oral cancer and y-axis denotes number of patients with PMDs and oral cancer.Majority of the patients were males (grey) in OSMF and females (purple) in lichen planus in PMD patients.(Chi--square value=1.034;p value=2.385) ,statistically not significant.

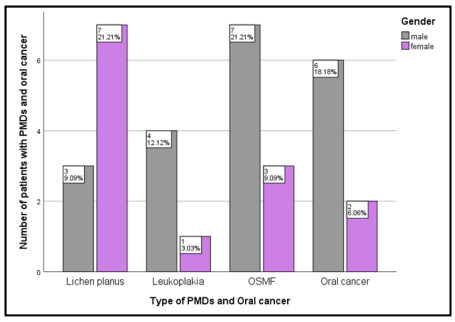


Figure 4. Bar graph shows association between age and anaemic status of PMD and oral cancer patients. X-axis denotes age and y-axis denotes number of patients with PMD and oral cancer based on haemoglobin level. Anaemia was present (blue) in majority of patients in the age group of 51-65 years with PMD and Oral cancer .Using chi square test,the association of age and hemoglobin levels is not statistically significant.(Chi--square value=1.034;p value=2.385).

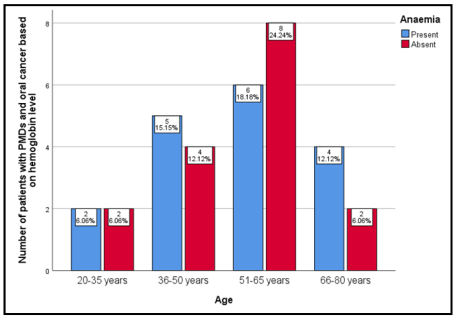


Figure 5. Bar graph shows association between gender variation andanaemic status of PMD and oral cancer patients.The x-axis denotes gender and y-axis denotes number of patients with PMDs and oral cancer based on hemoglobin level.Anaemia was present (blue) in majority of patients among males compared to females with PMDs and Oral cancer.(Chi--square value=5.475 ;p value=0.30),statistically not significant.

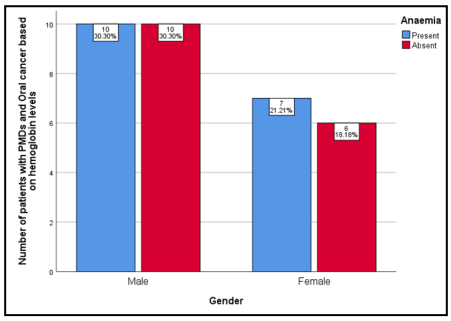


Figure 6. Bar graph shows the type of PMDs and oral cancer and anaemic status. X-axis denotes type of PMDs and oral cancer and Y-axis denotes number of patients with PMDs and oral cancer based on hemoglobin level. Anaemia was present (blue) in majority of patients with Oral cancer when compared to PMDs (Chi- square value= 0.047;p value=3.49) statistically not significant.

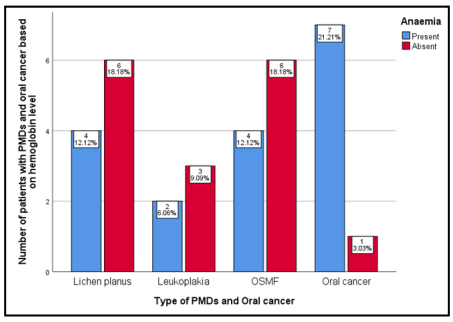
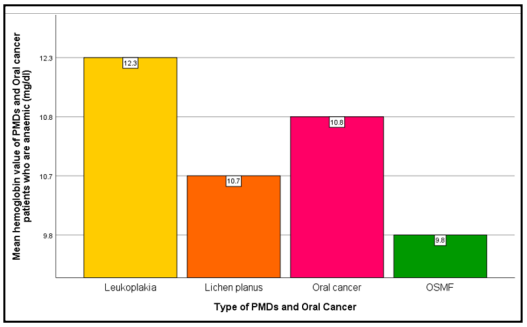


Figure 7. Bar graph shows distribution between mean hemoglobin in anaemic patients with PMDs,oralcancer.X-axis denotes type of PMDs and oral cancer and Y-axis denotes the mean value of hemoglobin in PMDs and oral cancer who are anaemic. Mean value of haemoglobin was lowest in OSMF(green) compared to other PMDs and Oral cancer.



PMDs and oral cancer is shown in Figure-7.According to One Way ANOVA,Mean hemoglobin value is 12.3 ± 1.20mg/dl, p-0.207 ($p<0.05$), was not statistically significant in leukoplakia, 10.7±0.801mg/dl, p-0.004 ($p<0.05$)mg/dl was statistically significant in lichen planus, 10.8±1.95mg/dl, p-0.229($p>0.05$) mg/dl was statistically not significant in oral cancer and 9.8±1.52 mg/dl, p-0.003 ($p<0.05$)was statistically significant in OSMF.

Patients who reported with lichen planus were more than the other patients with PMD and oral cancer. Male (50.61%) population in the current study were more compared to females (39.09 %). Patients who were anaemicand non-anaemic were in the age group of 51-65 years. Among the study population most of the patients who were anaemic were affected by oral cancer. Females who reported with Lichen planus were comparatively higher than males whereas among the other PMDs and oral cancer number of males reported higher than females. In the current study, patients with Lichen planus, Leukoplakia, OSMF and Oral cancer's hemoglobin levels were assessed. The haemoglobin value for men would be 13.2 mg/dl and women of all ages 12.2mg/dl.,(18).For our study the haemoglobin concentration value taken was 13.5 mg/dl or greater for males and 12 mg/dl or greater for females. The mean hemoglobin value according to one way ANOVA, was more in Leukoplakia,followed by oral cancer, lichenplanus and least is in OSMF compared to the other PMDs.

In the current study 30.33 % patients with lichen planus were included. In a study done by Sergey et al , 85% patients with lichen planus were taken into the study and rest 15 % patients without lichen planus for the reference group [19]. Similarly another study showed haemoglobin level deficiency among 21.9 % of oral lichen planus patients [20]. 30 patients with OSMF were used in the study done by hegdeKarthik et al., [21]. To assess haemoglobin levels ,the current study used 10 patients affected by OSMF.

In Ritutiwari's study in the PMD group (leukoplakia/EOLP/

Table 1. One-way ANOVA was done to compare between anemic and non anaemic status between different potentially malignant disorder and oral cancer.(*- statistically significant).

		N	Mean	Std. Deviation	Minimum	Maximum	F value	Significance value
Lichen planus	Anemic group	4	10.725	0.802	9.7	11.5	15.273	0.004*
	Non - anemic group	6	13.817	1.420	12.5	15.5		
	Total	10	12.58	1.971	9.7	15.5		
Leukoplakia	Anemic group	2	12.35	1.202	11.5	13.2	2.57	0.207
	Non - anemic group	3	13.8	0.866	12.8	14.3		
	Total	5	13.22	1.169	11.5	14.3		
Oral submucous fibrosis	Anemic group	4	9.875	1.526	8.6	11.8	17.688	0.003*
	Non - anemic group	6	14.733	1.931	12.1	16.8		
	Total	10	12.79	3.023	8.6	16.8		
Oral Cancer	Anemic group	7	10.8	1.958	7.3	13.4	1.79	0.229
	Non - anemic group	1	13.6	.	13.6	13.6		
	Total	8	11.15	2.065	7.3	13.6		

OSMF), females were 25% (10) and males formed 75% (30) of the subjects [22]. In the current study of PMDs and oral cancer, number of males were 60.61% [20] and females 39.39 % [13] subjects.

After 50 years of age, prevalence of anemia increases with advancing age and exceeds 20% in those 85 years and older. Anemia occurs more frequently in patients with tumor recurrence, at an advanced stage of disease [23, 24]. Average population age affected with PMD are between 50 to 69 years occurring five years earlier than oral cancer. But in another recent study 5 % of the PMD was seen among the younger age group of 30 years [25, 26].According to WHO, less than 10 % adults who are 65 years and above had anaemia, the prevalence of anaemia increases with increase in age [27-29]. Our study had 35 % patients who were anaemic with PMD and oral cancer in the age group between 51 to 65 years. This is because of increase of other chronic inflammation, renal insufficiency and in relation to oral cavity due to long-term usage of areca nuts.

In Oliver.D et al study, anaemia was more prevalent among men in India of 23.2 % [27]. The current study showed 59 % males were present in the study with reduced haemoglobin levels among PMDs and oral cancer.

In the European Cancer Anaemia Survey (ECAS), 39% of patients were anemic at the time of enrollment in the study, and 67% had anemia during chemotherapy and 12% patients had leukoplakia where the anaemic status was less [30]. In the present study 21.21% of oral cancer patients and 6.06 % of leukoplakia patients were anaemic.

Males (17.4%) were found to have a significantly higher prevalence of oral potentially malignant disorders compared to females. In a review done by Nair et al., [31], the prevalence of oral potentially malignant disorders and oral cancer was found to be more in males.Patients having leukoplakia have a malignant transformation rate of 3.6-7.5 %, while Indians have as low as 0.3 to 0.5 % [32, 33]. Leukoplakias are usually diagnosed after the fourth decade of life. They are more common in males. In our study, lesser cases were anaemic in leukoplakia group. 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 crosslinked insoluble collagen. This could be the reason why the mean haemoglobin level in our study was less in the OSMF group and patients were anaemic. As the stage of OSMF increased, the anaemic status were more as the fibrosis required more iron.

OSMF showed a significant low level of haemoglobin mean value-10.85 mg/dl in a study done by Hegde et al., The current study showed 9.8 ± 1.52mg/dl mean value of OSMF. In lichen planus, the imbalance of iron content in blood serum and in oral fluid of the pathological or adaptive nature has been found, which is of some importance in the pathogenesis of the disease.Our study showed mean value of oral lichen planus as 10.7 ± 0.801mg/dl .

In our study oral cancer were more anaemic compared to PMD due to nutritional deficiency in advanced stages reducing their quality of life,whichinturn can progress the disease from malignancy to invasive cancer. PMD patients can be diagnosed at early stage and periodic nutritional counselling can help prevent the progression to oral cancer.Patients in OSMF nad lichen planus were more anaemic compared to leukoplakia. Limitation of the study is smaller sample size. Further studies need to be done in early detection of haemoglobin levels to prevent further disease progression.

Conclusion

Within the limitation of the study it was observed that males were more anaemic compared to females and 51-65 years had majority of anaemic patients among PMD and oral cancer.Majority of Oral cancer patients had reduced haemoglobin levels. Among PMD patients, OSMF were most anaemic due to reduced mean hemoglobin level. It is of high importance to estimate and investigate the haemoglobin levels for early diagnosis and to prevent further disease progression.

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