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Altered Hematological Profile of Oral Lichen Planus Patients.

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ABSTRACT

The study highlights some salient epidemiological features of oral lichen planus observed in the South Indian population. Despite considering the gender ratio in the population, significant preponderance of the females towards this disease. It is mostly found in the buccal mucosa and the reticular form is most predominant ($p<0.0001$). All forms of OLP have been observed here with inflammatory infiltration form reigning in almost all the cases. Total WBC count, neutrophil and lymphocyte counts are significantly greater in the OLP patients than in the corresponding sex and age matched normal population. The difference in the ESR values of the female OLP patients with the normal females is highly significant ($p<0.0001$). The increase in eosinophil count in the adult males aged 30-60 years is significantly high compared to such non-diseased males. The decrease in haemoglobin level in the OLP patients do not vary to a significant level though. The alteration in the haematological parameters is of pertinent medical implication which has so far not been looked into.

Keywords: epidemiology, oral lichen planus, hematology

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INTRODUCTION

Lichen planus (LP) is a chronic inflammatory, autoimmune disorder that mainly affects the skin and mucous membranes. It is characterized by epithelial basal cell lesion that is mediated by type IV hypersensitivity reaction, which is mediated by T lymphocyte infiltration [1,2]. It occurs in 0.1 - 4% of the general population [3]. 50% patients of these patients have both skin and oral lesions and 25% of them have only oral lichen planus (OLP) (4). Epidemiological data on oral lichen planus have been found to vary widely. Population-based studies performed in Asia, Europe, North America and the Middle East reveal 1 – 3% such patients in their population [5].

OLP shows predominance among females and mainly affects adult patients between their fifth and sixth decades of life (6-9). The most frequently involved oral sites are mucosa of the cheek, tongue and gingiva. The mucosa of the palate and floor of the mouth is rarely affected [6,10,11). The clinical features of OLP are generally polymorphic and usually consist of bilateral and/or multiple symmetric lesions, with manifestation of associated clinical patterns [4,12-14]. Alternation between phases of exacerbation and quiescence has also been reported [13]. Clinically, OLP is classified into six forms [15]: reticular, plaque-like, papular, atrophic, erosive and bullous. The reticular form is the most common, followed by the erosive and atrophic form. Erosive and atrophic forms of OLP manifest painful symptoms and have been associated with possible malignant transformation of lichen planus [6,8,]). The basic histopathological features observed in OLP includes hyperorthokeratosis or hyperparakeratosis, acanthosis, thickening of the spinous layer, liquefaction of the basal layer accompanied by the degeneration of keratocytes (hydropic degeneration) and lymphocyte infiltration of the lamina propria, etc [4,12,13]. OLP also has the potentiality to develop into oral squamous cell carcinoma [5] and the frequency of malignant transformation varies from 0% to 12.5% [2].

The present study aims to assess the prevalence of oral lichen planus with its associated clinical features in South Indian (Kerela) population and to evaluate the chance of OLP with other diseases, if any. This work presents novelty in its depth of analysis of the epidemiology of this disease, especially with respect to the associated haematological parameters which has hitherto not been looked into.

METHODOLOGY

This cross-sectional and observational study was conducted by the Department of Physiology, PMS College of Dental Science and Research, Kerala, India, on 22,252 OLP patients (15938 adults and 6314 children) who attended the out-patient department of the college from January 2012 to April 2014. The data collection was approved by the Institutional Ethical Committee and written consent for publication was obtained.

The sample consisted of patients with initial diagnosis of OLP, aged 21 years to 70 years. Healthy subjects of different age groups, without any history of oral diseases were enrolled as control subjects. The patients having infectious diseases were excluded from this study. Information on habits and previous disease history of the study participants were acquired through interviewer-based questionnaire method.

The diagnosis of OLP was made by clinical evaluation and confirmed by histological examination based on WHO defined clinical criteria [16]. The basic six forms of OLP were classified as *reticular* due to the presence of lace-like keratotic lesions on the oral mucosa; papular, plaque-like, atrophic/erythematous, erosive or bullous. Biopsy was performed only in atypical cases. Histopathological criteria were followed according to WHO criteria [17] and eosin-haematoxylin staining was performed for the identification.

Routine blood tests were performed. Haemoglobin concentration was estimated by the *Sahli's* method [18], White blood cells (WBC) was counted manually in specially designed chambers (Neubauer) and differential count of WBC was assessed by Romanofsky staining method [19] and erythrocyte sedimentation rate (ESR) was measured by Westergreen method [20].

Collected data were statistically analyzed using GraphPad Prism software. The results were expressed as mean ± SD. Chi-square test was performed to observe the association among the variables and unpaired *t* test to test the level of significance. *P*-values of 0·05 or less were considered significant.

RESULTS

A total of 22,252 (15,938 adults and 6,314 children) patients visited the concerned dental hospital during the study period and 147 (0.66%) of them were suffering from OLP. Of these, 108 (70%) were females, 39 (30%) were males and the prevalence rate of OLP among the adult population was 0.92%. Figure 1 shows the gender-wise distribution of OLP patients of different age groups. The definite preponderance of females towards this disease has been observed and is in concurrence with other observations [6-8].

Incidentally, the population in this state has marginally high female to male ratio of 1084:1000 (21). Compared to other age groups, women in their fifth decade of life and men in their forties tend to be maximally affected by OLP. The gender ratio differs significantly. One tail t test shows that the prevalence of OLP in the females in the study population are significantly ($p<0.05$) more than in the males in all age groups.

OLP may be differentiated into six forms, often mildly overlapping with each other. Reticular form of OLP is of most common occurrence (55%) and the plaque-like form is rare (>4.5%), followed by the bullous form (<1%). Erosive form is found in a quarter of the newly reported OLP patients and half of their number shows the atrophic form, whereas papular form was not found during study period. The number of patients of the various forms significantly ($p<0.0001$) differ from each other.

OLP is most commonly (>45%) found only in the buccal mucosa and 20% patients initially report with tongue or gingival lesions. Less commonly seen are the combination forms as in the tongue (8.16%) or gingiva (4.76%) along with the buccal mucosa. Lips are a rare lesion site [1,7]. The number of patients of the various forms significantly ($p<0.0001$) differ from each other.

Figure 2 shows the different forms of histopathological features present in the OLP population. The inflammatory infiltration form is maximally found in these patients, followed by basal cell degeneration, parakeratosis and melanin incontinence in more than 50% cases. Atrophy and hyperplasia are found in more than 25% of the patients. Forms like orthokeratosis, mild dysplasia, Max-Joseph space and colloid bodies were observed in less than 5% of the patients. These features often overlapped with each other, contributing to the complexity of the disease.

OLP has been observed to co-exist with other systemic diseases too. >15% of the OLP patients also suffer from diabetes mellitus, 8.8% of them have high blood pressure and more than 5% of them were afflicted by all three diseases. 7.5% patients have history of hyperthyroidism whereas <2% of them are afflicted by hypothyroidism. Peptic ulcer has also been reported to exist in 2.7% of the patient population.

Upon comparison of the white blood cell (WBC) count, differential leukocyte count (DLC), neutrophil count and erythrocyte sedimentation rate (ESR) of the normal male and female South Indian population with such oral lichen planus patients of corresponding age groups, higher values are reflected in the OLP patients, with different levels of significance (Figures 3-5).

The WBC count of the female OLP patients is significantly ($p<0.0001$) higher than such normal ones of the age group 31-40 years and 61-70 years. WBC count of male patients of 41-50 years is significantly ($p<0.001$) more than that of the normal men. Such values of all the other groups of males and females are also significantly more ($p<0.05$) than the count recorded from the control group under study (Figure 3).

The percentage of lymphocytes has been observed to be significantly more in the patient group as compared to their control population. This difference is highly significant ($p<0.0001$) in the oral lichen planus affected females of 31-40 age group and 51-60 age group than those of OLP females of 21-30 years and all OLP patients of 41-50 years ($p<0.001$). In the rest of the patient groups the lymphocyte percentage is also significantly higher than the corresponding normal population ($p<0.05$)

The difference in the ESR of the female OLP patients with the normal females is highly significant ($p<0.0001$). The increase in eosinophil count in the adult males aged 30-60 years is significantly high compared to such non-diseased males. The increase in eosinophil count and decrease in haemoglobin level in the OLP patients do not vary to a significant level though.

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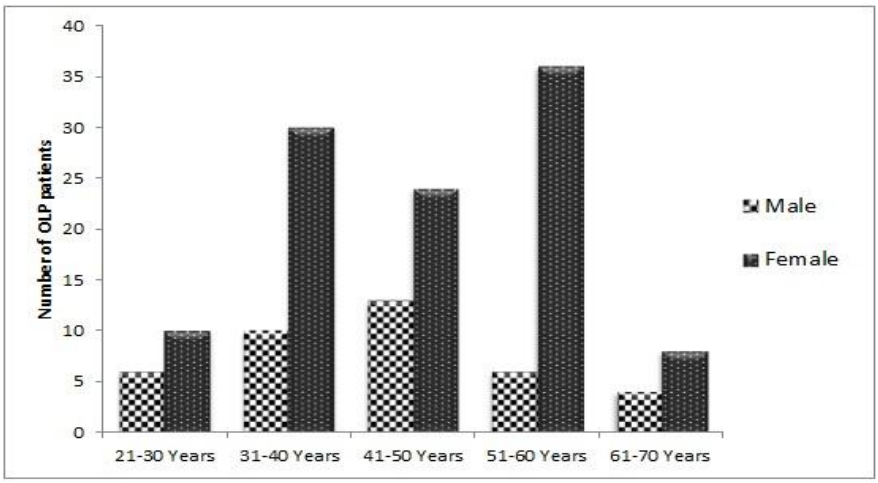

Fig 1: Prevalence of OLP in male and female patients of different age groups.

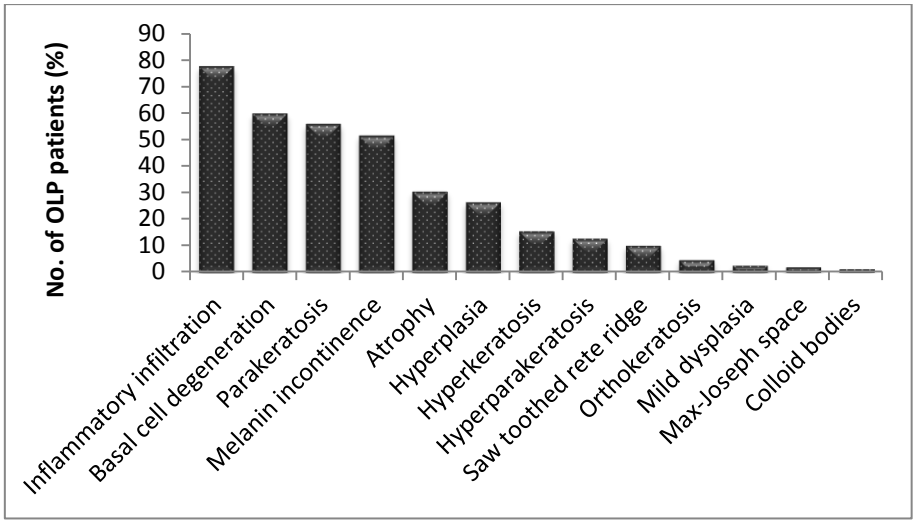

Fig 2: Distribution of histopathological features in OLP patients.

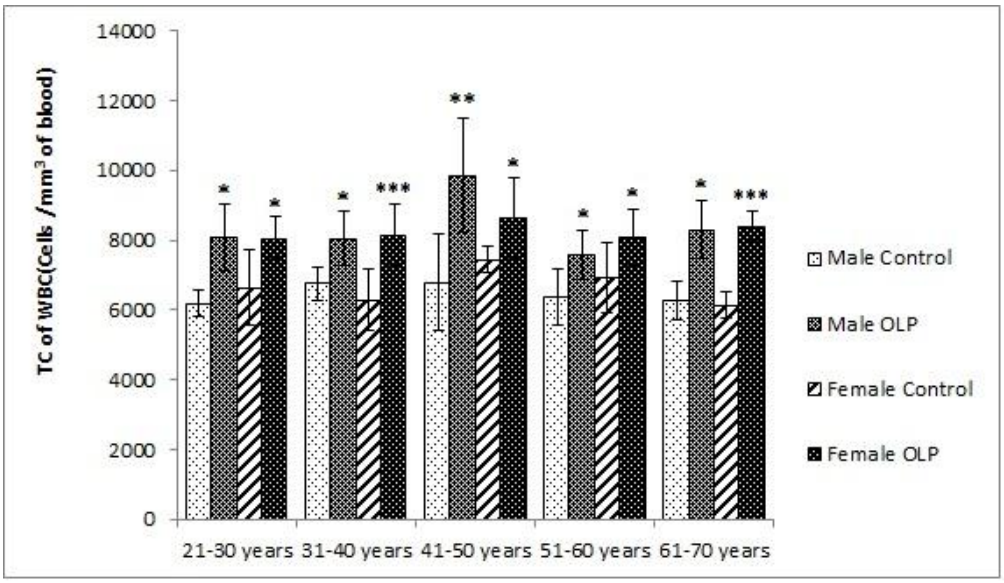

Fig 3: Total WBC count is significantly greater in the OLP patients than in the sex and age matched normal population (p<0.05*, p<0.001, p<0.0001***).**

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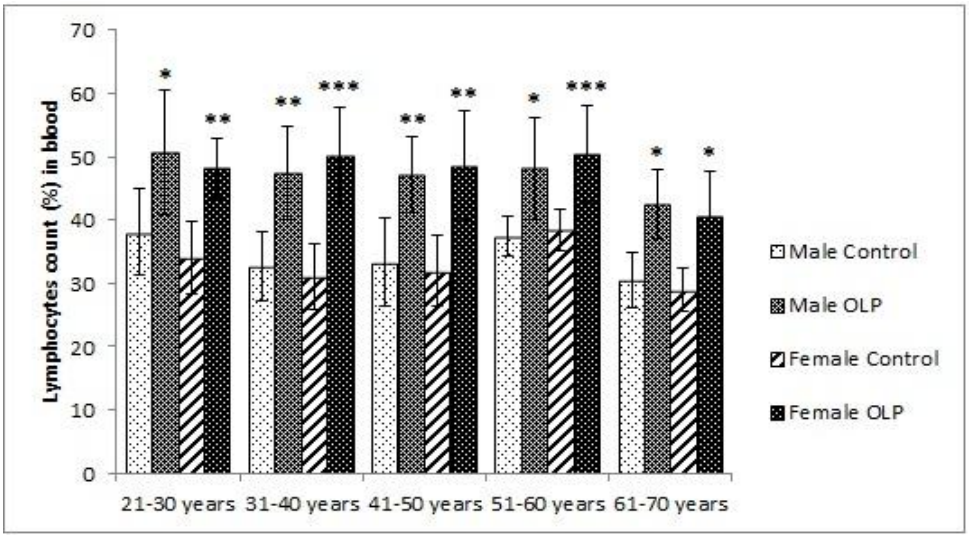

Fig 4: Lymphocyte count is significantly greater in the OLP patients than in the sex and age matched normal population (p<0.05*, p<0.001, p<0.0001***).**

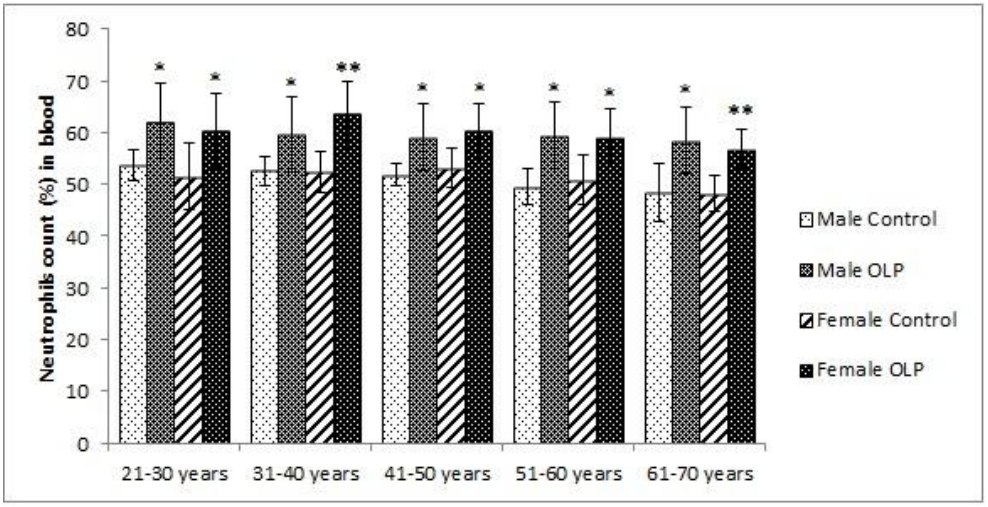

Fig 5: The neutrophil count has been observed to be significantly higher (p<0.05) in all the patient groups than the normal subjects.

DISCUSSION

The present study observed that 0.92% of the said population is affected by OLP. This is in concurrence with most observations (22, 5) but contradicts the finding that the Indian subcontinent has a particularly high incidence of the disease (23). There is a preponderance of females towards this disease as has been reviewed in almost all literature (6-9). Singh et al in 1976 (24) and Munde et al in 2013 (25) reported a higher frequency of OLP among men. In this study, the chi square test reveals that the difference between the genders is not significant. It is also to be considered that the females to males ratio in the said population is 1084:1000.

The women in their fifties are most common reporters of the disease [1, 26]. This could probably be due to the accumulation of random mutations over the period of 50 years of time. The sparse availability of new patients beyond 60 years of age is possibly due to less readiness to avail treatment at that age. Distribution of patients according to the age group has been observed to be highly significant (p<0.0001).

The reticular form of OLP is the most widely prevalent form observed worldwide [1, 26]. The other forms have been grossly tabulated earlier [27]. Here all probable 13 clinical forms have been assessed and

tallied for epidemiological analysis. The inflammatory infiltrated, basal cell degenerated, parakeratotic and melanin incontinence form are found in majority of the OLP patients, whereas, the atrophic, hyperplasic, hyperkeratotic, hyperparakeratotic, orthokeratotic, saw-toothed rete ridged, mild dysplasic, Max-Joseph spaced and colloid bodied forms are less common as in the order of mention.

The OLP patients may suffer from other ailments simultaneously, viz., diabetes, hypertension, thyroid imbalance or peptic ulcer but they have not yet been reported to have any role in the etiology of OLP. Manzoor et al in 2013 observed that a significant number of OLP patients suffer from hypothyroidism (28). According to Bagewadi and Bhoweer, diabetes or hypertension is not the causative of OLP though the patients may bear such comorbid diseases [29].

The haematological profile of the patients significantly deviates from the age and sex matched normal subjects. The broad normal range of blood profile has been considered prior to calculation of significance levels and standard deviations. Nevertheless, the patient blood picture tendencies towards the higher side in comparison to the normal and age / sex / locality matched population. The leukocyte count, neutrophil count and lymphocyte counts are significantly more than that of the normal subjects. High WBC count is accounted for by the immune system disorder or acute stress, both involved in the etiogenesis of OLP. The ESR of the female OLP patients is significantly high compared to corresponding non-diseased population. Such conditions prevail in autoimmune disorders and the deviation in women possibly indicates the severity of inflammation in female patients. The eosinophil count of the males aged 30-60 years is also significantly high indicative of the inflammation accompanying OLP. It might be plausible that erythrocytes play a dominating role in inflammation in females while eosinophils play similar role in the males, though an intensive patient recruitment will be required to conclude the possibility.

CONCLUSION

The cross-sectional epidemiological study on 147 OLP patients of Kerela, South India, for more than two years, reveal interesting features in the haematological profile but have various limitations. Longitudinal study and recruitment of a large cohort of patients from wider background may substantiate the haematological profile as a prognostic feature of the disease.

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