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Original Research

Risk factors associated with oral potentially malignant disorders: Five year analysis in a Pondicherry population

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ABSTRACT:
Introduction: India, country with diverse cultures, health beliefs, practices, habits and risk factors for disease is facing epidemiological and demographic translation in arena of rise of oral potentially malignant disorders and cancers. **Materials and methods:** Patients with clinically and histopathologically diagnosed oral potentially malignant disorders over the last five years in our department were included in the study and history of any harmful habits were retrieved from each patient record. For every patient histopathology report was obtained and strength of association of risk factors was analyzed. **Results:** In our study lichen planus were commonly found in females and most of the time associated with no harmful habits, leukoplakia were generally associated with tobacco smoking habit while erythroplakia were associated with both chewing and smoking tobacco habits. **Conclusion:** The habit of tobacco chewing and smoking showed a statistically significant association to oral potentially malignant disorders which are common in younger age group. There is an urgent need for awareness programs involving the community health workers, dentists and allied medical professionals.
Keywords: Malignant, precancerous, dysplasia, histopathology.

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INTRODUCTION

India, country with diverse cultures, health beliefs, practices, habits and risk factors for disease is facing epidemiological and demographic translation in arena of rise of Non communicable diseases. The use of tobacco and areca nut in various forms is very popular here (International Agency for Research on Cancer, 2004). Areca nut has a long history of use and is deeply ingrained in many socio-cultural and religious activities [1]. Gutka (Areca nut compound) is a commercially powdered mixture containing the same ingredients as paan with mock tail of various chemical carcinogenic compounds. Regular use of these leads to oral cancer and precancerous conditions [2]. The most important consideration is the relation between areca nut use and the development of mouth cancer (oral squamous cell carcinoma) and its precursor's leukoplakia and sub mucous fibrosis [3-4]. Prevalence of oral leukoplakia in India varies from 0.2%-5.2% [5-6,7-8].

A pre-cancerous lesion is a morphologically altered tissue in which oral cancer is more likely to occur than in its apparently normal counterpart. A pre-cancerous condition is a generalized state associated with a significant increased risk of cancer. According to a workshop co-ordinated by WHO in May 2005 at London the use of the term 'Potentially malignant disorders' was recommended. The usage of this terminology conveys that not all lesions and conditions described under this term may transform to cancer, instead there is a family of morphological alterations amongst which some may have an increased potential for malignant transformation (Warnakulasuriya et al., 2007; Chong et al., 2011).

Oral leukoplakia is a precancerous or potentially malignant lesion, which means that in this morphologically altered tissue, cancer is more likely to occur than its apparently normal counterpart [9]. In general, it is more or less accepted as an overall statement that approximately 5 percent of all

leukoplakias will transform into cancer in an average period of 5 years [10]. Tobacco smoking is an important risk factor for precancerous lesions of the mouth. Smokers have a significantly higher prevalence of leukoplakia compared with non-smokers [11-13], and the frequency of the habit has a positive dose-response relationship [14,15]. It has also been demonstrated that there is a dose-response relationship for tobacco use and the risk of malignant transformation of oral leukoplakia [15, 16].

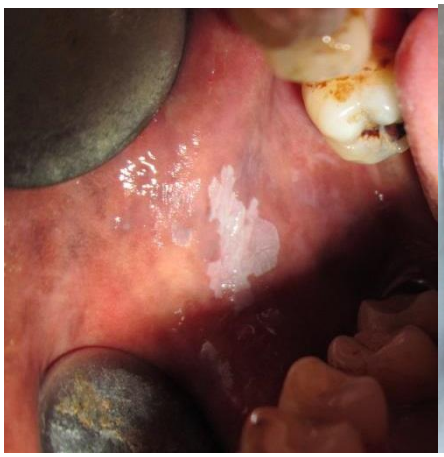


Fig.1 Homogenous leukoplakia

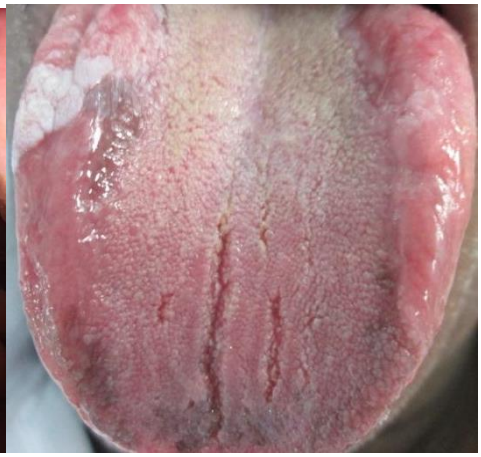


Fig.2 proliferative verrucous leukoplakia

The term 'erythroplakia' (erythroplasia) was coined to describe red lesions of the oral mucosa in contrast to oral leukoplakia. Cawson et al.[17] drew attention to the fact that lesions of this type (erythroplakia) do not form plaques—like oral leukoplakias— and therefore considered the term 'erythroplakia' inadequate. In contrast, these authors argued that the surface of oral erythroplakia is often depressed below the level of the surrounding mucosa. In addition to the term erythroplakia the term erythroleukoplakia has been introduced to describe a mixture of red and white areas of the oral mucosa.

Erythroplakia is an infrequent oral condition; its risk of malignant progression is the highest among all oral precancerous lesions. Erythroplakia is defined as 'any lesion of the oral mucosa that presents as bright red velvety plaques which cannot be characterized clinically or pathologically as any other recognizable condition'. It can appear anywhere in the oral cavity, but it predominately occurs in the floor of the mouth, the soft palate, the ventral tongue and the tonsillar fauces. Studies have shown that malignant transformation ranges from 20% to 68%.

The intermixed red and white lesions, called erythroleukoplakia or speckled leukoplakia, represents a pattern of leukoplakia that frequently reveals advanced dysplasia upon biopsy.

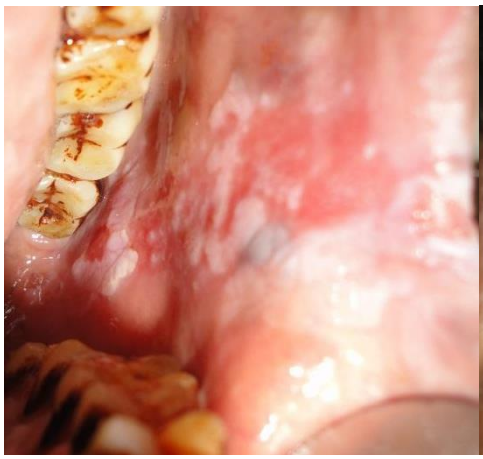


Fig.3 Erythroleukoplakia

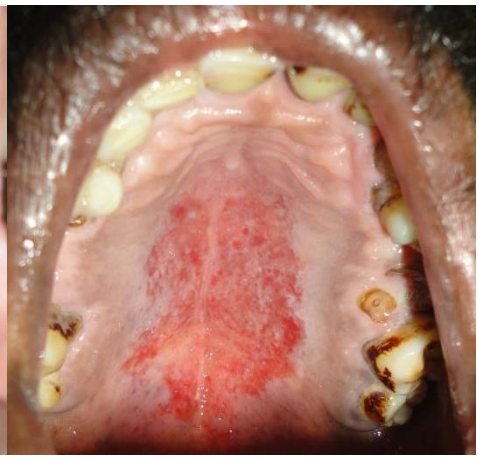


Fig.4 Erythroplakia

Lichen planus is a chronic inflammatory mucocutaneous disease which frequently involves the oral mucosa. In the majority of patients with oral lichen planus (OLP) there is no associated cutaneous lichen planus or lichen planus at other mucosal sites. This may be called "isolated" OLP [18]. This disease has most often been reported in middle-aged patients 30-60 years of age and is more common in females than in males [19]. OLP is also seen in children, although it is rare [20, 21].

The disease affects 0.5-2% of the population. The clinical history confirms the relationship between

OLP and oral cancer, although the degree of the risk involved is controversial. Therefore, OLP should be considered a precancerous lesion, emphasizing the importance of periodic follow-ups in all the patients [22]. Oral lichen planus (OLP) is a chronic inflammatory oral mucosal disease of unknown etiology. OLP typically presents as white striations, white papules or white plaques. Other more symptomatic clinical presentations include erythema, erosions, or blisters, which are generally very painful. OLP affect predominantly the buccal mucosa, tongue and gingiva, although other sites are occasionally involved. The potential malignant transformation of OLP has been a lasting controversial matter. Several retrospective studies have observed a higher incidence of oral cancer in patients with a specific subtype of OLP, mainly erosive OLP ranging from 2% to 8% which represents a greater risk of oral cancer than in the general population. In this regard, OLP should be considered a potentially malignant condition. Even though the World Health Organization classified OLP as a precancerous lesion the premalignant or malignant potential of OLP continues to be the subject of an ongoing and controversial debate.

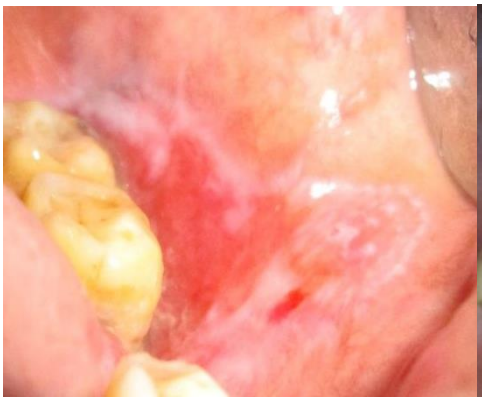


Fig. 5 Erosive lichen planus

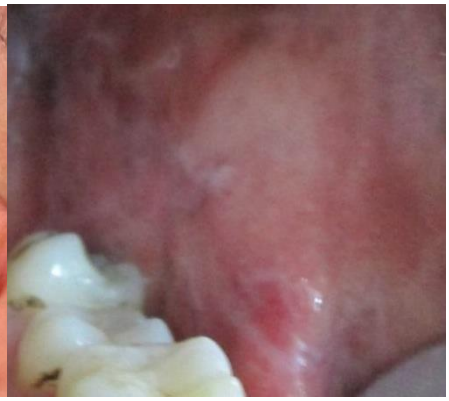


Fig.6 Reticular lichen planus

Histological examination is important not only in diagnosis of all potential premalignant disorder but also to determine whether there is evidence of malignancy, it provides information on the clinical behavior of the lesion and, in some instances, give prognostic information, all of which directly impact on patient management. The World Health Organization in 2005 graded precancerous changes into mild, moderate, severe and carcinoma in situ. The risk of malignant transformation has been reported to be between 6.6% and 36.4%, which recently reached up to12.1%.

With this background a retrospective study was done in our institution to review and analyze the association between various risk factors (Age, sex and harmful habits) and oral potentially malignant disorders as well as to obtain strength of association between risk factors and degree of dysplasia.

MATERIAL AND METHOD:

The study group comprised 71 patients (20 female and 51 male) aged from 20 to 70years, who visited the Department of Oral Medicine and Radiology, Mahatma Gandhi post graduate institute of dental sciences for the treatment in the last 5 years duration. Case history records for every patient were retrieved and a history of any harmful habit (Tobacco chewing, smoking and alcohol consumption) was taken from each patient, and the exact locations of all the lesions were noted down in a special pro-forma and patients were categorized on the basis of:

- Clinical appearance of the lesions.
- Symptoms associated with the lesions.
- Anatomical sites of the lesions.
- Type, duration and frequency of the habits.

Percentage distribution of oral potentially malignant disorders were obtained in association with age, sex and various habits as well as strength of association with given risk factors and degree of dysplasia of these lesions were obtained.

After the patients had provided their consent, biopsy procedure (excisional or incisional) was done. 10% buffered formalin was used as a fixative for biopsy specimen and histopathological examination was done. Reports were made according to the following histopathological criteria (Table 2).

Table 2: The criteria for histopathologic diagnosis of potentially malignant oral lesions.

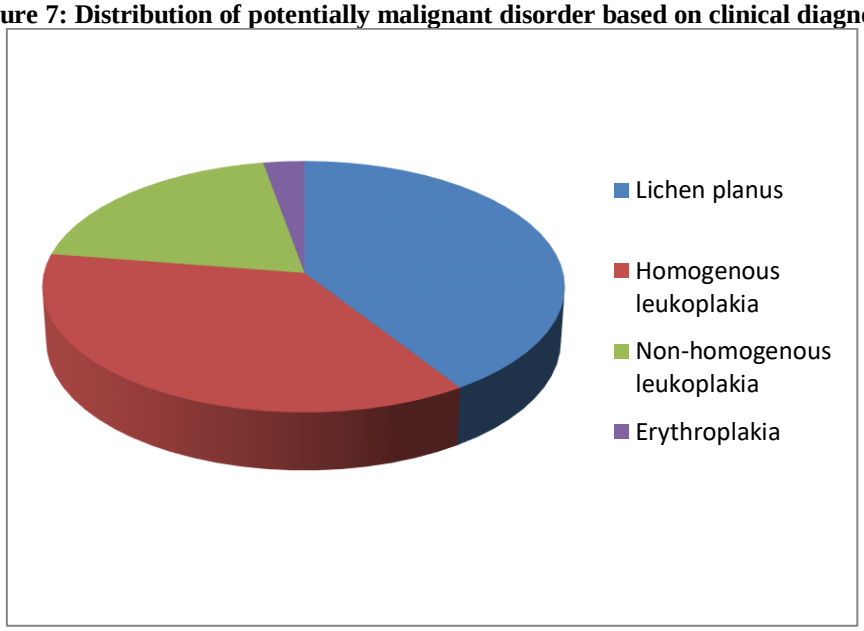
Histopathological diagnosis	Criteria
Benign keratosis	No specific changes, hyper or parakeratosis of epithelium, acanthosis, inflammatory infiltrate in lamina propria.
Epithelial dysplasia	Cytological epithelial dysplastic changes.
Lichen planus	Hyper/ parakeratosis, basal cell destruction, saw-tooth rete ridges, lichenoid T- lymphocytic inflammatory infiltrate.

Clinical and histopathological diagnoses were matched and discrepancy index (DI = the no. of incompatable diagnosis/the no. oftotal sample X 100) was calculated.

RESULTS

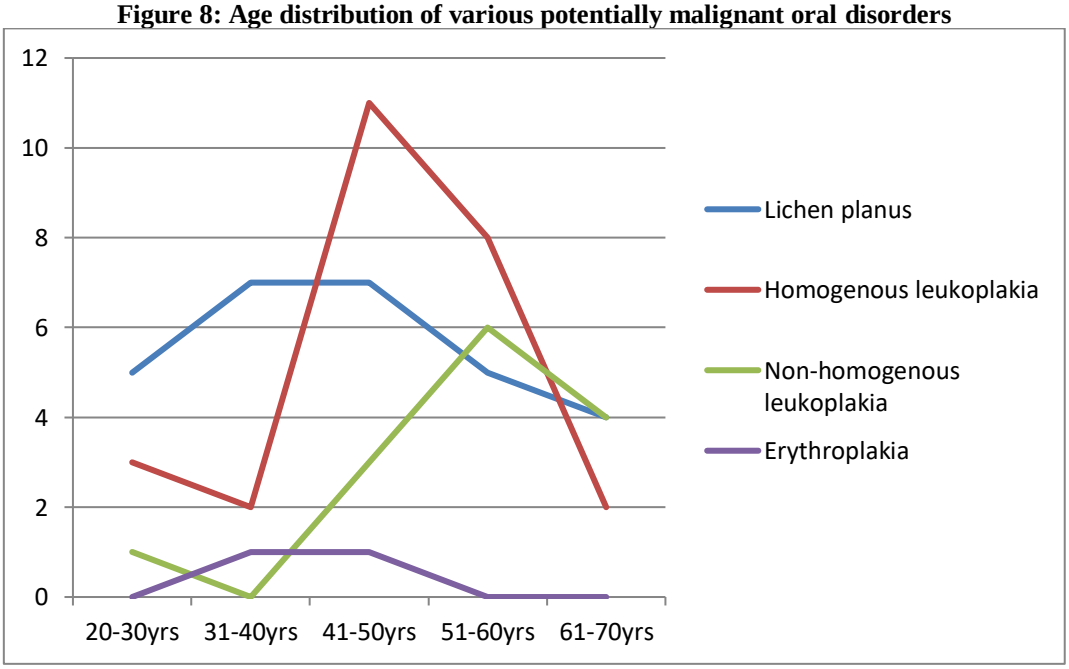
- In 71 clinically diagnosed cases 29 (40.84%) were lichen planus, 26 (36.61%) were homogenous leukoplakia, 14 (19.71%) were non-homogenous leukoplakia and 2 (2.81%) were erythroleukoplakia. [Fig.7]

Figure 7: Distribution of potentially malignant disorder based on clinical diagnosis



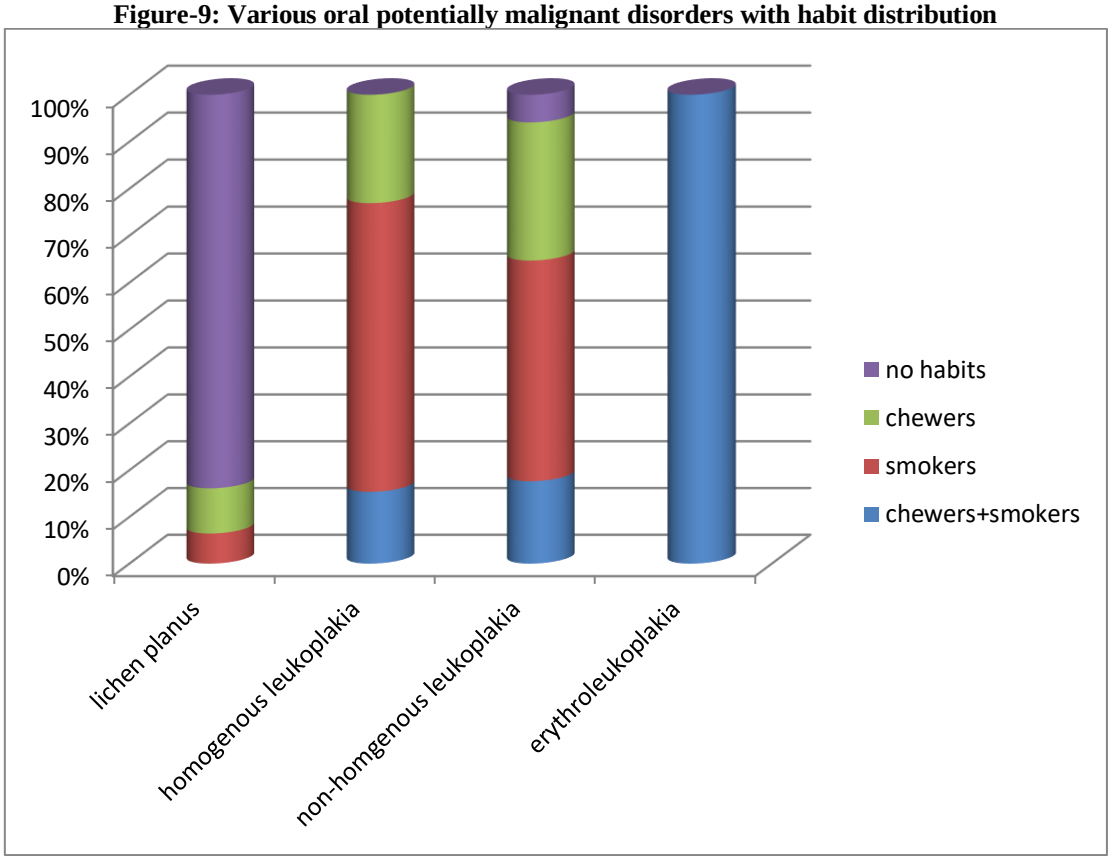
- Most of the lichen planus cases were diagnosed in 30-50yrs of age. Incidence of homogenous leukoplakia, non-homogenous leukoplakia and erythroplakia were increased as age advances. [Fig.8]

Figure 8: Age distribution of various potentially malignant oral disorders



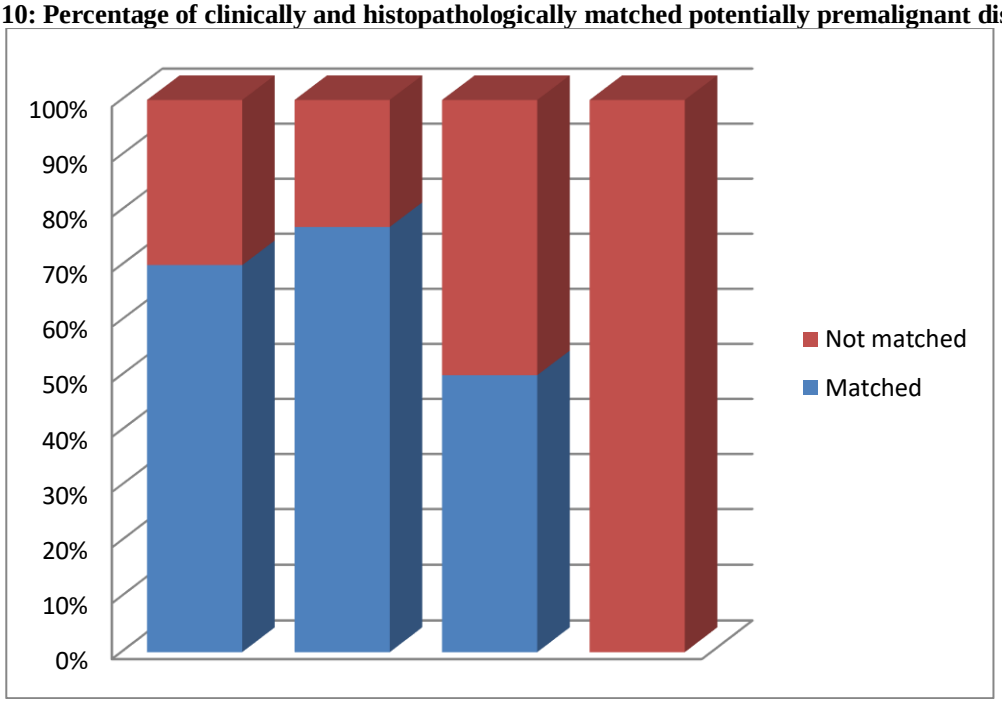
- Most of the lichen planus patients were with no history of habits, leukoplakia patients were smokers either homogenous or non-homogenous variety but erythroplakia patients were predominantly associated with both chewing and smoking habit simultaneously.[Fig-9]

Figure-9: Various oral potentially malignant disorders with habit distribution



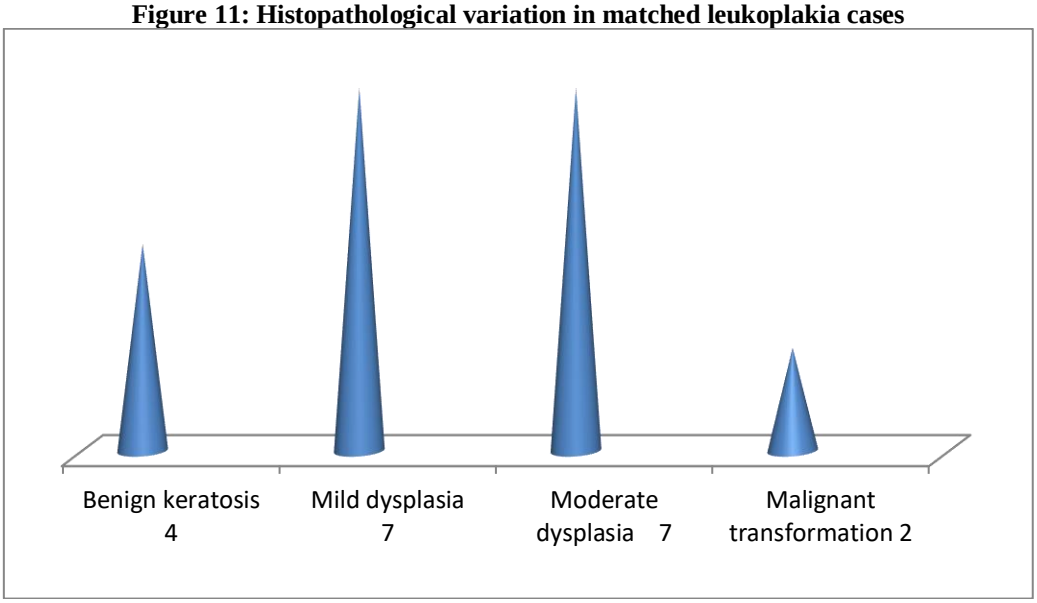
- 72.41% clinically diagnosed lichen planus cases were matched with histopathologic diagnosis. Similarly in 76.92% homogenous leukoplakia, 50% non-homogenous leukoplakia and 0% erythroplakia, clinical diagnoses were compatible with histopathological diagnosis. [Fig. 10]

Figure 10: Percentage of clinically and histopathologically matched potentially premalignant disorder.



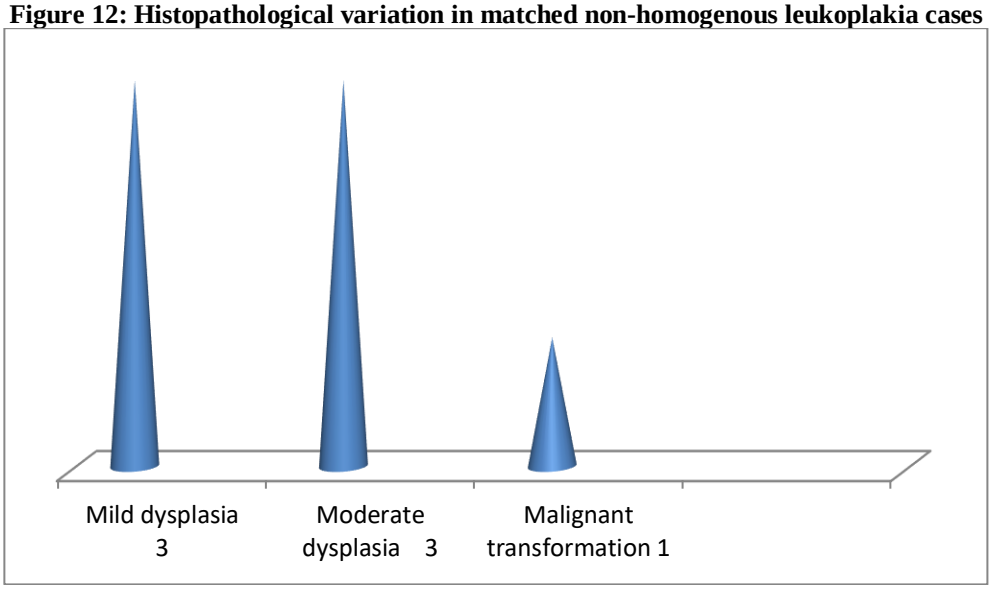
- Out of 20 clinically and histopathologically matched cases of homogenous leukoplakia 4 cases revealed benign keratosis, 7 cases with mild dysplasia, 7 cases with moderate dysplasia and 2 were with malignant transformation. [Fig.11]

Figure 11: Histopathological variation in matched leukoplakia cases



- In 14 clinically diagnosed non-homogenous leukoplakia cases, histopathogically mild dysplasia in 3 cases, moderate dysplasia in 3cases and malignant transformation in 1 case was reported. [Fig.12]

Figure 12: Histopathological variation in matched non-homogenous leukoplakia cases



DISCUSSION

It is widely understood that neither do all precancerous lesions progress to cancer nor all cancers necessarily originate from such lesions, but it has been proved that the majority of these lesions and conditions progress to cancer unless diagnosed early and treated. In our study the overall prevalence of precancerous lesions and conditions were 4.2% which is almost similar to the studies done by Warnakulasuriya *et al*., in the year 1984 (4.2%),[23] Rao *et al*., in 1998[24] (3.98%), and Lim *et al*., in 2003[25] (4.2%). In contrast, our prevalence of lesions and conditions were much higher when compared with the study done by Bhonsle *et al*., in 1976[26] (1.78%), suggesting that there is a slight regional variation in occurrence of the disease.

Occurrence of oral cancer is most frequently after the age of 40 years, with a peak at 60 years of age. It also affects males twice as often as females, and this holds true in case of our study also. The most common risk factors in this group are tobacco and smoking.

However rate of malignant transformation of oral lichen planus is the area of continues debate, frequency of this lesion is comparatively high. In the category of oral precancerous lesions homogenous leukoplakia is more common than erythroplakia and non-homogenous leukoplakia. In our study clinically 36.61% cases were diagnosed as homogenous leukoplakia and on histopathologic examination 76.92% cases were matched with clinical diagnosis which is slightly less than other studies. In three cases biopsy specimen was inadequate for histopathological examination and in other three cases clinically

diagnosed as leukoplakias were, in fact, OLP. In these cases, OLP appeared as a white plaque unilaterally located, without a reticular pattern, and therefore diagnosed as leukoplakia. This finding leads to a conclusion that a biopsy should always be taken from a plaque lesion. In additionthe differential diagnosis between plaque- like OLP and leukoplakia can be obtained by histopathologic analysis since these two conditions are clinically similar.

In case of oral lichen planus 72.41% clinically diagnosed cases were matched with histopathological examination. Unmatched cases on histopathologic diagnosis revealed non-specific chronic inflammatory process. In all these cases, the surface erosion existed, with the destruction of the epithelium, leaving only the fibrin-covered granulation tissue at the floor of the lesion. The biopsy of lesioned tissue, particularly if OLP is of an erosive form, can be challenging. A biopsy specimen of predominantly erythematous and ulcerated mucosal lesions should be taken few millimeters away from an ulcer so that the specimen's epithelium and connective tissue remains intact.

Most of the clinically diagnosed non-homogenous leukoplakia (50%) and erythroplakia cases, after histopathologic examination revealed non-specific inflammatory changes, secondary infection or early stage of oral submucous fibrosis, reason could be the similar clinical appearance ofthese lesions and secondary infections like erythematous candidiasis.

A lesion showing signs of dysplasia should be considered at high risk, but the absence of this parameter does not allowconsidering the lesion at low risk. In our study 53.84% homogenous leukoplakia cases were diagnosed with dysplastic changes and in 7.6% cases malignant transformation were evident similarly 42.85% non-homogenous leukoplakia cases were with dysplastic changes and 7.1% with malignant transformation.

The high variability of results compare to previous studies may be due to the limitations of the incisional biopsy technique that may reveal different histological patterns in a single lesion, depending on the surgical site. Additionally, a key factor that may misestimate the overall risk of malignant transformation is the presence of multiple lesions in the same oral cavity. So all lesions in the same oral cavity must be evaluated, but it is not unusual in clinical practice for both diagnosis and prognosis to be formulated on the basis of a single biopsy from a single lesion that is thought to be the most representative.

In our study the DI was 32.34%. The discrepancy between the clinical and the histopathologic diagnoses of non-homogenous leukoplakia and erythroplakia significantly contributed to the increase in the DI. However, Onofre and coworkers found a DI of 24.4%, and the higher DI was detected among the non-homogeneous leukoplakias which show agreement with our study.

CONCLUSION

Leuko/erythroplakias and lichen planus lesions are the potentially malignant disorders that most frequently turn into oral squamous cell carcinoma.Despite a similar clinical aspect they differ in etiology and in their risk of developing into oral squamous cell carcinoma.Quantifying the risk of malignant transformation in a single lesion is challenging and often based on the clinical aspect, and the histological features of the lesion in addition to the diagnosis.

Recent advancements in oral cancer research have led to the development of potentially useful diagnostic tools at the clinical and molecular level for the early detection of early oral potentially malignant disorders. There is urgent need for awareness programs involving the community health workers, dentists and allied medical professionals. The public should be made aware of the high risk of oral malignancy in oral lesions induced by tobacco, gutkha and different habits.

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