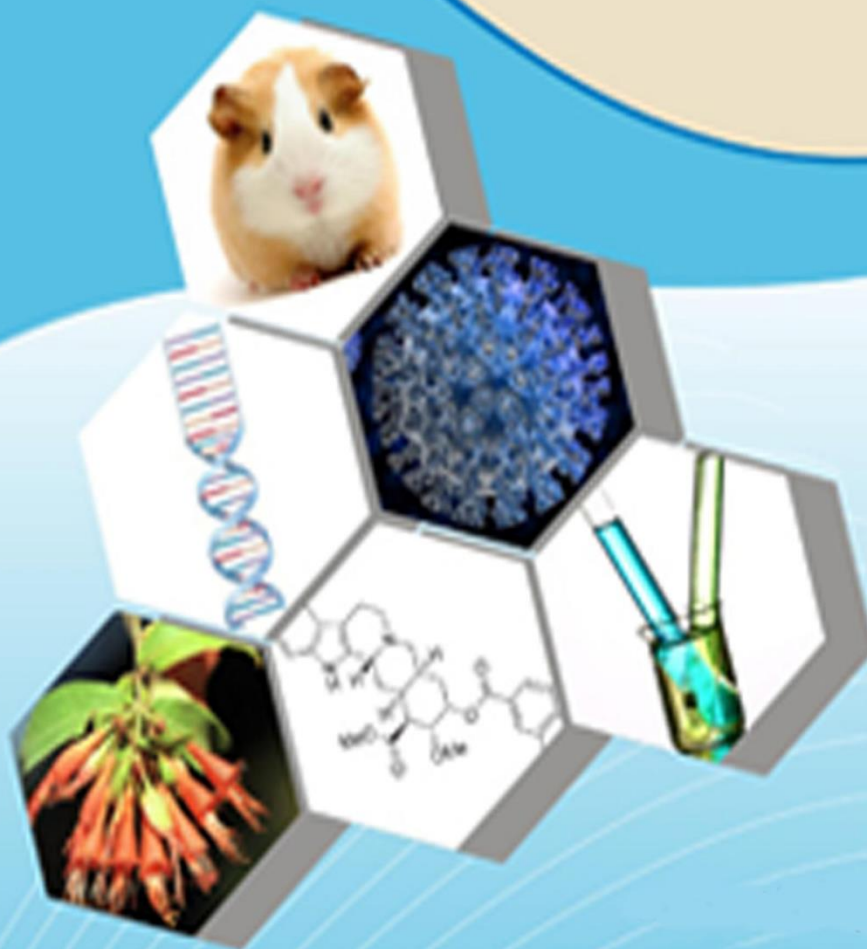




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Analysis Of Awareness Of Oral Potentially Malignant Disorders And Oral Squamous Cell Carcinomas Reported To A Private Teaching Hospital- A Retrospective Study

Type of study: Original research

Running title: Analysis of patient awareness in cases of oral potentially malignant disorders and oral cancer

Suvarna Kizhakkottu, Pratibha Ramani, Gheena.S, Abilasha.R

ABSTRACT

Background: Oral Squamous cell carcinoma (OSCC) can be preceded by clinically obvious oral potentially malignant disorders. The significant malignant transformation rates of Oral Potentially Malignant Disorders (OPMD) demands early diagnosis and proper management not only to reduce the symptoms but also to prevent its aggressive outcome. The objective of this retrospective study was to quantify the need of patient related awareness in identifying OPMD by analyzing the association between the type of referral in OSCC and OPMD cases and also to analyze the gender predilection, prevalent age and habits associated with OPMD and OSCC. **Methods:** This retrospective study included a sample size of $n = 226$ (70-OSCC, 156-OPMD). Data regarding the sample cases were selected after the review and analysis of records of about 86000 patients between June 2019 and march 2020. The retrieved data were tabulated and exported to SPSS software for statistical analysis. **Result:** Analysis showed a statistically significant correlation between the type of referral in OSCC and OPMD cases ($P < 0.0009$). Among all cases, the self-referred cases were found to be higher for females (61.8%) when compared to males (45.03%) and a statistically significant correlation existed between the gender and type of referral ($P=0.03$). **Conclusion:** To the best of our knowledge, this is the first study to analyze the association between type of referral in OSCC and OPMD patients. Quantification of awareness on OPMD and interventions at institutional level to improve this will have a significant impact on early diagnosis and better prognosis of OPMD patients.

Keywords: Awareness; Early diagnosis; Oral potentially malignant disorders; Oral squamous cell carcinoma; Referral

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1. INTRODUCTION

Oral cancer is emerging as one of the serious health problems and accounts for 2-4% of types in the world [1,2,3]. Oral Squamous cell carcinoma accounts for more than 90% of the reported oral cancer cases in the world with the prevalence of 300,000 oral squamous cell carcinoma cases annually[1,4,5]. One of the main problems

with this neoplasm is, it can go unnoticed during its early stages [1]. OSCC can develop in apparently normal mucosa and can also be preceded by clinically obvious potentially malignant lesions such as erythroplakia and leukoplakia [1,6].

The term oral potentially malignant disorder (OPMD's) was proposed by WHO in 2005 and this includes potentially

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malignant lesions and potentially malignant conditions. OPMD is defined by WHO in 2005 as "The risk of malignancy being present in a lesion or condition either at the time of Initial diagnosis or at a future date "[7,8]. The spectrum of OPMD's includes mainly oral leukoplakia, erythroplakia, erythroleukoplakia, oral submucous fibrosis (OSF), palatal lesions in reverse smokers, oral lichen planus and oral lichenoid reactions [9,10]. This OPMD's under certain altered tissue microenvironments for a specific time duration can grow and progress to aggressive oral cancer[11].Progression of an oral potentially malignant disorder into cancer depends on the progression of epithelial dysplasia, which does not follow a predictable sequential progression from mild to moderate to severe dysplasia and in some cases may revert to normal [12,13]. The malignant transformation of OPMD's depends on various factors which can be patient related or lesion related [14–17]. In 2014, Dost et al studied the malignant potential of oral epithelial dysplasia and found that 7.1 % of patients with oral epithelial dysplasia progressed to OSCC [18]. In a systematic review by Warnakulasuriya and Ariyawardana stated that the overall malignant transformation rate of leukoplakia is 1.5 % to 34% and 3% in homogenous lesions and 14.5 % in inhomogeneous lesions [19,20]. In the oral submucous fibrosis the rate of malignant transformation was estimated to be between 2 % – 8 % [21]. The reason for this malignant transformation in OPMDs can be associated with factors like gender, site and type of the lesion and habits[14,22].

The significant malignant transformation rates of OPMD demands early diagnosis and proper management not only to reduce the symptoms but also to prevent its aggressive outcome[23,24]. Early diagnosis of OPMD

and its awareness among patients was evaluated in this study

This retrospective study aimed to quantify the need of patient related awareness in identifying OPMD by analysing the association between the type of case referral in OSCC and OPMD cases and also analysed the gender predilection, most affected age range and habits associated with OPMD and OSCC. The present study also evaluates the need of the early diagnosis of OPMD and its treatment before progressing into adverse outcomes.

2. MATERIALS AND METHODS

The present study was conducted with approval from the Institutional Human Ethical Committee, Saveetha dental College and Hospitals (SDC), Chennai. This was a retrospective study which included n=226 samples (OSCC: n=70, OPMD: n=156) [Table-1] and the data regarding the sample cases were selected after the review and analysis of records of about 86000 patients who visited our institution between june 2019 and march 2020. All the retrieved case sheets were verified by an external reviewer in order to minimize the errors in data recording.

Sample Groups	Sample size (n)	Percent
OSCC	70	31%
Leukoplakia	96	42.5%
Oral Lichen Planus	60	26.5%

Total	226	100%
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Table 1 showing the frequency and percentage of OSCC and OPMD (Leukoplakia and Oral lichen planus) cases included in the study

OPMD and OSCC cases with specific diagnosis, properly recorded habit history and clinical details were included. OPMD and OSCC cases with non specific diagnosis and improperly recorded case sheets were eliminated from the present study. Cross verification of the retrieved data was done by photographs and direct communication.

The data collected from the n= 226 of age, gender, habit history, referral type and diagnosis were tabulated in Microsoft Excel software. This tabulated data was then transported to SPSS-Statistics 23 software and frequency analysis were done for age range, gender, habit history, referral type and diagnosis. For analysing the correlation of referral type with diagnosis and gender, chi-square test was performed and the results were analysed statistically and interpreted as tables and bar graphs.

3. RESULT

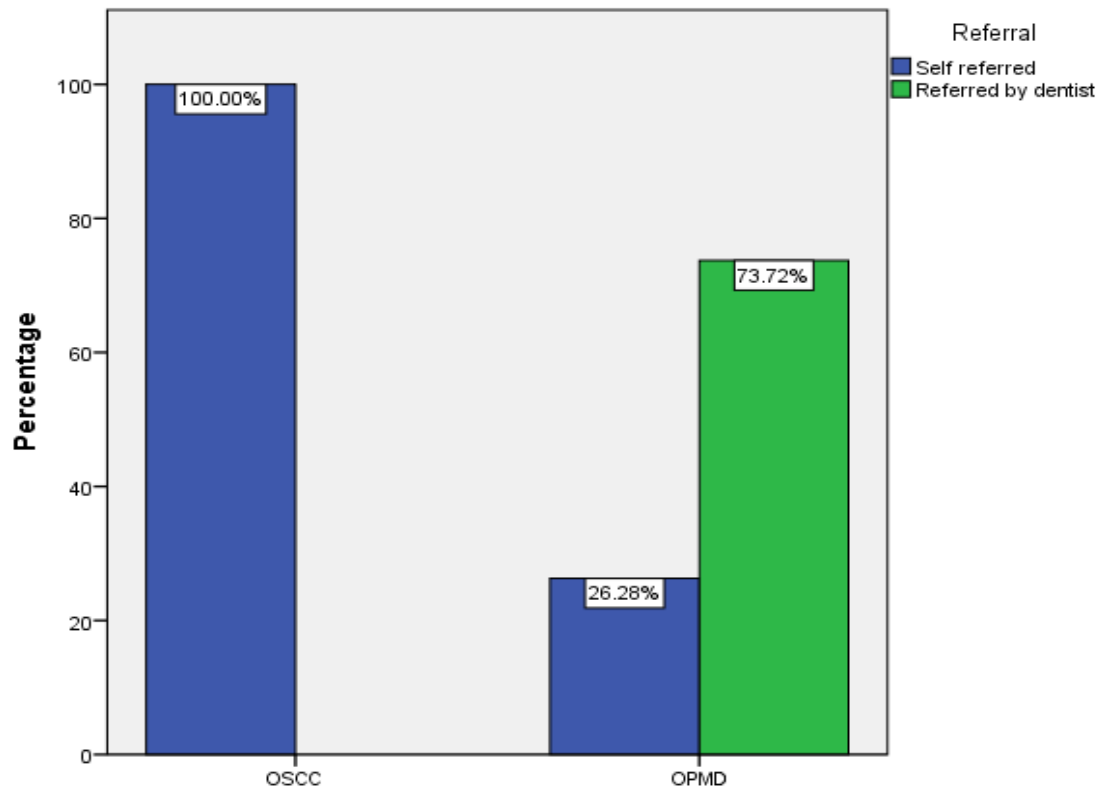
On analysing the demographic and clinical data from n = 70 samples of OSCC and n = 156 samples of OPMD. It was found that 100% of the OSCC cases were self-referred

and 73.70% of OPMD samples were identified, diagnosed and referred by dentists. In the present study, we found a statistically significant relation between the type of referral in OSCC, leukoplakia and lichen planus with p value less than 0.0009.

The frequency and percentage of distribution of self referred and dentist referred cases among selected samples of OSCC, leukoplakia and lichen planus were given in Table-2 and also percentage of the same were represented in bar graph (Graph 1).

Type of Referral	Diagnosis		
	OSC C	Leukop lakia	Oral Lichen Planus
Self-referred	100%	6.3%	58.3%
Referred by dentist	0%	93.7%	41.7%

Table 2 showing the percentage of distribution of self-referred and Dentist referred cases among selected samples of OSCC, Leukoplakia, and Oral lichen planus



Graph 1 showing percentage of self-referred cases and doctor referred cases among OSCC and OPMD cases, X axis showing OSCC and OPMD, Y axis depicting percentage. Self referred cases are represented by Blue and Dentist referred cases are represented by Green colour.

On analyzing the gender predilection, males were found to be predominantly affected in OSCC and OPMD with 82.9% and 72.4% respectively when compared to females. The gender distribution among the selected samples were represented in Table 3.

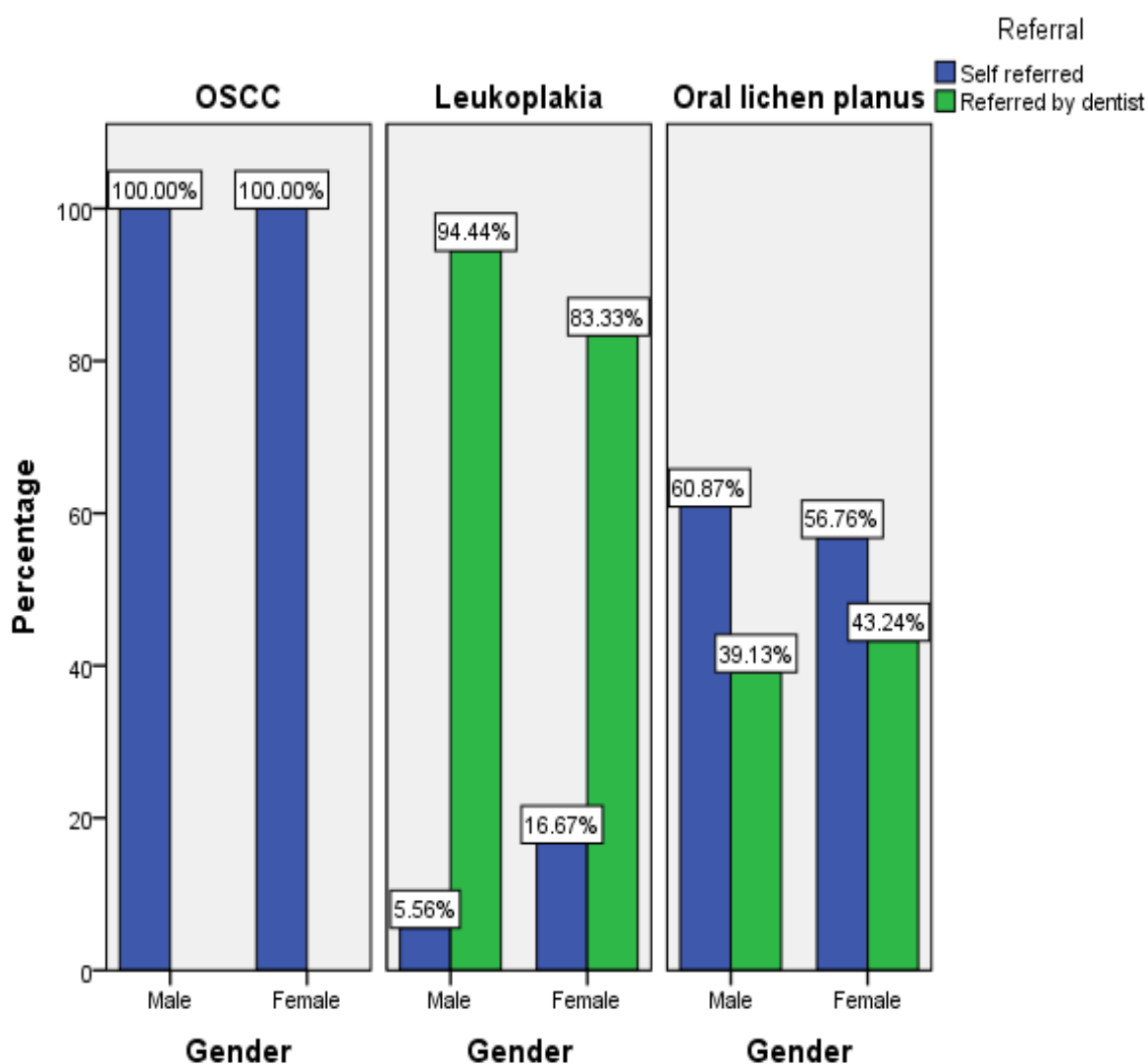
Gender	Diagnosis		
	OSCC	Leukoplakia	Oral Lichen Planus
Male	82.9%	93.75%	38.3%

Female	17.1%	6.25%	61.7%
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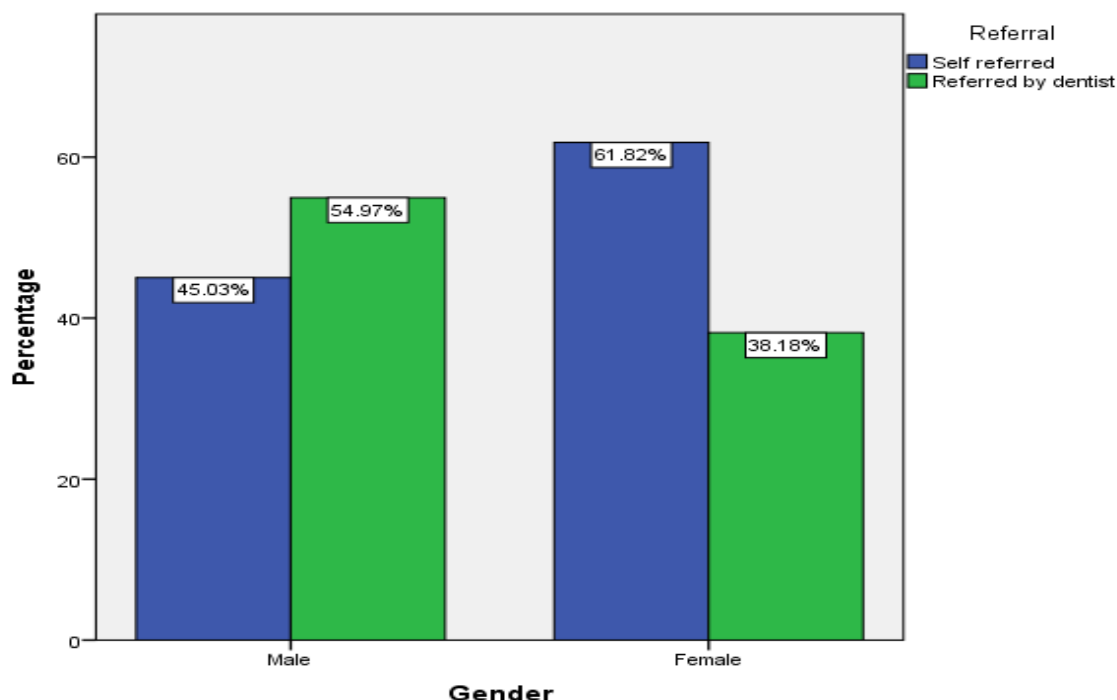
Table 3 showing the percentage of distribution of gender among the selected samples of OSCC, Leukoplakia and Oral lichen planus

Analysis of type of referral against gender showed that 100 % of OSCC samples were self-referred irrespective of gender. In leukoplakia 94.4% of males and 83.3 % of females were referred by dentists. Among

lichen planus cases, 60.87% of males and 56.76% of females were found to be self-referred. The frequency of distribution of referral type among males and females were depicted in Graph 2.



Graph 2 showing the percentage of distribution of self-referred and dentist referred cases among males and females in OSCC, leukoplakia and oral lichen planus. X axis depicting gender wise distribution of OSCC,leukoplakia and oral lichen planus. Y axis showing percentage. Self referred cases are represented by Blue and Dentist referred cases are represented by Green colour.



The self-referred cases were found to be higher in females (61.8%) than in males (45.03%) when considering the total sample size (Graph 3).

Graph 3 showing the frequency of self-referred and dentist referred cases among males and females in the overall sample (n=226). X axis representing the gender and Y axis showing percentage of cases. Self referred cases are represented by Blue and Dentist referred cases are represented by Green colour.

The association between gender and the type of referral was statistically significant with p value = 0.03 (Table 4).

SL No	Variables compared	Statistical test used	*P value
1	Type of referral and Diagnosis	Chi-square test	<0.0009
2	Type of referral and Gender	Chi-square test	0.03

Table 4 depicting the correlation between different variables using Chi-square test; *P value less than 0.05 considered as statistically significant

67.1 % of the affected OSCC samples were above 50 years of age. The most affected age range in OSCC was found to be 50-60 years and more than 60 years. In OPMD also 50-60 years was found to be the most

affected age range. The percentage of distribution of OSCC , leukoplakia and oral lichen planus cases among different age groups were described in Table 5.

Age Groups	Diagnosis		
	OSCC	Leukoplakia	Oral Lichen Planus
18-30yrs	0	6.3%	16.7%
30-40yrs	5.7%	16.7%	15%
40-50yrs	28.6%	29.2%	23.3%
50-60yrs	32.86%	27.08%	30%
>60yrs	32.86%	20.8%	15%

Table 5 showing the percentage of distribution of OSCC, Leukoplakia, and Oral lichen planus cases among different age groups

45.7 % of the OSCC cases and 44.9 % of OPMD cases were found to be associated with habits. Among OSCC cases, pan chewing habits was found in 34.3 % pan and smoking habits were found in 5.7 % and smoking was found in 5.7%. Among OPMD cases, pan chewing was found in 13.5%, pan

and smoking in 6:4% and smoking in 25 %. The percentage of distribution of various types of habits among selected samples of OSCC, leukoplakia and oral lichen planus were given in Table 6.

Habits	Diagnosis		
	OSCC	Leukoplakia	Oral Lichen Planus
Pan	34.3%	19.8%	3.3%
Pan and smoking	5.7%	10.4%	0%
Smoking	5.7%	37.5%	5%
No habits	54.3%	32.3%	91.7%

Table 6 showing the percentage of distribution of various types of habits among selected samples OSCC, Leukoplakia and Oral lichen planus

4. DISCUSSION

The terminology OPMD was recommended and defined by WHO in 2005 as the risk of malignancy being present in a lesion or condition either at the time of initial diagnosis or at a future date[7] . Later in 2017, WHO defined OPMD as a clinical presentation that carries a risk of cancer development in the oral cavity whether in a clinically definable precursor lesion or in a clinically normal mucosa[25]. Among OPMDs oral leukoplakia is the most common type [25]. The other OPMDs of concern are erythroplakia, erythroleukoplakia, oral submucous fibrosis, palatal lesions of reverse cigar smoking and oral lichen planus [26]. The malignant potential of oral lichen planus still remains as a topic of controversy[26,27] . According

to recent studies the malignant transformation potential of oral leukoplakia, oral lichen planus and oral submucous fibrosis was found to be 3.5 % [19,28], 1.1% [29]and 7 -13 % [30] respectively. The factors associated with increased risk of malignant transformation include gender, site and type of the lesion, habits such as smoking, pan chewing and alcohol consumption, and the presence of epithelial dysplasia on histological examination [14]. Early identification of suspicious lesions by the specialist is highly recommended to identify any malignant changes in early stages to reduce the aggressive outcomes[31].

As for best of our knowledge, this was the first study to analyse the awareness among the South indian population about OSCC and OPMD by quantifying the self-referred

cases among them. In the present study, all the OSCC cases were self-referred whereas in OPMD only 26.3% of the cases were self-referred. Among OPMD, self-referred cases in leukoplakia (6.3%) were found to be less when compared to lichen planus (58.3%), even though the malignant potential of leukoplakia is more [32]. The reason for this could be the more symptomatic presentation of oral lichen Planus when compared to leukoplakia. Oral lichen planus is usually presented as a burning sensation during eating spicy foods [33] but leukoplakia is a white patch or plaque which is usually found as an asymptomatic lesion.

In the present study, the type of referral was found to be correlated to the diagnosis with a statistically significant p value < 0.0009 . This suggested that 73.7% of the OPMD cases failed to self-identify the lesion and seek treatment when compared to OSCC where all the cases were self-referred. Few studies have also reported low awareness levels about OPMD ranging from 19 % [34], 22.7 % [34,35] and 44.9% [36]. A survey conducted by Rai A et al in 2017 to identify the self awareness of oral potentially malignant disorder and oral cancer among high risk patients, found that 70.4 % of the study participants were aware of oral cancer but only 33.4 % were aware of OPMD [36,37]. Failure of self identification of the lesion and self referral to a hospital among 73.7% of OPMD cases indicated the low awareness of OPMD and its increased probability of transforming into a malignant lesion. The results obtained in this study were based on the actual patient cases reported to a single institution. The authenticity of the results obtained from the actual patient data analysis were more when compared to surveys which are double edged. This study gives a more precise idea

about the underlying problem of lack of awareness about OPMDs.

The gender predilection analysis in this present study showed that the males were more affected in OSCC and OPMD with 82.9% and 72.4% respectively. This was in concordance with several other studies [38,39,40,41,42,43,44] in which they stated that males were found to be more affected than females in the case of OSCC. The male dominance was also discussed in studies by G.Kiran Kumar et al in 2019 [45] and Fernanda weber Mello in 2018 [46]. The male predilection among OPMD and OSCC cases in this study could be due to the increased prevalence of habits in males. Males are considered to be more exposed to risk factors, such as smoking, drinking and chewing tobacco than females.

Asymptomatic nature and less amount of self-referral (6.3%) in leukoplakia cases were already discussed in this study. In the present study, out of 90 cases of Leukoplakia in males, 94.4% were referred by dentists. Among 23 cases of oral lichen planus in males 57.5% were found to be self-referred. We observed a statistically significant correlation between the gender and the type of referral (P value = 0.03). There had been no previous study which showed a statistically significant relation between the gender and the type of referral. The overall percent of self referred cases among females were more when compared to males. There are few other studies to support this observation. Armanda Deeks et al in 2009 stated that women were more likely to feel that it was their responsibility to seek advice on disease prevention compared to men [47]. The increased number of self-referred cases in females when compared to males in this study may be due to augmented observation power of females. One more reason for this could be due to the availability of more time to take

care of themselves as many of the female population in south india are homemakers.

Age also plays a major factor in OSCC and OPMD development [14]. In this study, the OSCC was found to be predominant for individuals of age group greater than 50 years. This was found to be similar to the result of the previous study by Riaz abdulla et al in 2018 (Abdulla et al., 2018). Increased prevalence of OSCC in older age groups in the present study can be correlated with the increased positive history of different types of habits among older age groups. However in the case of OPMD, the dominant age group of diagnosis was found to be 50-60 years. These results were in contrast with some of the previous studies in which most of the cases of OPMD reported were of the age group 20-30 years [48,49]. In this study, the increased predilection of OPMD in the 5th decade could be due to the increased influence of systemic conditions like diabetes mellitus and habit patterns on OPMD. Smaller sample size and geographical limitations of sample selection could also have an impact on the age predilection.

The association of habits with OSCC and OPMD have been a topic of study for a long time. This study also confirms the association of OSCC and OPMD cases to the individual's habits. The OSCC cases were found to be more commonly associated with pan chewing habit, followed by pan chewing and smoking. Some of the previous studies confirmed the relation of pan chewing and OSCC risk [49,50]. The dependency of OSCC with habits in this study could be due to geographical and social factors. But in the case of OPMD, smoking was found to be more predominant than pan chewing. Lin Li et al in 2011stated that smoking can also act as a substantial risk factor for the development of OPMD [51]. The predominance of smoking in

OPMD patients in this study could be due to lifestyle changes and geographical variations in presentation of habits.

Some researchers also focused on the non habit related etiologies of OSCC, one of which was by T.Smitha et al and Ramashankar et al and they stated that the majority of the patients with tongue cancer had no habit history [52,53]. Similarly more than 50 % of the OSCC and OPMD cases in this study were also not associated with any habits. This could be due to an increased prevalence of other factors like chronic trauma, familial factors and genetic predisposition [54]. The small sample size, geographical limitations of sample selection, biases in recording habit history and single institution type study design could also be the reason for dominance of non habit related OSCC and OPMD in the present study.

The quantitative evaluation of awareness among patients for OPMD in this study can be used as an educational aid at institutional level to improve the awareness among patients. Awareness programs at institutional level and dental camps emphasising on the need of early diagnosis of suspicious oral lesions can be conducted to bridge the gap so that many OPMD cases can be treated at Initial stages without progressing to aggressive outcomes like cancer.

The use of clinical diagnosis rather than more confirmatory histopathological diagnosis in OPMD cases can be considered as a limitation of the present study. Other limitations include smaller sample size, limited geographical area of sample selection, biases in history taking, errors in data recording and single institution based research.

5. CONCLUSION

To the best of our knowledge, this is the first study to analyse the association between type of referral in OSCC and OPMD patients. The present study obtained a statistically significant association between the type of referral and diagnosis. The lack of awareness of OPMD among patients can result in delayed diagnosis and treatment, which may further result in progression to aggressive outcomes. Building awareness at both Institutional level and public level on OPMDs is the need of the hour. In the absence of such campaigns, early diagnosis of OPMDs still remains a distant possibility.

AUTHOR CONTRIBUTIONS

SK wrote the manuscript and PR reviewed the data provided by SDC. PR corrected and reviewed the manuscript. GS gave suggestions for structuring the manuscript. PR, GS, AR and HR reviewed the final manuscript.

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CONFLICT OF INTEREST

The authors have no potential conflict of interest.

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