

PREVALENCE OF ORAL CANDIDIASIS IN ORAL LEUKOPLAKIA IN PATIENTS REPORTED IN PRIVATE DENTAL INSTITUTION: A RETROSPECTIVE STUDY

Nauma Hafeez¹, Dr. T. N. Uma Maheshwari²

Abstract

Aim: To assess the prevalence of candidiasis in oral leukoplakia in patients reporting to Saveetha Dental College.

Background: Candidiasis is an opportunistic infection caused by the *Candida albicans* species. It occurs when there is an imbalance in the microbiome, resulting in excessive growth of the species and causes white scrapable lesions. The study thus aims at assessing its prevalence in oral leukoplakia cases.

Materials and Methods: The study was conducted from June 2019 to March 2020 at Saveetha Dental College amongst a sample size of 97 patients between the ages of 21 to 18 years of which 92 male and 5 female patients diagnosed as leukoplakia were included in the study. The hospital database was used to retrieve data and tabulation of the data was done using excel sheets. Statistical analysis was done using SPSS software. Descriptive frequency test and inferential statistics was done using Chi square test and a p value of < 0.05 was considered statistically significant.

Results: The study reveals the prevalence of oral candidiasis in oral leukoplakia. The majority of candidiasis and oral leukoplakia occurs in the age group of 31 to 50 years and males are found to be more affected than females.

Conclusion: The prevalence rate agrees with other studies done on candidiasis and leukoplakia, being conscious of the prevalence rate helps in better diagnosis and identification of dysplastic condition in potentially malignant disorders as it is proved in earlier studies that candidal invasion is common in malignant changes.

Keywords: candidiasis; dysplasia; leukoplakia; leukokeratosis.

Introduction

Fixed prosthodontic treatment deals with the replacement of teeth by artificial substitutes that are not readily

¹ Saveetha Dental College & Hospitals, Saveetha Institute of Medical and Technical Sciences, Saveetha University, Chennai-77, Email: 151501002.sdc@saveetha.com

² Corresponding author: Professor & Head of Admin, Dept. of Oral Medicine and Radiology, Saveetha Dental College & Hospitals, Saveetha Institute of Medical and Technical Sciences, Saveetha University, Chennai-77, Email: umamaheshwaritn@saveetha.com

The human body is a host to many microorganisms [1], from healthy gut microbiome to unbalanced and disease-causing parasites. The body over its evolutionary period has learned to use microorganisms for various metabolic processes and in turn, provide these organisms a place to live and food to feed on. A delicately balanced process occurs called the symbiotic relationship, where a perfect ratio of microorganisms is maintained, even a slight imbalance can result in various levels of diseases in the human body.

One such organism to which the human body plays host is the candida albicans species[2]. It belongs to the yeast family and is a common inhabitant of human beings. It is evident from previous studies, the benefits of *C. albicans* species, which helps break down food to a certain extent. The various microorganisms in the body keep each other organisms in check, and hence some microorganisms are shown to help maintain the levels of *C. albicans* [3]. Dysregulation of these microorganisms may cause its overgrowth and result in its imbalance. It is interesting to note that studies have linked the increased antibacterial usage to Candida/yeast infections in humans. Thus it can be stated that a complex system is at play to control the yeast population.

At right amounts, candida is beneficial[4], it helps aid digestion and maintains gut flora keeping them in check. However, if an overgrowth is present candidal infection may occur in various parts of the body. The present study will focus on association of oral leukoplakia with candidiasis.

Oral candidiasis, also known as oral thrush is a commonly prevalent condition affecting the human population. It is commonly seen in infants and prevalent among the adult population as well. It clinically presents as a white scrapable patch in the oral cavity [5]. In people with weak immune systems [6] the mouth can serve as a hotspot for the spread of disease to other parts of the body since all food passes down through it, a significant exchange of microbiome takes place, and thus the need to treat this condition. The symptoms include bleeding, soreness of the mouth, loss of taste, etc. There is evidence to suggest diet plays an important role in yeast infections [7,8]. Diet is known to greatly enhance and affect the gut bacteria which in turn affects the yeast growth. Candidiasis being a white lesion has stirred some confusion in relation to another white lesion, namely leukoplakia. Although both have similarities, leukoplakia is an established premalignant lesion and thus accurate diagnosis is necessary [9,10].

This study looks over the prevalence of candidiasis and leukoplakia [11]. Since both these conditions have been linked to diet by many studies it can be safely said that there is a correlation between the two conditions [12]. It is also important to note that previous studies have correlated dysplasia and candida species, thus providing another link between the two lesions[13]. The study thus aims to correlate oral candidiasis and oral leukoplakia and assess the reason for its correlation. This helps in better understanding the condition and diagnosis of the early malignant changes in oral leukoplakia even when clinically appears as homogeneous with low risk for cancer.

Materials and Methods

The study has been thoroughly planned for methodology. The study has been conducted retrospectively and Saveetha Dental Hospital using the patient database, both data collection and analysis were done from June 2019 to March 2020. Using the Hospital database provides a large dataset to work on with reducing the hassle and time to evaluate patients independently. Since the study involves patients reporting to Saveetha Dental Hospital the population study is mostly centered around the hospital thus it lacks diversity in terms of location and socioeconomic status and may not directly represent the general population. Permission to access patient reports was obtained and ethical clearance was provided by the ethical board (ethical approval number SDC/SIHEC/2020/DIASDATA/0619-0320). The hospital patient database was used to review and analyze data specific to candidiasis and leukoplakia. Verification of the data was done using histopathological reports and clinical pictures. The collected data were tabulated in excel sheets and statistical analysis was done using the SPSS software. Incomplete reports were excluded from the study to prevent distortion and bias. The frequency distribution test was done in terms of age, gender, type of tobacco used and the presence of candidiasis in leukoplakia, further Chi square test was performed for the association of candidiasis and leukoplakia to comprehend its present trends.

Results

This study looked into the association of candidiasis with leukoplakia with respect to age, gender, and tobacco associations, in order to analyze its prevalence and thus assess its course. This also gives an idea of the causes

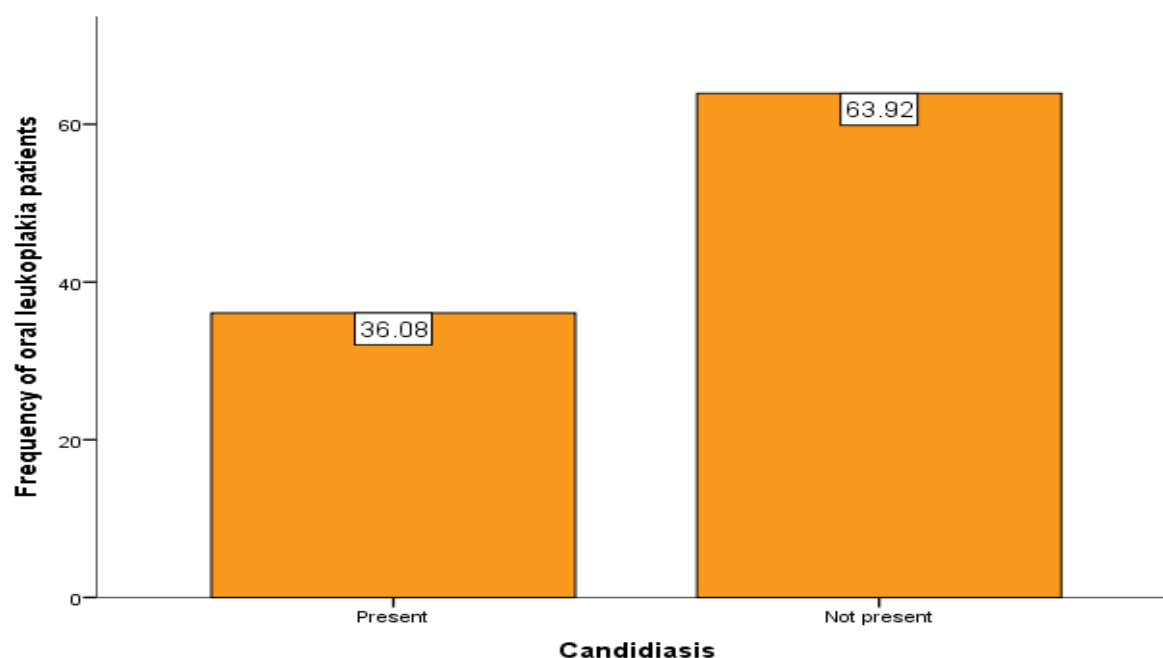
specific to the study population and suggests steps that need to be taken to effectively identify/ diagnose this condition.

The present study involves a total of 97 patients that were reported positive for leukoplakia, this was confirmed using the patient reports and clinical pictures. The study population varied in age from 21 - 80, with the mean affected age being 31-50, with 94 % males, 6% females affected. The study has been thoroughly analyzed and can be summarized into 5 main points as seen from graphs 1-5.

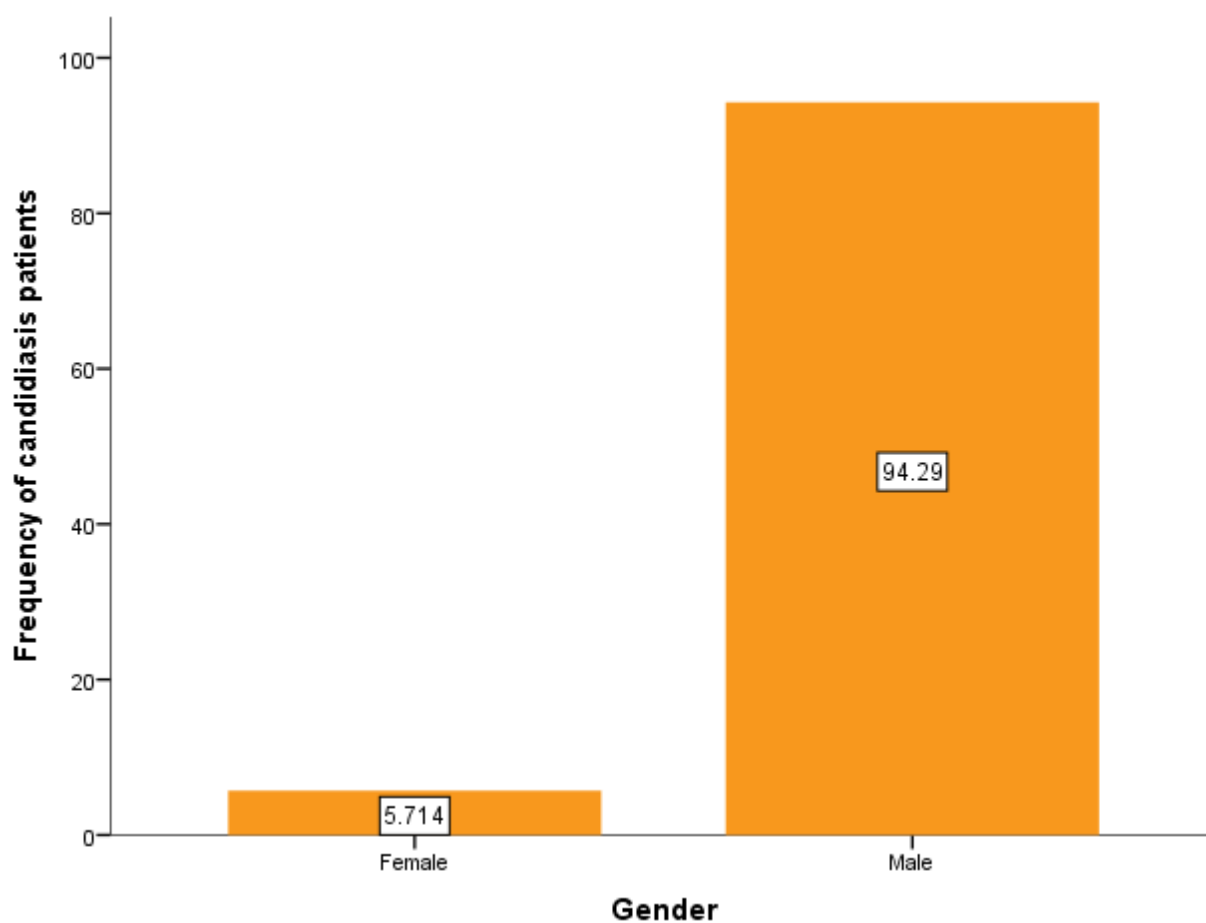
The prevalence of oral leukoplakia in oral candidiasis was found to be 36% (graph 1). Coming to the next finding that looks at gender predilection for candidiasis, it was found that males are more affected at 94% compared to a 6% occurrence rate in females (graph 2).

Looking at the prevalence of candidiasis by age, the Majority of the patients are in the 31 - 40 and 41 - 50 age groups at 29% each. The 21 - 30 and 51 - 60 age groups had an occurrence rate of 17% each and 8% in 61 - 70 years age groups (graph 3).

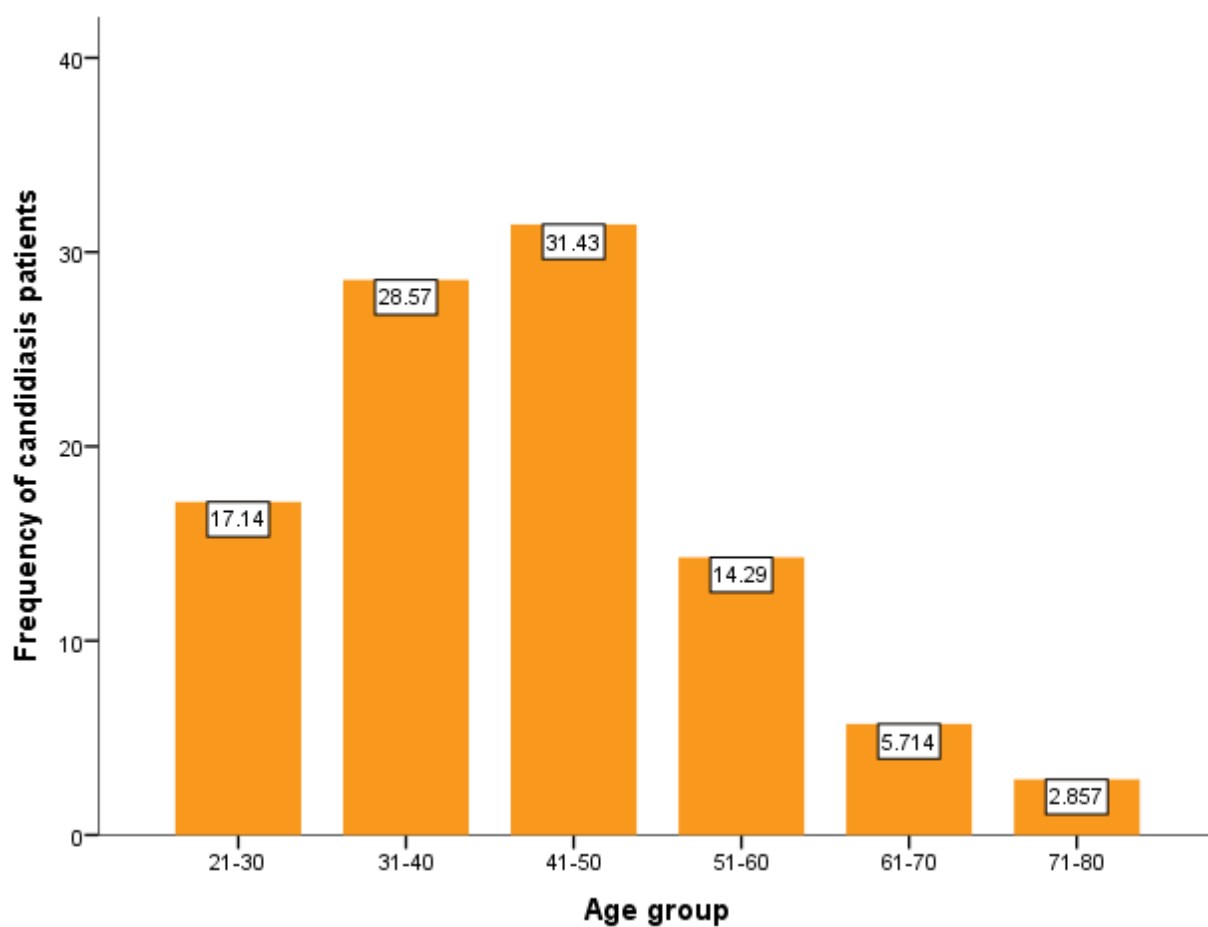
Next, looking at the prevalence of candidiasis by tobacco usage, the majority of the patients having candidiasis do not use tobacco - 37%, followed by paan usage in 34%, smoking tobacco in 23%, and gutka in 5%. (graph 4). The study further assessed the correlation of candidiasis and leukoplakia using the Chi-square test (Chi square value - 3.445 , p-value =0.328) and was found to be statistically not significant. It is observed that majority of the candidiasis cases occurs in homogeneous leukoplakia at 31% occurrence rate followed by verrucous leukoplakia (3.1%) and nodular and speckled leukoplakia (1% each) (graph 5 and 6) however narrowing the observation to include candida cases alone, 86% of candidiasis occurs in homogeneous leukoplakia and the remaining 8.5% in verrucous leukoplakia and 3% in nodular and speckled leukoplakia each . The study further analysed the association between presence/absence of candidiasis and type of tobacco product used. Association between candidiasis and type of tobacco was done using Chi-square test (Chi square value - 5.771 , p-value =0.123) and was found to be statistically not significant. It was observed that pan chewing habit was highly prevalent among oral candidiasis patients.



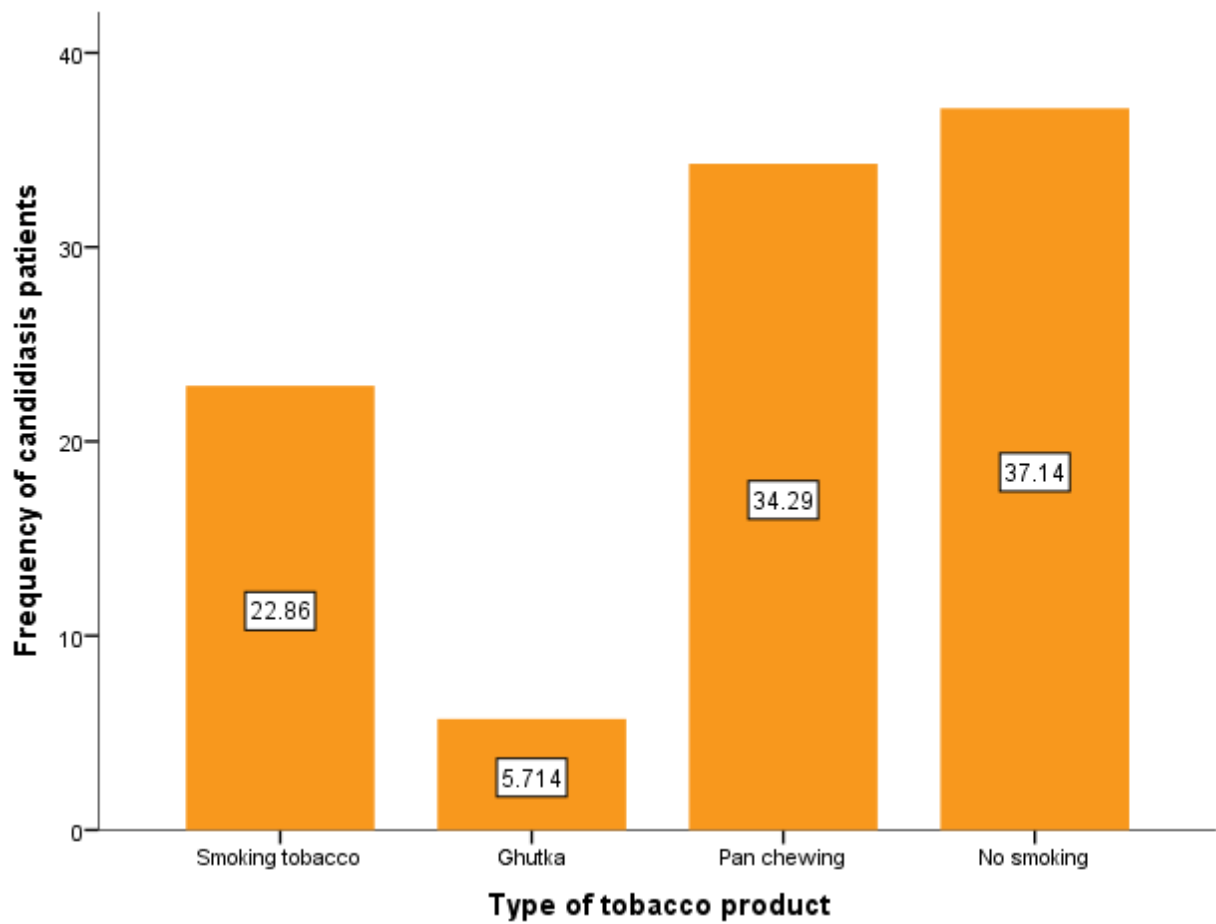
Graph 1 represents the frequency distribution of oral candidiasis among oral leukoplakia patients. The X-axis represents presence or absence of candidiasis and the Y-axis represents the frequency of candidiasis among the leukoplakia patients . It is observed that oral candidiasis is present in 36% of oral leukoplakia patients.



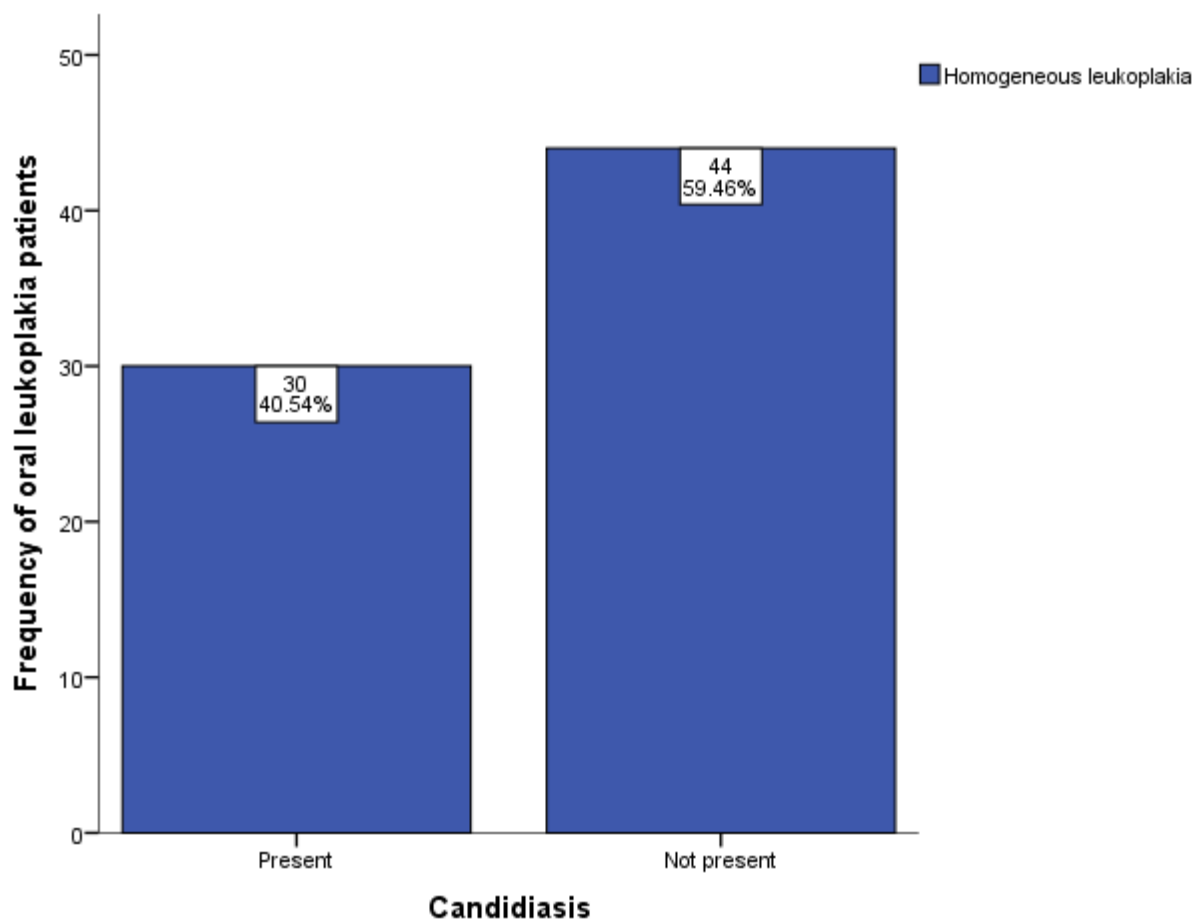
Graph 2 represents the frequency distribution of oral candidiasis patients in males and females. The X-axis represents the gender and the Y-axis represents the frequency of the oral candidiasis cases. It is observed that males (94.3%) have a higher prevalence of leukoplakia when compared to females (5.71%).



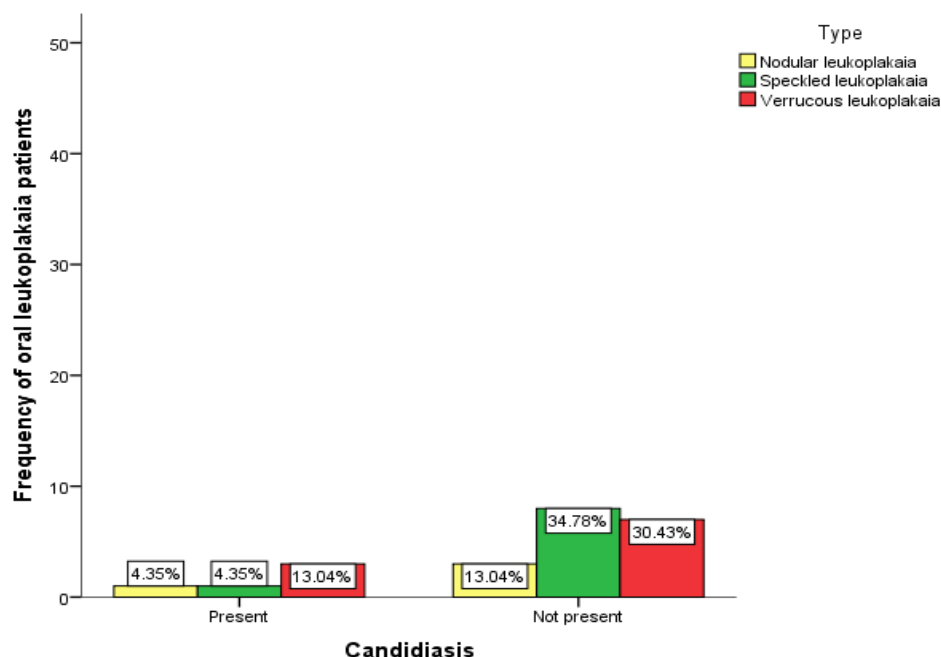
Graph 3 represents the frequency distribution of oral candidiasis patients in various age groups. The X-axis represents the age group and the Y-axis represents its frequency of candidiasis in oral leukoplakia. It is observed that the 41-50 years age group (31.4%) have the highest prevalence rate followed by 31-40, 21-30, 51-60, 61-70 and 71-80 age groups having a prevalence rate of 28.57, 17.14, 14.3, 5.71 and 2.9 respectively.



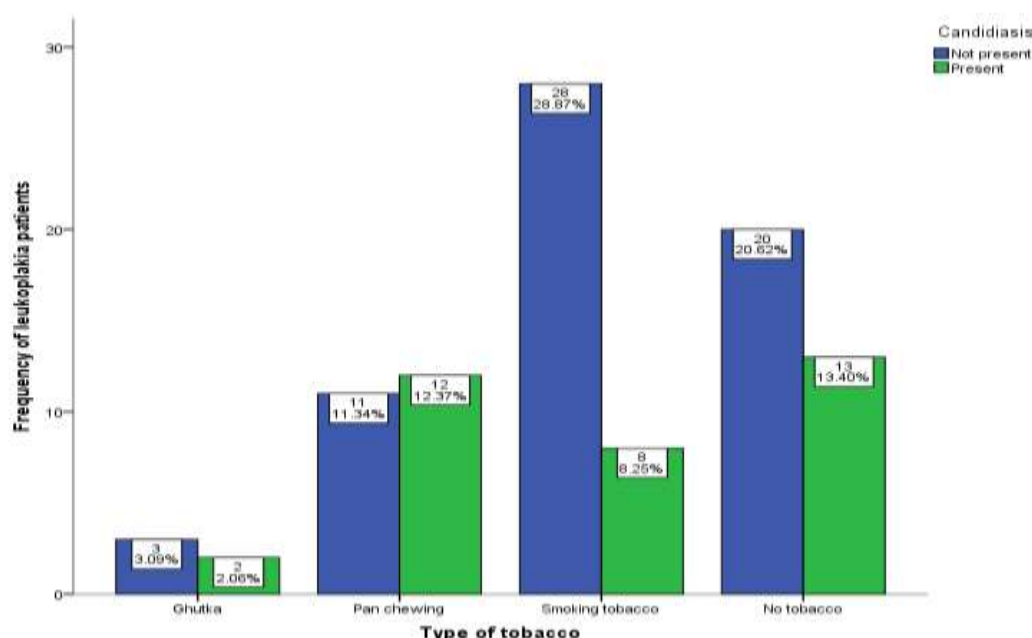
Graph 4 represents the frequency distribution of oral candidiasis patients based on the type of tobacco product used. The X-axis represents the type of tobacco product used and the Y-axis represents the frequency of candidiasis patients. It is observed that non tobacco users have the highest prevalence (37.14%) followed by pan chewing habit (34.3%), smoking tobacco (22.9%) and gutka (5.7%).



Graph 5 represents the association between presence/absence of candidiasis and homogeneous leukoplakia. The X-axis represents the presence /absence of candidiasis and the Y-axis represents the frequency of oral leukoplakia patients diagnosed with homogeneous leukoplakia. Association between candidiasis and type of homogeneous leukoplakia was done using Chi-square test (Chi square value - 3.445 , p-value =0.328) and was found to be statistically not significant. It was observed that 40.5% of homogeneous leukoplakia patients were also diagnosed with candidiasis.



Graph 6 represents the association between presence/absence of candidiasis and type of non homogeneous leukoplakia. The X-axis represents the presence /absence of candidiasis and the Y-axis represents the type of non homogeneous leukoplakia namely nodular leukoplakia, speckled leukoplakia and verrucous leukoplakia (depicted in yellow, green and red respectively). Association between candidiasis and type of oral leukoplakia was done using Chi-square test (Chi square value - 3.445 , p-value =0.328) and was found to be statistically not significant. It was observed that verrucous leukoplakia had the highest prevalence among the oral candidiasis patients.



Graph 7 represents the association between presence/absence of candidiasis and type of tobacco product used. The X-axis represents the type of tobacco namely gutka , paan , smoking tobacco and no tobacco and the Y-axis represents its frequency among candidiasis patients (presence of candidiasis in green and absence of candidiasis in blue). Association between candidiasis and type of tobacco was done using Chi-square test (Chi square value - 5.771 , p-value =0.123) and was found to be statistically not significant. It was observed that pan chewing habit was highly prevalent among oral candidiasis patients.

Discussion

Candidiasis is an opportunistic infection. Understanding its epidemiology can greatly help in diminishing its prevalence. This study has thus aimed at correlating leukoplakia and candidiasis in order to understand how age, gender, and tobacco usage can affect its occurrence [14,15].

The study reveals a 36% prevalence of oral Candidiasis in oral leukoplakia. Studies by various authors show candidiasis is directly linked to leukoplakia. The results of the current study are in consensus with other study results which reveal oral candidiasis and oral leukoplakia to be associated to some degree. A study by Shah et al in the year 2018 shows a 47.5% correlation between the two lesions [16]. The entity candidal leukoplakia is often used to describe a combination lesion, this proves the hypothesis of them linked by a common causative factor to a certain extent. The study suggests a higher male predilection when compared to females [17]. Of the 36% affected by candidiasis 94% are male and only 6% females which reveals a very strong male predilection. To better comprehend this, it has to be noted that the sample population has to be observed carefully, the study population is predominantly male considering the percentage of affected females independently gives a 40% prevalence of candidiasis, and 33% of males affected which results in quite the opposite finding i.e. female affected more than males (within leukoplakia patients) when independently analyzed. However, the percentage of prevalence is within 30 to 40%, and thus not significantly different. This is in consensus with other studies [18].

The study further reveals 31 - 50 years of age groups are most commonly affected, however, some studies suggest a higher prevalence rate for the above 50 years owing to their reduced immunity. Although some studies confirm the present findings and thus is in consensus with other studies. The study assesses candidiasis prevalence by type of tobacco use [19], the majority of the candidiasis occurs in non-tobacco users at 37% and paan is the most commonly associated tobacco followed by smoking. Gutka however is the least used amongst the candidiasis patients at 5%. Many studies disapprove of the association of smoking and tobacco with candidiasis, and is in agreement with the present study.

The study reveals 86% of candidiasis occurs in homogeneous leukoplakia and the remaining 8.5% in verrucous leukoplakia and 3% in nodular and speckled leukoplakia each [20]. The previous study suggests speckled leukoplakia has a high incidence rate in candidiasis however not many studies have been done in this regard which necessitates the importance of conducting similar studies on a larger scale. However, it has been established by other studies that candidal invasion is common in non-homogeneous leukoplakias. Given the association of candidiasis with dysplasia and leukoplakia, it suggests an increased risk of transformation of non-homogeneous leukoplakia into a carcinoma[20]. The study observed that pan chewing habit was highly prevalent among oral candidiasis patients. This finding is agreed upon by other research studies [21]

This study was performed in a retrospective manner, and thus has certain limitations to it. Since the study was performed in Saveetha Dental Hospital, the sample population is restricted to the people living in close proximity to the hospital, this drastically limits the sample diversity (similar socio-economic status and location) which in turn affects the study outcome. Also, this may not depict the general population precisely. Another drawback of this study is the limited sample size. The future scope of this study is thus to perform a prospective study on a much larger scale to better understand the epidemiology of the disease. This will greatly help in advance in the diagnosis and treatment front [22,23], as early diagnosis is key to combating any disease [24,25]

Conclusion

The study reveals the prevalence and association of leukoplakia and oral candidiasis. Study reveals that candidiasis is significantly associated with homogenous leukoplakia and the 31 - 50 years age group is found to be most affected compared with the other age groups. A total of 36% candidiasis prevalence rate was seen amongst the leukoplakia patients. However further studies are required to confirm gender predilection and tobacco usage and its overall effects. The future scope is to conduct more studies in a prospective manner on a larger scale to study the prevalence of candidiasis in oral leukoplakia to evaluate the malignant risk potential.

Acknowledgments:

The study was supported by Saveetha Dental College and Hospitals, Saveetha Institute Of Medical and Technical Sciences, Saveetha University, Chennai.

Author Contributions:

First author Nauma Hafeez contributed towards the data collection, data analysis, and manuscript preparation, The second author Dr. Uma Maheswari contributed towards the study design, key concepts, critical analysis, and review of the study.

Conflicts of Interests:

There were no conflicts of interest as declared by the authors.

References

1. Cani PD. Human gut microbiome: hopes, threats and promises. *Gut*. gut.bmj.com; 2018;67:1716–25.
2. Lohse MB, Gulati M, Johnson AD, Nobile CJ. Development and regulation of single- and multi-species *Candida albicans* biofilms. *Nat Rev Microbiol*. nature.com; 2018;16:19–31.
3. Sam QH, Chang MW, Chai LYA. The Fungal Mycobiome and Its Interaction with Gut Bacteria in the Host. *Int J Mol Sci* [Internet]. mdpi.com; 2017;18. Available from: <http://dx.doi.org/10.3390/ijms18020330>
4. Shao T-Y, Ang WXG, Jiang TT, Huang FS, Andersen H, Kinder JM, et al. Commensal *Candida albicans* Positively Calibrates Systemic Th17 Immunological Responses. *Cell Host Microbe*. Elsevier; 2019;25:404–17.e6.
5. Subashri A, Maheshwari TN. Knowledge and attitude of oral hygiene practice among dental students. *Research Journal of Pharmacy and Technology*. A & V Publications; 2016;9:1840–2.
6. Dharman S, Muthukrishnan A. Oral mucous membrane pemphigoid - Two case reports with varied clinical presentation. *J Indian Soc Periodontol*. 2016;20:630–4.
7. Chaitanya NC, Muthukrishnan A, Krishnaprasad CMS, Sanjuprasanna G, Pillay P, Mounika B. An Insight and Update on the Analgesic Properties of Vitamin C. *J Pharm Bioallied Sci*. 2018;10:119–25.
8. Chaitanya NC, Muthukrishnan A, Babu DBG, Kumari CS, Lakshmi MA, Palat G, et al. Role of Vitamin E and Vitamin A in Oral Mucositis Induced by Cancer Chemo/Radiotherapy- A Meta-analysis. *J Clin Diagn Res*. 2017;11:ZE06–9.
9. Maheswari TNU, Venugopal A, Sureshbabu NM, Ramani P. Salivary micro RNA as a potential biomarker in oral potentially malignant disorders: A systematic review. *Ci Ji Yi Xue Za Zhi*. 2018;30:55–60.
10. Misra SR, Shankar YU, Rastogi V, Maragathavalli G. Metastatic hepatocellular carcinoma in the maxilla and mandible, an extremely rare presentation. *Contemp Clin Dent*. 2015;6:S117–21.
11. Muthukrishnan A, Bijai Kumar L. Actinic cheilosis: early intervention prevents malignant transformation. *BMJ Case Rep* [Internet]. 2017;2017. Available from: <http://dx.doi.org/10.1136/bcr-2016-218654>
12. Venugopal A, Uma Maheswari TN. Expression of matrix metalloproteinase-9 in oral potentially malignant disorders: A systematic review. *J Oral Maxillofac Pathol*. 2016;20:474–9.
13. Hebbar PB, Pai A, D S. Mycological and histological associations of *Candida* in oral mucosal lesions. *J Oral Sci*. jstage.jst.go.jp; 2013;55:157–60.
14. Subha M, Arvind M. Role of Magnetic Resonance Imaging in Evaluation of Trigeminal Neuralgia with its Anatomical Correlation [Internet]. *Biomedical and Pharmacology Journal*. 2019. p. 289–96. Available from: <http://dx.doi.org/10.13005/bpj/1640>
15. Muthukrishnan A, Bijai Kumar L, Ramalingam G. Medication-related osteonecrosis of the jaw: a dentist's

nightmare. BMJ Case Rep [Internet]. casereports.bmj.com; 2016;2016. Available from: <http://dx.doi.org/10.1136/bcr-2016-214626>

16. Shah KM. Association of Candida species with Oral submucous fibrosis and Oral leukoplakia: a case control study. *Annals of Clinical and Laboratory Research*. researchgate.net; 2018;6:248.

17. Nakamura S, Okamoto MR, Yamamoto K, Tsurumoto A, Yoshino Y, Iwabuchi H, et al. The Candida species that are important for the development of atrophic glossitis in xerostomia patients. *BMC Oral Health*. bmcoralhealth.biomedcentral.com; 2017;17:153.

18. Loster JE, Wieczorek A, Loster BW. Correlation between age and gender in Candida species infections of complete denture wearers: a retrospective analysis. *Clin Interv Aging*. ncbi.nlm.nih.gov; 2016;11:1707–14.

19. Muthukrishnan A, Warnakulasuriya S. Oral health consequences of smokeless tobacco use. *Indian J Med Res*. 2018;148:35–40.

20. Dilhari A, Weerasekera MM, Siriwardhana A, Maheshika O, Gunasekara C, Karunathilaka S, et al. Candida infection in oral leukoplakia: an unperceived public health problem. *Acta Odontol Scand*. 2016;74:565–9.

21. Abduljabbar T, Hussain M, Adnan T, Vohra F, Javed F. Comparison of oral Candida species prevalence and carriage among gutka-chewers and betel-quid chewers. *J Pak Med Assoc*. jpma.org.pk; 2017;67:350–4.

22. Choudhury P, Panigrahi RG, Maragathavalli, Panigrahi A, Patra PC. Vanishing roots: first case report of idiopathic multiple cervico-apical external root resorption. *J Clin Diagn Res*. ncbi.nlm.nih.gov; 2015;9:ZD17–9.

23. Patil SR, Maragathavalli G, Araki K, Al-Zoubi IA, Sghaireen MG, Gudipani RK, et al. Three-Rooted Mandibular First Molars in a Saudi Arabian Population: A CBCT Study. *Pesqui Bras Odontopediatria Clin Integr*. 2018;18:4133.

24. Rohini S, Jayanth Kumar V. Incidence of dental caries and pericoronitis associated with impacted mandibular third molar-A radiographic study [Internet]. *Research Journal of Pharmacy and Technology*. 2017. p. 1081. Available from: <http://dx.doi.org/10.5958/0974-360x.2017.00196.2>

25. Steele JC, Clark HJ, Hong CHL, Jurge S, Muthukrishnan A, Kerr AR, et al. World Workshop on Oral Medicine VI: an international validation study of clinical competencies for advanced training in oral medicine. *Oral Surg Oral Med Oral Pathol Oral Radiol*. 2015;120:143–51.e7.