ECRONICON OPEN ACCESS

EC DENTAL SCIENCE
Research Article

Areca Nut and Smokeless Tobacco: Identifying Addiction and Mucosal Changes in Habitual Chewers

Ayesha Basit[1], Sadia Mahmood[2], Maham Naeem[3], Abdur Rehman[4]*, Syed Muzzamil Ali Shah[5], Amna Farrukh[6], Danish Muzaffar[7] and Rafey Ahmed Jameel[8]

[1]Associate Professor, Department of Oral and Maxillofacial Surgery, Hamdard University Dental Hospital, Hamdard University Karachi, Pakistan

[2]Lecturer, Department of Oral Biology, Hamdard University Dental Hospital, Hamdard University, Karachi, Pakistan

[3]Lecturer, Department of Oral and Maxillofacial Surgery, Hamdard University Dental Hospital, Hamdard University, Karachi, Pakistan

[4]Associate Professor, Science of Dental Material Department, Hamdard University Dental Hospital, Hamdard University Karachi, Pakistan

[5]Associate Professor, Department of Community Dentistry, Hamdard University Dental Hospital, Hamdard University Karachi, Pakistan

[6]Senior Registrar, Department of Orthodontics, Hamdard University Dental Hospital, Hamdard University Karachi, Pakistan

[7]Senior Lecturer, Faculty of Basic Sciences, Segi University, Kota Damansara Selangor, Malaysia

[8]Assistant Professor, Department of Oral Biology and Tooth Morphology, Foundation University College of Dentistry and Hospital, Islamabad, Pakistan

***Corresponding Author:** Abdur Rehman, Associate Professor, Science of Dental Material Department, Hamdard University Dental Hospital, Hamdard University, Karachi, Pakistan.

Received: September 28, 2020; **Published:** October 22, 2020

Abstract

The objective of this study is to identify the addiction potential and mucosal changes in the habitual chewers of areca nut and smokeless tobacco with emphasis on the importance of clinical diagnostic skills and documentation of such patients. A proforma was filled for each chewer reporting to Hamdard University Dental Hospital, consisting of information regarding chewers demography, chewing habit, and identification of oral changes due to these substances. After an orientation session, patients were assigned to final year BDS students and house officers. Data was analyzed using SPSS version 25. Out of 664 study participants, predominant age group was 26 - 45 years (49.5 %), males 65% and literate up to the level of matriculation 35.8%. The chewers were predominantly housewives 25% followed by field workers 24.8% in terms of occupation. Significant relationships were found between age and substance consumed and so between substance consumed and withdrawal symptoms. Areca nut alone most commonly chewed 31.7% and 75% participants consuming one or more substances for more than five years. Taste was the predominant cause of the habit 44.7%. Withdrawal symptoms were reported by 40.6% participants. 80.1% chewers knew about the potential harm of these substances. The predominant clinical finding 45% was restricted mouth opening, followed by fibrous bands 25.7%. No significant relationship was found between the type of substance chewed and the type of clinical findings. Chewers lack of awareness and failure to recognize the harmful effects of areca nut and SLT, necessitates clinical diagnostic skills training of young doctors with documentation and long term follow up of these patients.

Keywords: *Areca Nut; Smokeless Tobacco; Oral Sub Mucous Fibrosis; Oral Cancer; Gutka; Malignant Transformation; Oral Mucosal Lesions; Addiction; Dependency Syndrome; Burning Sensation*

Introduction

Areca nut and Smokeless Tobacco (SLT) in the form of Gutka are known as strong and independent risk factors for the development of potentially malignant mucosal changes and eventually oral cancer, the 6th most common cancer worldwide [1-4]. Romana., *et al*. found a prevalence of oral cancer ranging from 2 - 19% depending on the area of study [5].

The alkaloids, polyphenols, tannins and copper present in areca nut promote collagen synthesis and crosslinking and decreased collagen degradation leading to oral submucous fibrosis, a potentially malignant condition [6].

According to Pakistan Health Research Council Cancer Registry (2015-16) oropharyngeal cancer was the second most common cancer in Pakistan and its association with smokeless tobacco was found to be 35% [7]. The carcinogenic potential in Smokeless Tobacco (SLT) is due to the presence of tobacco-specific N-nitrosamines, cadmium, polonium-210, formaldehyde, benzo(a)pyrene and lead. It is also reported to possess cancer inhibiting constituents like carotenoids and phenolic compounds but in very low concentrations [8]. Local irritation and chronic inflammation from SLT coupled with the effects of nitrosamines cause leukoplakia, erythroplakia and autoimmune conditions like lichen planus; all having potential for malignant transformation. As a result of chronic inflammation induced by these substances, levels of oxygen free radicles and cytokines increase, leading to increased cell proliferation and DNA damage and hence oral cancer [6].

It has been found that nicotine from chewed tobacco is absorbed more readily and hence more exposure as compared to systemic absorption from snuff and that from smoking. As a result of this increased nicotine exposure, tobacco with or without areca nut, exerts a toxic effect on reproductive system as well as a potential for adverse pregnancy outcome [9]. In a survey conducted on one thousand habitual gutka and areca nut chewers by Nigam., *et al*. 6.3% developed oral submucous fibrosis. Other complications observed were altered taste, limited mouth opening and problems in hearing ability [10].

Research has shown that areca nut possesses a psychoactive potential, primarily caused by its active are choline. It is a partial agonist of muscarinic receptors. The stimulant and anxiolytic effects of areca nut are thought to be the cause of a rapid increase in its consumption [11]. The stimulation of central and autonomic nervous system results in subjective effects of increased wellbeing, improved stamina and concentration. It is also believed to be a hunger suppressant, aphrodisiac and a digestant [12]. Javed and coworkers point towards another possible interesting consequence of areca nut use. According to them, the hunger suppression caused by areca nut users, leads to a state of malnutrition and more importantly vitamin D deficiency. This deficiency is a risk factor for metabolic syndrome and diabetes mellitus [13]. The addictive potential of areca nut has been supported by its activity on nicotinic acetylcholine receptor (nAChR) subtypes [14] and the reports of nicotine like withdrawal symptoms in chewers trying to quit the habit [15]. The areca nut dependency increases with addition of tobacco or when the chewer is also a smoker [16]. Areca nut has also been reported to show cariostatic, and antimicrobial properties in the oral cavity [17].

Different commercial preparations of Gutka, containing areca nut, dried and finely chopped tobacco, slaked lime and catechu along with some sweeteners and flavoring agents have been in use since 1975 by South-Asian people. The same product without tobacco is known as pan masala [5].

The effects of gutka chewing on cellular morphology of buccal keratinocytes including alterations in cellular diameter (CD), cytoplasmic area (CA), nuclear shape, nuclear texture, nuclear diameter (ND), nuclear area (NA), nuclear membrane continuity, NA/CA ratio and optical density have been reported by Acharya., *et al*. and Noufal., *et al* [18,19].

In the oral and maxillofacial surgery department in our institute, the authors very frequently come across the habitual users of areca nut and smokeless tobacco products with or without mucosal changes. Very commonly they visit the department for extraction of carious

teeth which becomes a difficult task because of the restricted mouth opening due to oral submucous fibrosis. Sometimes it was realized that a potentially malignant change in mucosa was left unrecognized by a general dental practitioner outside our institute or final year student or house officer during routine OPD. It is pertinent that young dental healthcare professionals be capable of recognizing the mucosal changes developed as a result of these products at as early stage as possible in order to reduce possible complications. The importance of counselling towards habit cessation of these harmful products before appearance of mucosal changes cannot be forgotten.

Aim of the Study

The aims of the study were, to gain an insight of some important factors related to the chewing habit of areca nut and SLT, to identify potentially malignant mucosal changes in these habitual chewers even if they are not aware of it and to train young dentists and final year students in recognition of mucosal changes developing as a result of areca nut and SLT.

Materials and Methods

The study was conducted in the Oral and Maxillofacial Surgery department, Hamdard University Dental Hospital, Karachi. The duration of the study was 2 years (2017 - 2019). Sample size was calculated by using Openepi software version 3. Mean and standard deviation was used 44.1 (± 16.2) and 29.4 (± 12.5) respectively [20].

The Proforma of the study (Annexure) consisted of the three parts.

Consent form in English and Urdu to be filled by the patient.

Second part of the proforma, to be filled by the examiner, included the following information:

1. Demographic data of the participants including name, age, gender, contact information, education and occupation. For the purpose of data analysis, all the occupations reported by our participants were broadly categorized into student, office work (working with pen and paper), field workers (including all sorts of labor work and drivers), speakers (teachers, lawyers and media persons), shopkeepers, housewives and unknown (including unemployed, retired and those who did not inform about their occupation).

2. Type of substance chewed, namely pan with tobacco, pan without tobacco, areca nut, gutka, niswar, or any combination of two or more products.

3. Oral consequences associated with chewing habit including, burning sensation, Interincisal distance, cheek flexibility (distance from maxillary incisal midline to the cheek retractor during retraction), blanching, fibrous bands, ulceration, white and or red patches and exophytic lesions at different mucosal subsites.

Third part of the proforma, to be filled by the patient, was a questionnaire designed in Urdu language and included 10 questions regarding, duration and cause of chewing habit, daily expenditure on the substance, withdrawal symptoms (what happens if substance is not consumed), knowledge about harmful effects of the chewed substance, and willingness towards quitting the use of these substances.

At the beginning of data collection, the proforma was validated with 10 patients for understanding and clarity of questions.

The study was approved by the Ethical Committee of Hamdard University Dental Hospital.

The inclusion criteria was all new patients reporting to the oral and maxillofacial surgery department with history of any form of areca nut and/or tobacco chewing habit regardless of the primary complain and chewers not consenting to participate in the study.

Exclusion criteria was patients already diagnosed with oral cancer and patients not consenting to participate in the study.

A structured orientation session on the proforma, with identification of history and clinical findings was delivered to each group of final year BDS students and house officers at the beginning of their rotation in Oral and Maxillofacial Surgery department prior to assigning them patients.

Data was analyzed by using SPSS version 25. All descriptive analyses were done. Statistical significance evaluated by using Chi Square Test (P-value = 0.05).

Results

Total number of participants consenting for the study, was 664. The demographic information is presented in table 1. Out of 664 patients, 49.5 % (n = 329) patients were aged between 26 - 45 years and the predominant gender was male 65% (n = 432). The educational status of majority of participants was matriculation (n = 238, 35.8%). Housewives 25% (n = 166) followed by field workers 24.8% (n = 165) were the predominant chewers. Significant relationships were found between age of participants to substance consumed and between substance consumed to the withdrawal symptoms.

S. No.	Variable name	Frequency	Percentage %
1.	**Age**		
	Less than 16	25	3.7
	16-25	115	17.3
	26-45	329	49.5
	More than 45	195	29.3
2.	**Gender**		
	Male	432	65
	Female	232	34.9
3.	**Education**		
	None	154	23.1
	Matriculation	238	35.8
	Intermediate	113	17
	Graduation	125	18.8
	Postgraduation	34	5.1
4.	**Nature of work**		
	Student	54	8.1
	Office work	45	6.7
	Speakers	17	2.5
	House wives	166	25
	Field workers	165	24.8
	Shopkeepers	80	12
	Unknown	135	20.3
5.	**Tests of significance**	P- Value	
	Age to Substance chewed	0.001	
	Substance chewed to Withdrawal symptoms	0.001	

Table 1: *Demographic data of the participants.*

Information about the chewing habit and the clinical findings related to it are depicted in table 2. Majority of the participants 31.7% (n = 211) were areca nut chewers. The predominant number of participants 75% (n = 500) had been consuming these substances for more than five years. The predominant causes of consuming these substances were, taste 44.7%, (n = 297) followed by friends/company 30.7% (n = 204). Less than Rs 100 were being spent daily by 88.4% (n = 587) chewers.

S. No.	Variable Name	Frequency	Percentage
1.	**Substance**		
	Pan with tobacco	132	19.8
	Pan without tobacco	17	2.6
	Areca nut	211	31.7
	Gutka	88	13.2
	Niswar	8	1.2
	Combination	208	31.2
2.	**Duration (Years)**		
	less than 1	39	5.9
	Up to 2	29	4.4
	2-5	96	14.5
	More than 5	500	75
3.	**Cause**		
	Home Environment	72	10.8
	Friends/company	204	30.7
	Workload	25	3.8
	Suppress hunger	9	1.4
	Taste	297	44.7
	Mental stress	29	4.4
	For toothache	2	0.3
	To be alert	1	0.2
	Combination	19	2.9
4.	**Daily Expenses (Rs)**		
	Less than 100	587	88.4
	More than 100	77	11.5
5.	**Willingness to Quit**		
	No	68	10.2
	Yes	596	89.8
6.	**Withdrawal**		
	No	394	59.3
	Yes	270	40.6
7.	**Awareness of Harm**		
	No	128	19.3
	Yes	532	80.1

8.	**Clinical Findings**		
	Burning sensation	195	29.3
	Interincisal distance (less than 35 mm)	299	45
	Cheek flexibility L (less than 30 mm)	103	15.5
	Cheek flexibility R (less than 30 mm)	106	15.9
	Blanching of mucosa	100	15
	Fibrous bands	171	25.7
	Ulceration	88	13.2
	White patches	93	14
	Red patches	46	6.9
	Relationship of oral consequences with the type of substance used	**P-Value**	
	Burning sensation	0.830	
	Blanching of mucosa	0.333	
	Interincisal distance	0.371	
	Fibrous bands	0.671	
	Ulceration	0.156	
	White patches	0.020	
	Red patches	0.077	

Table 2: *Chewing habits and clinical findings of the participants.*

Out of 664 participants, 40.6% (n = 270) complained of different types of withdrawal symptoms. Predominant number of chewers 80.1% (n = 532) were aware of the potential harm of these substances. 89.8% (n = 596) were willing to quit the habit, and they had tried at least once for this purpose. 94.7% (n = 629) showed willingness to accept help with clinical follow ups and habit cessation.

The predominant clinical finding 45% (n = 299) was restricted mouth opening, followed by fibrous bands 25.7% (n = 171).

No significant relationship was found between the type of substance chewed and the type of clinical findings.

Discussion

Participants of all ages and both genders with history of areca nut and smokeless tobacco (SLT) chewing habit were included in our study and their level of education noted. The trend we found in our study was predominantly literate males up to the level of matriculation in the age range 26 - 45 years consuming most commonly areca nut alone. Researches done in other parts of the world show variations in terms of age range and gender. Mohan., *et al*. had majority of gutka chewers below 30 years, whereas Singhvi., *et al*. while surveying gutka chewing school children, found the majority between 11 - 18 years [21,22]. Rehan and coworkers reported male predominance in gutka chewing habits [23]. In contrast, in Bangladesh; Abdullah and coworkers studying the use of SLT, found a pattern of predominant illiterate females, increasing age, with the beliefs of social acceptance and less harm as compared to smoked tobacco [24].

During the study, we realized the fact that it is difficult to consider areca nut and smokeless tobacco separately because the products used by the chewers contain mostly both major constituents. For example, pan with tobacco has areca nut as well and any form of gutka has both tobacco and areca nut. Both the major constituents have psychoactive and addictive effects and lead to similar mucosal changes.

We enquired about the occupation of the participants with the objective of finding out if there is any relation between the nature of work with the chewing habit considering the psychoactive and stimulant effect of these substances. In our study, the chewers were pre-

dominantly housewives followed by field workers, mostly consuming areca nut alone or consuming multiple forms. Huang., *et al*. in their study in Taiwan found increased prevalence of betal quid (betal leaf, areca nut and slaked lime with or without tobacco) chewing habit among drivers, construction and mine workers and they related this finding to the psychoactive and stimulant benefits during stressful jobs and long working hours [25]. Rehan and coworkers also relate the chewing habits to occupation, psychological stress and socioeconomic conditions [23]. Our study had some different findings. Majority of our study participants labelled taste and influence of friends/company as the cause of their chewing habit as compared to workload or hunger suppression. Gunaseelan., *et al*. in their study on areca nut use in a rural population found that fun and peer pressure were the causative factors of this habit in people younger than 30 years; but in older population, it was boredom and stresses [26].

The ease of availability in terms of cost at the expense of health hazard coupled with the fact that these carcinogenic substances are also an important source of income for people of low socioeconomic status is depicted in our results as well as other researches. Regardless of the type of substance used, majority of our participants spent less than 100 rupees daily on their habit. Similarly, Shah., *et al*. and Misbahuddin., *et al.* found usage of areca nut and its products to be very high among school going children belonging to families of low socioeconomic status [27,28]. Schensul., *et al*. found selling of smokeless tobacco with addictive properties to be an important source of income in slum communities with people of low socioeconomic status [29].

According to Farlex Medical Dictionary, "Addiction is a persistent, compulsive dependence on a behavior or substance. The term has been partially replaced by the word dependence for substance abuse" [30]. Our study participants reported different problems when they do not consume these substances including headache, drowsiness, anxiety, irritability, weakness, sleepiness, stomach upset, palpitations and toothache. There was no significant difference between the two predominant groups (areca nut and gutka chewers). Bhat., *et al*. reported positive relationship between the dependence scores and the quantity chewed daily [20].

Despite the fact that more than 80% of our study participants were aware of the harmful effects of these substances, they continued to consume them even in the absence of withdrawal symptoms. This indicates participants' careless approach towards their health. Similarly, Khan and coworkers found that awareness regarding the harmful effects of areca nut was satisfactory amongst the subjects, but the population was not willing to quit the habit [31].

Mutti., *et al*. and Pant., *et al*. reported gutka to be the most commonly used form of smokeless tobacco in India and pan masala in Bangladesh and similar to our findings, they also related the widespread use of these substances to the issue of the chewers believing that the quantity being consumed is not harmful enough to cause cancer [32,33].

Liaqat., *et al*. related the chewing habit of smokeless tobacco despite being aware of the its harmful effects, to psychological dependency and addiction [34]. Shah., *et al*. in their survey, reported extensive use of areca nut and pan masala by school children of low socioeconomic status despite knowing its harmful effect. The reasons they revealed were very similar to our results, that is taste, friends/company, low cost and easy availability [28].

SLT in the form of gutka has been found to be associated with oral submucous fibrosis and its malignant transformation which can extend beyond the oral cavity [35].

Oral submucous fibrosis manifests itself initially as burning sensation, xerostomia, ulceration and restricted mouth opening [36]. Malignant transformation of OSF to squamous cell carcinoma (SCC) has been estimated to be between 2 - 8% [37]. Upon detailed clinical examination of 664 participants in our study, the most common clinical findings were restricted mouth opening followed by fibrous bands. Next in line was burning sensation. The reduction in membrane associated mucins because of fibrosis of minor salivary glands leads to insufficient lubrication and protection of oral mucosa. The impaired protective barrier of oral mucosa with rapid loss of superficial cells in response to minor trauma leads to the nerve endings in the epithelium getting closer to the surface. The substances in the food absorb

more readily through the thin epithelium to reach the nerve ending and hence the symptom of burning sensation [38]. All the symptoms are logically related to oral submucous fibrosis. Reddy and coworkers reported mucositis followed by submucous fibrosis as the most common findings in tobacco chewers [3]. Patil and coworkers reported that there are 11.92 times more chances of developing oral leukoplakia and oral submucous fibrosis in people with tobacco chewing habit as compared to those who do not consume it [39].

With all the knowledge regarding the addictive and carcinogenic potential of areca nut and SLT, the most important question arises; how to deal with this difficult situation? There have been different strategies in use worldwide including mass media campaigns and bans on these products [40,41]. The dental healthcare professionals bear the responsibility to have a critical eye on identifying people at risk. The policy review by Mehrtash., *et al*. agrees with our study objectives by discussing the importance of dental healthcare professionals trained in oral clinical examination targeted towards identification of potentially malignant oral mucosal changes to reduce cancer burden on the society. As this method does not cost much to the patient as compared to other testing modalities, it is more acceptable to the people. In addition, documentation of different aspects of the consumption of these addictive substances and the subsequent harms, lead to a better understanding of the situation [42].

For this purpose, as part of the study we focused on training the final year students and house officers in identification of such patients. They were supervised by the authors during clinical examination of the study participants and the chewers were requested to adhere to the follow up protocol provided to them.

The authors have noticed a lack of compliance of the chewers towards the follow up visits during the study despite their acceptance in the proforma, but as the follow ups are still in progress, it is still an opinion until documented.

Conclusion

Because of the addictive and psychoactive potential, areca nut and smokeless tobacco are consumed widely either alone or in combination. The ease of availability relates to the low cost and therefore the members of low socioeconomic group are both users and sellers. In this era of massive information, the chewers are still failing to realizing the potential harm of these substances and recognizing the changes happening in their oral cavity. We recommend that the dental healthcare professionals working in any setting, must critically look for oral mucosal changes in the chewers' oral cavities even if they do not complain of any. For this purpose, we also recommend holding workshops focused on identification and documentation of oral mucosal changes in habitual chewers of areca nut and SLT. Further researches based on long term follow ups of areca nut and SLT chewers are the need of the day, to evaluate chewers compliance towards habit cessation, efficacy of preventive and therapeutic measures for potentially malignant oral mucosal changes and rate of malignant transformation in these areas.

Bibliography

1. Li Yi-Chen., *et al*. "Multifaceted Mechanisms of Areca Nuts in Oral Carcinogenesis: The Molecular Pathology from Precancerous Condition to Malignant Transformation". *Journal of Cancer* 10 17 (2019): 4054.

2. Gupta Bhawna and Newell W Johnson. "Systematic Review and Meta-Analysis of Association of Smokeless Tobacco and of Betel Quid without Tobacco with Incidence of Oral Cancer in South Asia and the Pacific". *PloS one* 9 11 (2014): e113385.

3. Reddy Sujatha S., *et al*. "Prevalence of Oral Mucosal Lesions among Chewing Tobacco Users: A Cross-Sectional Study". *Indian Journal of Dental Research* 26.5 (2015): 537.

4. Asthana Smita., *et al*. "Association of Smokeless Tobacco Use and Oral Cancer: A Systematic Global Review and Meta-Analysis". *Nicotine and Tobacco Research* 21.9 (2019): 1162-1171.

5. Idrees Romana., *et al*. "Cancer Prevalence in Pakistan: Meta-Analysis of Various Published Studies to Determine Variation in Cancer Figures Resulting from Marked Population Heterogeneity in Different Parts of the Country". *World Journal of Surgical Oncology* 16.1 (2018): 129.

6. Sankhla Bharat., *et al*. "Genotoxic and Carcinogenic Effect of Gutkha: A Fast-Growing Smokeless Tobacco". *Addiction and Health* 10.1 (2018): 52.

7. Pakistan Health Research Council (2020).

8. Janbaz Khalid Hussain., *et al*. "Risk for Oral Cancer from Smokeless Tobacco". *Contemporary Oncology* 18.3 (2014): 160-164.

9. Kumar Sunil. "Tobacco and Areca Nut Chewing-Reproductive Impairments: An Overview". *Reproductive Toxicology* 36 (2013): 12-17.

10. Nigam Nitin Kumar., *et al*. "Prevalence of Oral Submucous Fibrosis among Habitual Gutkha and Areca Nut Chewers in Moradabad District". *Journal of Oral Biology and Craniofacial Research* 4 1 (2014): 8-13.

11. Papke Roger L., *et al.* "Nicotinic Activity of Arecoline, the Psychoactive Element of" Betel Nuts", Suggests a Basis for Habitual Use and Anti-Inflammatory Activity". *PLoS One* 10.10 (2015): e0140907.

12. Benegal Vivek., *et al.* "Does Areca Nut Use Lead to Dependence?" *Drug and Alcohol Dependence* 97.1-2 (2008): 114-121.

13. Javed F., *et al.* "Areca-Nut Chewing Habit Is a Significant Risk Factor for Metabolic Syndrome: A Systematic Review". *The Journal of Nutrition, Health and Aging* 16 5 (2012): 445-448.

14. Horenstein Nicole A., *et al*. "Cracking the Betel Nut: Cholinergic Activity of Areca Alkaloids and Related Compounds". *Nicotine and Tobacco Research* 21.6 (2019): 805-812.

15. Little MA and RL Papke. "Betel, the Orphan Addiction". *Journal of Addiction Research and Therapy* 6.3 (2015): 130-132.

16. Mirza Saira S., *et al*. "Areca Nut Chewing and Dependency Syndrome: Is the Dependence Comparable to Smoking? A Cross Sectional Study". *Substance Abuse Treatment, Prevention, and Policy* 6.1 (2011): 23.

17. Chandak Rakhi Manoj., *et al.* "Current Concepts About Areca Nut Chewing". *Journal of Contemporary Dentistry* 3.2 (2013): 78-81.

18. Acharya Swetha., *et al.* "Cytomorphometric Analysis of the Keratinocytes Obtained from Clinically Normal Buccal Mucosa in Chronic Gutkha Chewers". *Journal of Cranio-Maxillary Diseases* 2.2 (2013): 134-141.

19. Noufal Ahammed., *et al*. "Cytomorphometric Analysis of Oral Buccal Mucosal Smears in Tobacco and Arecanut Chewers Who Abused with and without Betel Leaf". *Substance Abuse* 35.1 (2014): 89-95.

20. Bhat Shrihari JS., *et al*. "Areca Nut Dependence among Chewers in a South Indian Community Who Do Not Also Use Tobacco". *Addiction* 105.7 (2010): 1303-1310.

21. Mohan P Ram., *et al.* "Clinical, Cytological and Histopathological Correlation of Oral Mucosal Changes in Gutka Chewers-a Prospective Study" 5.11 (2018): 70-76.

22. Singhvi Abhishek., *et al*. "The Insight for Initiation and Maintenance of Areca Nut Chewing Habit and Its Effects on Oral Health Status among School Age Population in Western Rajasthan, India". *Journal of Clinical and Diagnostic Research: JCDR* 10.11 (2016): ZC15.

23. Rehan Faisal., *et al*. "Habitual Risk Factors in Gutka Chewers". *International Dental and Medical Journal of Advanced Research* 3.1 (2017): 1-5.

24. Abdullah Abu S., *et al*. "Patterns and Predictors of Smokeless Tobacco Use among Adults in Bangladesh: Findings from the International Tobacco Control (Itc) Bangladesh Survey". *PloS one* 9.7 (2014): e101934.

25. Huang Yu-Ting., *et al*. "Determining High Prevalence of Betel-Quid Chewing and Cigarette Smoking by Occupation Using the Taiwan National Health Interview Survey". *Substance Use and Misuse* 55.9 (2020): 1472-1482.

26. Gunaseelan R., *et al*. "Areca Nut Use among Rural Residents of Sriperambudur Taluk: A Qualitative Study". *Indian Journal of Dental Research* 18.1 (2007): 11.

27. Misbahuddin Syed M., *et al*. "The Menace of Betel Nut and Gutka: An Oral Health Survey of School Children to Assess Prevalence of Oral Lesions in Chewers Versus Non-Chewers". *International Dental Journal of Students Research* 3 (2015): 163-169.

28. Shah Sameena., *et al.* "Is Chaalia/Pan Masala Harmful for Health? Practices and Knowledge of Children of Schools in Mahmoodabad and Chanesar Goth, Karachi". *Journal of the Pakistan Medical Association* 59.8 (2009): 550.

29. Schensul Jean J., *et al*. "Availability, Accessibility and Promotion of Smokeless Tobacco in a Low-Income Area of Mumbai". *Tobacco Control* 22.5 (2013): 324-330.

30. Farlex Medical dictionary.

31. Khan Muhammad Shahzeb., *et al*. "Comparison of Knowledge, Attitude and Practices of Betelnut Users in Two Socio-Economic Areas of Karachi". *JPMA. The Journal of the Pakistan Medical Association* 63.10 (2013): 1319-1325.

32. Mutti Seema., *et al*. "Patterns of Use and Perceptions of Harm of Smokeless Tobacco in Navi Mumbai, India and Dhaka, Bangladesh". *Indian journal of community medicine: official publication of Indian Association of Preventive and Social Medicine* 41.4 (2016): 280.

33. Pant Nirdosh Kumar., *et al*. "Evaluation of the Knowledge and Perceptions with Regards to Pictorial Health Warnings on Tobacco Products among Tobacco Users Diagnosed with Head and Neck Carcinoma: A Study from the Kumaon Hills of India". *Asian Pacific Journal of Cancer Prevention* 15.18 (2014): 7891-7895.

34. Liaquat Nida., *et al*. "Knowledge and Perception of Areca/Smokeless Tobacco Users About Oral Cancer". *Journal of Ayub Medical College Abbottabad* 28.1 (2016): 164-167.

35. Javed Fawad., *et al*. "Oral Mucosal Disorders Associated with Habitual Gutka Usage: A Review". *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology* 109.6 (2010): 857-864.

36. Shih Yin-Hwa., *et al*. "Oral Submucous Fibrosis: A Review on Etiopathogenesis, Diagnosis, and Therapy". *International Journal of Molecular Sciences* 20.12 (2019): 2940.

37. Ray Jay Gopal., *et al.* "Malignant Transformation of Oral Submucous Fibrosis: Overview of Histopathological Aspects". *Oral Surgery, Oral Medicine, Oral Pathology And Oral Radiology* 122.2 (2016): 200-209.

38. Sarode Sachin C and Gargi S Sarode. "Burning Sensation in Oral Submucous Fibrosis and Its Possible Association with Mucin Secreted by Affected Minor Salivary Glands". *Oral Oncology* 49.4 (2013): e16.

39. Patil Prashant B., *et al.* "Prevalence of Oral Mucosal Lesions in Dental Patients with Tobacco Smoking, Chewing, and Mixed Habits: A Cross-Sectional Study in South India". *Journal of Family and Community Medicine* 20.2 (2013): 130.

40. Mishra GA., *et al*. "Impact Of'gutkha and Pan Masala Ban'in the State of Maharashtra on Users and Vendors". *Indian Journal of Cancer* 51.2 (2014): 129.

41. Murukutla Nandita., *et al*. "Results of a National Mass Media Campaign in India to Warn against the Dangers of Smokeless Tobacco Consumption". *Tobacco Control* 21.1 (2012): 12-17.

42. Mehrtash Hedieh., *et al*. "Defining a Global Research and Policy Agenda for Betel Quid and Areca Nut". *The Lancet Oncology* 18.12 (2017): e767-e75.

Volume 19 Issue 11 November 2020