



Determining the Risk Factor of Oral Cancer on Chewing Smokeless Tobacco Kharra: A Case-control Study

Jonathan Lalnunsanga^{a#}, Lalruatzela^{a#}, James Lalduhawma^{a#},
Kumar Gaurav Chhabra^{b*#} and Priyanka Paul Madhu^{b#}

^a Sharad Pawar Dental College And Hospital, Datta Meghe Institute Of Medical Sciences (Deemed To Be University), Sawangi (Meghe), Wardha 442001, Maharashtra, India.

^b Department of Public Health Dentistry, Sharad Pawar Dental College And Hospital, Datta Meghe Institute Of Medical Sciences (Deemed To Be University), Sawangi (Meghe), Wardha 442001, Maharashtra, India.

ABSTRACT

Background: Oral cancer is the sixth most common cancer globally; however, the incidence is much higher in the developing countries, including Pakistan, India, Sri Lanka. The etiology of oral cancer is multifactorial with majority of the cases attributable to separate and combined use of tobacco (smoked and smokeless), excessive alcohol consumption, betel quid, and betel quid substitutes. Among this, Kharra chewing (areca nut and tobacco) is the most prevalent addiction and the most common risk factors of oral cancer in central India.

Objectives: To evaluate the risk of oral cancer associated with kharra users and non-tobacco user. To evaluate the association for the risk factors of oral cancer with kharra and non-tobacco user.

Methodology: A hospital based case control study will be carry out in the study, the study will be conducted among the patient who had confirmed diagnosis of oral cancer and visited the hospital in AVBRH and SPDC Sawangi (Meghe) Wardha. Non- probability convenient sampling technique will be used for selecting the sample. The structured questionnaire will be used for collection of the data.

Expected results: This study is mainly planned to evaluate the effects of Kharra chewing on oral cancer risk with the help of structured questionnaire. Hence, it is expected to identify the effects of Kharra chewing on the risk of oral cancer.

Keywords: Oral cancer; kharra; structured questionnaire.

1. INTRODUCTION

Kharra chewing (areca nut and tobacco) is the most prevalent addiction in central India. Arecoline, a natural alkanoid in areca nut, has genotoxic, carcinogenic, embryotoxic, and immunotoxic potential. Several epidemiological and experimental investigations have established that quid chewing causes oral and oropharyngeal cancer, interferes with the microbial mechanism of neutrophils, and inhibits protein synthesis and attachment of fibroblasts. This in turn promotes bacterial colonization and periodontal infection.

As a result, the harmony between various periodontal structures is disrupted that leads to induced gingivitis and periodontitis. It also exerts excessive masticatory load on the tissues, leading to wearing facets, attrition, sensitivity, food lodgement, and food impaction. The extracts also stain teeth and affects oral aesthetics and social confidence. Arecoline also generates reactive oxygen species due to which lipid peroxidation is initiated and leads to oral cancer.

Oral cancer is the sixth most common cancer globally; however, the incidence is much higher in the developing countries, including Pakistan, India, Sri Lanka [1,2]. In Central and Southeast Asia, oral cancer accounts for up to 40% of all cancers compared to less than 4% reported in most developed countries [3,4]. The etiology of oral cancer is multifactorial with majority of the cases attributable to separate and combined use of tobacco (smoked and smokeless), excessive alcohol consumption, betel quid, and betel quid substitutes [5-9]. Moreover, the pattern of tobacco consumption in India is probably more diverse than any other country in the world, which is the reason for the regional variations in the consequential burden of tobacco-related diseases and deaths [10]. 15 Studies in India have reported that five million children under the age of 15 years are addicted to gutka [11]. Recently with increased availability and use of many different forms of ST products, it has become imperative to evaluate their harmful effects. Moreover, there is a paucity of data on research related to new tobacco products, especially related to kharra. There are not many studies in the published literature that have reported evidences on risk of oral cancer related to kharra. Therefore, the aim of the present study was to identify the prevalence of the risk of oral cancer and its association with kharra [11].

2. METHODS

A hospital based case control study will be carry out in the study, the study will be conducted among the patient who had confirmed diagnosis of oral cancer and visited the hospital in AVBRH and SPDC Sawangi (Meghe),Wardha. Non-probability convenient sampling technique will be used for selecting the sample. The structured questionnaire will be used for collection of the data.

Sample selection-

Odds ratio r	=	2
Exposed controls	=	20%
One-sided alpha risk	=	5%
Number of pairs	=	80

Probability of an exposure-discordant pair = 40%

$$\text{Sample size} = \frac{r + 1 (Z_{1-\alpha} + Z_{1-\beta})^2 p_1 (1 - p_1)}{r (p_1 + p_2)^2}$$

Estimated Number of case controls on the basis of Case control 1: 1 distribution

Hence a sample size of 60 cases and 60 controls were evaluated.

2.1 Inclusion Criteria

1. Patient who had confirmed clinical and histopathological diagnosis of oral cancer and visited the hospital during the study period.
2. Patient who have habit of chewing kharra.
3. Patient who can speak Marathi, Hindi and English.

2.2 Exclusion Criteria

1. Patient who are not willing to participate in the study.

2.3 Selection of Participants

All the confirmed clinical and histopathological diagnosis of oral cancer and patient who visit the hospital during the study period will be assign randomly by sequential numbered system.

2.4 Statistical Analysis

Statistical analysis will be done by descriptive and inferential statistics with the help of SPSS software. SPSS software will be used for statistical analysis. After completion of the questionnaire, all the data will be recorded and will be analyzed from the number of responses received by using Chi Square test and will be analyze for Odds ratio.

2.5 Measurement

The questionnaire is arranged according to examine respondents' socio-demographic characteristics, dental service specifics, and a self-assessment of service quality. The items used in the self-assessment of service quality will be graded using a five-point Likert Scale {13}. Participants will be asked to complete a questionnaire in a particular period and demographic information was included at the start of the survey.

Bias: All the potential sources of bias has been removed.

Quantitative variables: all the demographic details and the questions in relation to the questionnaire will be recorded with the

help of electronic forms and record in the excel sheet.

3. EXPECTED RESULTS

This study is mainly planned to evaluate the effects of Kharra chewing on oral cancer risk with the help of structured questionnaire. Hence, it is expected to identify the effects of Kharra chewing on the risk of oral cancer.

4. DISCUSSION

Tobacco products which are used in a way other than smoking are known as smokeless tobacco. The most common smokeless tobaccos are chewing tobacco, naswar, snuff, snus, gutka, kharra and topical tobacco paste. Any product which contain tobacco is not safe for human health.

According to Surekha Rathod, Ishita Wanikar, Anubha Raj, Shweta Maske, Vivek Harkare on the topic of Association between kharra chewing and periodontal health status in oral submucous fibrosis patients of Central India, Nagpur. The aim of this study was to evaluate and compare the effects of kharra chewing on periodontal status in patients with OSMF. The study was concluded that The habit of chewing kharra is found to be associated with poor periodontal health in patients with OSMF [12].

KH Awan, QA Hussain, Shankargouda Patil, Mahesh Maralingannavar on the topic of Assessing the Risk of Oral Cancer associated with Gutka and Other Smokeless Tobacco Products: A Case-control Study. Participants who consumed other ST products also showed 2 to 4 times higher odds ratio of developing oral cancer than compared to those who did not consume these products. The study concluded that the study provided strong evidence that gutka and other ST products are independent risk factors for oral cancer [13].

Jang Bahadur Prasad & Murali Dhar was conducted a systematic review and meta-analysis on the topic of Risk of major cancers associated with various forms of tobacco use in India. The result shows that smoking was found to be associated with a 5-fold higher risk of oropharynx, larynx, and lung, a 3-fold higher risk of hypopharynx, and esophagus, and a 2-fold higher risk of oral cancer. Esophagus (OR = 3.5) and oral cancer were the only sites significantly associated with tobacco chewing. The OR associated with bidi smoking was highest for lung (6-fold) followed by esophagus (3.5-fold) and oral

cancer (3-fold). Lung cancer was also significantly associated with cigarette smoking [14].

A study was conducted by Ashish Sharma, Kumar Gaurav Chhabra, Sunita Agarwal, Suman Bhansali, Pooja Singh, Renuka G Nagrale on the topic of association between health-related quality of life and sense of coherence among health professionals working in primary health centers consuming tobacco in Jaipur, India. It was a cross-sectional descriptive study where sampling technique used was systematic stratified random sampling. Jaipur District has 37 PHCs retrieved from site of NRHM Rajasthan. A close-ended questionnaire was prepared to conduct the interview. The study results showed that Majority of study participants (57; 37.01%) were of 36–40 years of age. Males respondents (86; 55.85%) consuming tobacco were more in number than female respondents. Majority of study subjects (91; 59.09%) consumed smoked kind of tobacco, in which most contributed were nurses (49; 62.82%). On applying a linear regression model, it was determined that all subscale of SF-36 was significantly ($P \leq 0.000$) associated with SoC. It was concluded that there was a strong association between HRQOL and SoC among health professionals working in primary health centers consuming tobacco [15].

A cross-sectional study was carried out on the knowledge attitude and practice regarding tobacco cessation methods among the dental professionals by Dr. Priyanka Paul Madhu. It shows that more than half of the respondents had an average level of knowledge on smoking cessation interventions while a majority had a positive attitude towards the provision of smoking cessation interventions. Hence it's a need of hour to influence the students for generating interest in attaining knowledge about tobacco cessation methods [16]. Many studies have been reported on the tobacco abuse and related pathologies in Indian population [17-20]. Thakare et. al. reported as study on variation in the changes induced by different forms of tobacco in dental hard tissues [21]. Hande et. al. reported on cytomorphometric analysis of buccal mucosa of tobacco chewers [22]. Some more interesting studies were reported by Lohe et. al.[23], Quazi et. al. [24] and Teni et. al.[25].

5. CONCLUSION

The evaluation of the effects of smokeless tobacco on oral health helps to understand the various risk factors associated with oral cancer. Hence, the determination of the frequency of tobacco consumption and its relation with oral cancer can help the patients to quit the habit and prevent further occurrence of the disease.

CONSENT

As per international standard or university standard, respondents' written consent will be collected and preserved by the author(s).

ETHICAL APPROVAL

As per international standard or university standard written ethical approval will be collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Parkin DM, Whelan SL, Ferlay J, Teppo L, Thomas DB. Cancer incidence in five continents Volume VIII. IARC scientific publication. 2002(155).
2. Awan KH, Patil S, Islam SA, Jafer M. Early Detection of Oral Cancer-Guidelines for Dental Practitioners. *Journal of International Oral Health*. 2016;8(3):399.
3. Warnakulasuriya S. Global epidemiology of oral and oropharyngeal cancer. *Oral oncology*. 2009;45(4-5):309-16.
4. Downer MC. Patterns of disease and treatment and their implications for dental health services research. *Community dental health*. 1993;10:39-46.
5. Zygogianni AG, Kyrgias G, Karakitsos P, Psyri A, Kouvaris J, Kelekis N, Kouloulis V. Oral squamous cell cancer: early detection and the role of alcohol and smoking. *Head & neck oncology*. 2011 ;3(1):1-2.
6. Lambert R, Sauvaget C, de Camargo Cancela M, Sankaranarayanan R. Epidemiology of cancer from the oral cavity and oropharynx. *European journal of gastroenterology & hepatology*. 2011;23(8): 633-41.
7. World Health Organization, IARC Working Group on the Evaluation of Carcinogenic Risks to Humans, International Agency for Research on Cancer. Betel-quid and areca-nut chewing and some areca-nut-derived nitrosamines. IARC; 2004.
8. IARC Working Group on the Evaluation of Carcinogenic Risks to Humans, World Health Organization, International Agency for Research on Cancer. Smokeless tobacco and some tobacco-specific N-nitrosamines. World Health Organization; 2007.
9. Awan KH. Effects of tobacco use on oral health-an overview. *Annals of Dentistry University of Malaya*. 2011;18(1):18-23.
10. Sinha DN, Gupta PC, Pednekar MS, Jones JT, Warren CW. Tobacco use among school personnel in Bihar, India. *Tobacco control*. 2002;11(1):82-3.
11. Kumar S, Pandey U, Bala N, Tewar V, Oanh KT. Tobacco habit in northern India. *Journal of the Indian Medical Association*. 2006;104(1):19-22.
12. Rathod S, Wanikar I, Raj A, Maske S, Harkare V. Association between kharrha chewing and periodontal health status in oral submucous fibrosis patients of Central India, Nagpur. *Journal of Indian Society of Periodontology*. 2018;22(4):345.
13. Awan KH, Hussain QA, Patil S, Maralingannavar M. Assessing the risk of Oral Cancer associated with Gutka and other smokeless tobacco products: a case-control study. *J Contemp Dent Pract*. 2016;17(9):740-4.
14. Prasad JB, Dhar M. Risk of major cancers associated with various forms of tobacco use in India: a systematic review and meta-analysis. *Journal of Public Health*. 2019;27(6):803-13.
15. Sharma A, Chhabra KG, Agarwal S, Bhansali S, Singh P, Nagrale RG. Association between health-related quality of life and sense of coherence among health professionals working in primary health centers consuming tobacco in Jaipur, India. *Journal of Family Medicine and Primary Care*. 2020;9(6):2963.
16. Madhu PP, Kumar PN, Prashant G, Sushanth V, Imranulla M, Nair AR. Knowledge, attitude and practice regarding tobacco cessation methods among the dental professionals: A cross-sectional study. *J Oral Health Comm Dent*. 2019;13:21-6.
17. Deolia, Shravani, Surbhi Agarwal, Kumar Gaurav Chhabra, Gunjan Daphle, Sourav Sen, and Ashish Jaiswal. Physical and Psychological Dependence of Smokeless

- and Smoked Tobacco. *Journal of Clinical and Diagnostic Research*. 2018;12(3):ZC01–4. Available: <https://doi.org/10.7860/JCDR/2018/28583.11233>.
18. Nigudkar, Rashmi, Minal Chaudhary, Madhuri Gawande, Swati Patil, Alka Hande, and Lalit Kanthale. Incidence of Tobacco Chewing in Families of Patients with Oral Squamous Cell Carcinoma. *Clinical Cancer Investigation Journal*. 2016;5(6):513–15. Available: <https://doi.org/10.4103/2278-0513.200110>.
 19. Gulhane, Prachi Kishor, Renu B. Rathi, and Bharat Rathi. Assessment of Prevalence and Psychosocial Behaviour of Tobacco Addictive School Going Children with Awareness for Deaddiction. *International Journal of Ayurvedic Medicine*. 2020;11(2):300–305.
 20. Chole, Revant H, Ranjithkumar N. Patil, Anjan Basak, Kamlesh Palandurkar, and Rahul Bhowate. Estimation of Serum Malondialdehyde in Oral Cancer and Precancer and Its Association with Healthy Individuals, Gender, Alcohol, and Tobacco Abuse. *Journal of Cancer Research and Therapeutics*. 2010;6(4): 487–91. Available: <https://doi.org/10.4103/0973-1482.77106>.
 21. Eesha, Thakare, Chaudhary Minal, Gawande Madhuri, Wadhwan Vijay, and Gadbail Amol. Variation in the Changes Induced by Different Forms of Tobacco in Dental Hard Tissues-A SEM-EDAX Study. *Journal of Oral Biosciences*. 2011;53(4):348–55. Available: <https://doi.org/10.2330/joralbiosci.53.348>.
 22. Hande, Alka Harish, and Minal S. Chaudhary. Cytomorphometric Analysis of Buccal Mucosa of Tobacco Chewers. *Romanian Journal of Morphology and Embryology*. 2010;51(3):527–32.
 23. Lohe, Vidya K, Shirish S. Degwekar, Rahul R. Bhowate, Ravindra P. Kadu, and Suwarna B. Dangore. Evaluation of Correlation of Serum Lipid Profile in Patients with Oral Cancer and Precancer and Its Association with Tobacco Abuse. *Journal of Oral Pathology & Medicine*. 2010;39(2):141–48. Available: <https://doi.org/10.1111/j.1600-0714.2009.00828.x>.
 24. Quazi Syed, Zahiruddin, Abhay Gaidhane, Shilpa Bawankule, Khatib Nazli, and Sanjay Zodpey. Prevalence and Pattern of Tobacco Use among Tribal Adolescents: Are Tobacco Prevention Messages Reaching the Tribal People in India? *Annals of Tropical Medicine and Public Health*. 2011;4(2):74–80. Available: <https://doi.org/10.4103/1755-6783.85756>.
 25. Teni TR, Mallick S, Palve V, Pawar S, Patil R, Agarwal JP. Mcl-1 Expression Is Associated with Pathogenesis and Radiotherapy Treatment Response in Chewing Tobacco-Associated Oral Carcinomas. *Oral Oncology*; 2009:70. Available: <https://doi.org/10.1016/j.oos.2009.06.127>.