

Original Article

## The Incidence of Oral and Oropharyngeal Cancers in Betel Quid-Chewing Populations in South Myanmar Rural Areas

Nobuyoshi Mizukawa<sup>a\*</sup>, Swe Swe Win<sup>b</sup>, Zaw Moe Thein<sup>c</sup>, Moe Thida Htwe<sup>d</sup>,  
Yohsuke Yoshioka<sup>e</sup>, Yoshihiro Kimata<sup>f</sup>, Seiji Iida<sup>e</sup>, Myo Khin<sup>g</sup>,  
Shigeru Okada<sup>g</sup>, and Than Sein<sup>h</sup>

Department of Oral and Maxillofacial Reconstructive Surgery, <sup>a</sup>Okayama University Hospital, and  
<sup>e</sup>Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences,  
<sup>f</sup>Department of Plastic and Reconstructive Surgery, Okayama University Graduate School of Medicine,  
Dentistry and Pharmaceutical Sciences, Okayama 700-8558, Japan, <sup>b</sup>Myanmar Dental Association, Myanmar,  
<sup>c</sup>Department of Oral Medicine, University of Dental Medicine, Yangon, Myanmar,  
<sup>d</sup>Department of Oral Medicine, University of Dental Medicine, Mandalay, Myanmar,  
<sup>g</sup>NPO Myanmar-Japan Collaboration Project for Fostering Medical Human Resources, <sup>h</sup>People's Health Foundation, Myanmar

Oral cancer is a very common disease in South and Southeast Asia. Betel quid (BQ)- chewing and tobacco-smoking habits are etiological factors for oral cancer patients in these regions. We conducted an oral cancer screening in BQ-chewing endemic rural areas in South Myanmar for the early detection of oral cancer in BQ-chewing and smoking individuals. We examined 105 subjects who were at high risk of oral cancer due to their oral habits (BQ users and/or smokers). Three carcinoma cases were detected, and there were 8 dysplasia cases. The carcinoma detection rate was 2.9%, and the carcinoma and precancerous lesion detection rate was 10.5%. In Myanmar, oral cancer screening has been conducted sporadically on a voluntary basis, and nationwide surveys have never been performed. There are also few reports of oral cancer screening for high-risk groups among the general population in Myanmar. Our present findings highlight the need for further screening and surveys. Education on betel quid chewing- and tobacco- related oral diseases and screening for the early detection of oral cancer are of the utmost importance in the control and prevention of oral cancer.

**Key words:** oral cancer screening, betel quid (BQ), Myanmar, oral cancer, smoking

Oral (including pharyngeal) cancer is the sixth most common cancer in the world [1], and four-fifths of oral cancer cases occur in developing countries [2]. Oral cancer is a very common disease in South and Southeast Asia [3]. In India, among the 30-69- year-old population of males, the three most common fatal cancers are oral (including lip and pharynx, 22.9%), stomach (12.6%), and lung (11.4%) [4].

Oral carcinoma and oropharyngeal carcinoma are

also reported to be very common in Myanmar by hospital- based studies [3]. Sein *et al.* confirmed that oral cancer ranked fifth among all cancers for the period between 1985 and 1988 [5]. Oo *et al.* reported that oral cancer ranked 6th for males and 10th for females, with males predominating at a ratio of 2.1 : 1 [6].

Cigarette smoking and alcohol consumption are the most recognized risk factors for oral squamous cell carcinoma in developed western countries [7, 8], and cigarette smoking causes 30% of all cancer deaths in devel-

oped countries [9]. In addition to lung cancer, smoking is an important cause of oral and oropharyngeal cancers [6,9]. However, in South and Southeast Asian countries, betel quid (BQ) chewing and smoking are the major contributory risk factors for carcinoma incidence [7,10,11].

BQ chewing is a widespread habit in South- and Southeast Asia, with approx. 600 million people still indulging in this habit [12].

For example, among men in Taiwan, oral carcinoma is the fourth leading malignancy due to the popularity of BQ chewing [2]. There is a high-risk group of 2.5 million people in Taiwan who both chew BQ and smoke tobacco [2]. BQ chewing has been clearly implicated as a cause of oral cancer [3,13]. Because of the scarcity of dentists in Myanmar, essentially only patients visiting hospitals with late advanced (rarely early) cases of oral cancer have been treated. Oral cancer screenings for early detection and treatment have been neglected. There are few reports in the literature of oral cancer screening for high-risk groups among the general population in Myanmar. Here we present the results of an oral cancer screening program among high-risk populations in South Myanmar rural Areas.

## Materials and Methods

Oral cancer screening was conducted for regional residents at Hpa-an General Hospital, Kayin State, Myanmar in 2015 and Mawlamyaing General Hospital, Mawlamyaing, Mon State, Myanmar in 2016 with the cooperation of the Myanmar Dental Association, the University of Dental Medicine in Yangon and Mandalay,

the People's Health Foundation, and the NPO Myanmar-Japan Collaboration Project for Fostering Medical Human Resources. Ethical approval by the People's Health Foundation in Myanmar was obtained.

Hpa-an and Mawlamyaing are areas with a high prevalence of BQ-chewing habits. The subjects were persons who hoped to receive free dental treatment including oral cancer screening on a specific day when Myanmar dentists provide necessary dental treatments free of charge to all subjects.

We surveyed the age, gender and oral habits using questionnaire, including the duration and level of consumption of all types of smoked tobacco, BQ and alcohol.

There were a total of 106 subjects, of whom 51 were males and 55 were females. The average ages were  $48.5 \pm 13.9$  years for the men and  $52.3 \pm 11.2$  years for the women (Fig. 1).

Of the 106 subjects, 96 were BQ chewers (90.6%, Table 1). The users of BQ and/or smokers comprised 99.1% of the subjects in the present cancer screening (Table 1). We examined the participants principally via ocular inspection and palpation. Toluidine blue staining and brush biopsy were conducted for lesions suggesting carcinoma. We referred participants with suspicious cancers or cancer-like lesions to a specialized medical hospital.

## Statistical analysis

We examined the relationship between oral habits and cancer and pre-cancer incidence in the high-risk group. One subject who was in the low-risk oral habits

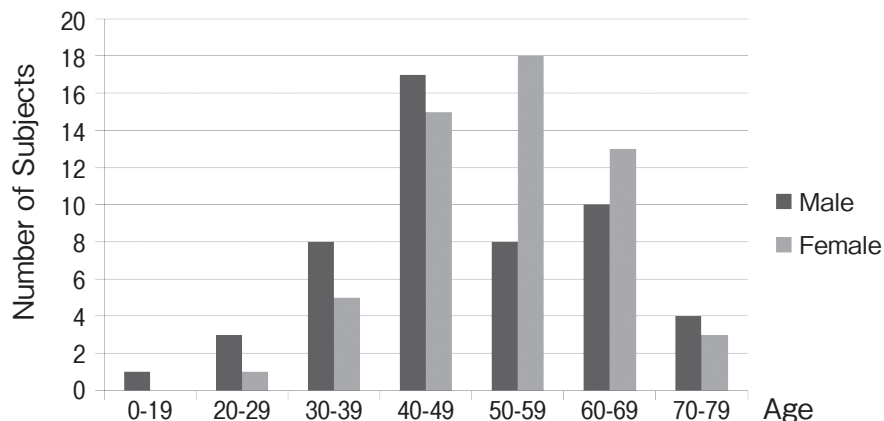


Fig. 1 Age and Sex distribution of subjects.

group (non-smoking + non-BQ-chewing) was excluded from the analysis. We thus examined 105 subjects of the high-risk group (Smoking or BQ-chewing), and divided them into the BQ group (non-smoking), Smoking group (non-BQ), and BQ + Smoking group. The group's values were analyzed using the Chi-square test, and *p*-values < 0.05 were considered significant. The analyses were performed using the SPSS 15.0 J software program for Windows (IBM Japan, Tokyo, Japan).

### Results

Thirty-nine lesions were detected by this oral cancer screening in the high-risk oral habits group (Table 2). We found not only 2 oral carcinomas but also 1 oropharyngeal carcinoma (Fig.2). Other lesions included 7 cases of leukoplakia, 4 lichen planus lesions, and 1 submucous fibrosis. In addition, 1 case of chewer's mucosa was diagnosed as dysplasia after a biopsy was performed. Therefore, 8 cases of precancerous lesions

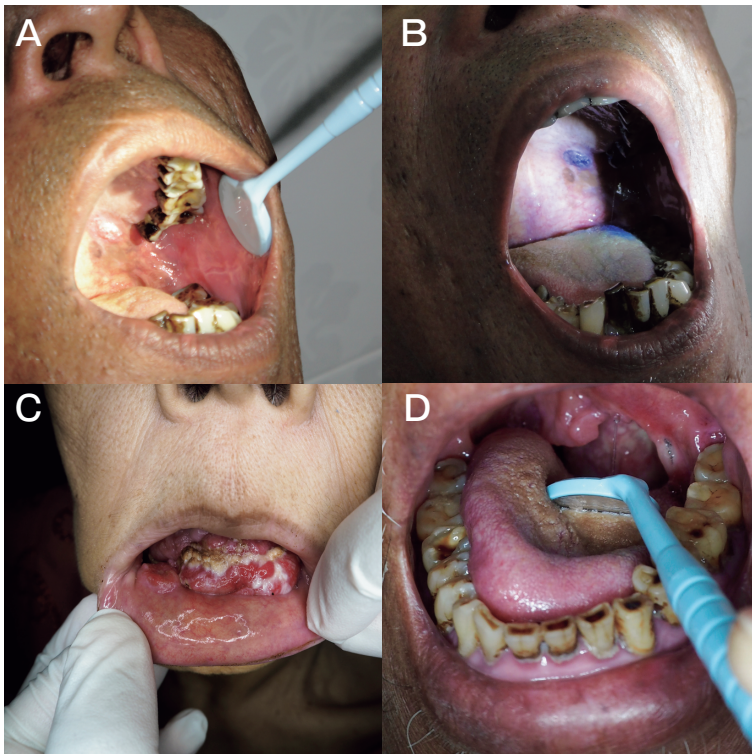
**Table 1** Oral Habits of Subjects

Oral habit	Male	Female	Total	Total (%)
Smoking only	3	3	6	5.7
BQ chewing only	28	41	69	65.1
Smoking and BQ chewing	6	7	13	12.3
Smoking, BQ chewing and Drinking	10	2	12	11.3
BQ chewing and Drinking	2	0	2	1.9
Smoking and Drinking	2	1	3	2.8
Drinking only	0	0	0	0
None	0	1	1	0.9
Total	51	55	106	100

**Table 2** Lesions detected by oral cancer screening (High-risk oral habits group)

Oral Lesion	Male	Female	Total
Chewer's mucosa	13	9	22
Leukoplakia	5	2	7
Lichen Planus	2	2	4
Submucous fibrosis	1	0	1
Candidiasis	1	0	1
Ulcer	0	1	1
Oral Carcinoma	1	1	2
Oropharyngeal Carcinoma	1	0	1
Total	24	15	39

(Total Subjects 105)



**Fig. 2** A, Case 1, carcinoma at left palate; B, Case 1, the lesion was dyed with toluidine blue stain; C, Case 2, carcinoma at lower gingiva; D, Case 3. oropharyngeal carcinoma.

(leukoplakia and dysplasia) and 5 cases of precancerous conditions (lichen planus lesions and submucous fibrosis) were detected by the present screening.

The carcinoma detection rate was thus 2.9%, and the carcinoma and precancerous lesion detection rate

was 10.5% (Table 3).

As for the oral habits of the three subjects in whom cancer was identified (Table 4), one subject was a BQ user, smoker and alcohol user. Of the others, one subject used only BQ, and the other smoked. As for the oral habits of the eight subjects with oral dysplasia cases with precancerous lesions, all used BQ (Table 5). Three of these subjects were also smokers.

The oral cancer and precancerous lesion detection rates according to oral habits are presented in Table 6. The BQ-chewing + smoking group showed the highest rate of carcinoma and precancerous lesion detection at 16.0%. However, there were no significant differences in these rates among the 3 groups ( $p = 0.569$ ).

**Table 3** Carcinoma, precancerous lesion, and precancerous condition detection rates (High-risk oral habits group)

Detection rates	%
Carcinoma	2.9
Carcinoma and precancerous lesion	10.5
Carcinoma, precancerous lesion, and precancerous condition	15.2

**Table 4** Oral habits of carcinoma cases

Case	Age	Sex	Site	Pathological diagnosis	BQ chewing	Smoking	Drinking
1	58	Male	Palate	SCC	8 quids/day for 7 years	Cheroots 5/day for 14 years Cigarettes 7/day for 14 years	Traditional alcohol 4 pec/days
2	72	Female	Lower gingiva	SCC	3-5 quids/day for 10 years	None	None
3	70	Male	Oropharynx	SCC	None	5 cheroots/day for 50 years	Occasionally for 50 years

**Table 5** Oral habits of oral dysplasia cases (Leukoplakia 7 cases, Chewer's mucosa → Dysplasia 1 Case)

Case	Age	Sex	Site	BQ chewing	Smoking
1	41	Male	Buccal mucosa	10 quids/day for 5 months	None
2	61	Female	Buccal mucosa	10 quids/day for 15 years	None
3	32	Male	Buccal mucosa	10 quids/day for 6 years	5 cigarettes/day for 6 years
4	41	Male	Buccal mucosa and retromolar region	15 quids/day for 5 years	None
5	38	Female	Buccal mucosa	3 quids/day for 20 years	2 cheroots/day for 28 years
6	63	Female	Buccal mucosa	15 quids/day for 8 years	None
7	60	Male	Buccal mucosa	20 quids/day for 15 years	None
8	48	Male	Buccal mucosa	10 quids/day for 6 years	Occasionally

**Table 6** Carcinoma and Precancerous lesion detection rates by oral habit

Oral Habit	Total Subjects	Carcinoma	Precancerous lesion	Carcinoma and Precancerous lesion	Carcinoma and Precancerous lesion Detection Rates
Smoking (non-BQ chewing)	9	1	0	1	11.1%
BQ chewing (non-Smoking)	71	1	5	6	8.5%
BQ chewing +Smoking	25	1	3	4	16.0%

## Discussion

An epidemiologic hospital-based study of 70 oral cancer cases in Myanmar demonstrated that the prevalence of smoking (regular and occasional) was 67.1% in the group of oral cancer cases, whereas the prevalence of BQ chewing (regular and occasional) was 71.4% in the same group [5]. In addition, 70% of the oral cancer patients were Stage IV (advanced stage), whereas only 7.1% were Stage I (early stage) [5].

Therefore, preventive medicine and oral cancer screening of high-risk groups are needed for early detection [2]. There are few reports of oral cancer screening for high-risk populations in Myanmar. Our present findings showed the utility of oral cancer screening in high-risk populations. In our screening, oral lesions were detected in 39 subjects (37.1%) in the high-risk group. Oral carcinoma mainly afflicts patients older than 40 years of age. In the present study, the average ages of the men and women were 48.5 years and 52.3 years, respectively. Furthermore, 83.0% of the subjects were 40 years of age or older.

An unexpected finding in our high-risk population was the high incidence of lichen planus lesions. Although not widely recognized, the existence of lichen planus lesions in a BQ-chewing population may be another precancerous condition leading to oral cancers [14, 15].

Betel quid consists of 3 major ingredients: the betel 'nut' (areca nut), the betel leaf (*Piper betle*), and lime (calcium hydroxide) [3]. Tobacco is often added [3].

Betel quid is associated with chemical carcinogenesis, and BQ ingredients have been shown to induce cytotoxicity and DNA strand breakage [2]. The genesis of oral squamous cell carcinoma is a complex process involving multiple genetic and epigenetic alterations, which can be affected by various risk factors [7].

The customs of BQ chewing seen in many Asian countries does not occur in Japan. As such, the situation in Japan differs markedly from Myanmar. The oral cancer detection rate in populations subjected to oral cancer screening in Japan has been reported to be 0.09-0.4% [16]. Nagao *et al.* reported that the cancer detection rate was 0.05% in an oral cancer screening in Japan, and that precancerous lesions were detected in 0.42% of cases (leukoplakia 0.4% and erythroplakia 0.02%) [17]. Their subjects were a general population of citizens (over 40 years age) [17]. In Japanese subjects, a signifi-

cantly higher prevalence of oral pre-cancer was found among male smokers (2.5%) compared to male non-smokers (0.8%) ( $p < 0.005$ ) [17]. However, in our oral cancer screening of a high-risk group in Myanmar, the cancer detection rate and the cancer and precancerous lesion detection rate were 2.9% and 10.5%, respectively. Furthermore, the detection rate of cancer and precancerous lesions was 16.0% in the BQ chewing + smoking group ( $p = 0.569$ , Table 6). Of course, we cannot simply compare our data with other cancer screening data, but it is clear that nationwide oral cancer screening projects for high-risk groups are necessary in Myanmar in contrast to Japan, where oral carcinoma is uncommon, accounting for only 1-2% of all cancer deaths [18].

To reduce the incidence of oral cancer in Myanmar, education on tobacco- and BQ- related oral diseases along with oral cancer screening are of the utmost importance. However, BQ chewing is often related to manners and customs in the Myanmar population, especially among individuals of low socioeconomic status, some of whom rely on the sale of BQ to sustain their daily lives. Therefore, livelihood support should be considered in order to achieve the successful eradication of BQ use. The cooperation of the school education system, news media, and government support will also be necessary. In conclusion, we expect that oral cancer screening will contribute to oral cancer awareness, the early detection of oral cancer and thus to improvements in the quality of life.

**Acknowledgments.** We appreciate the cooperation of the Myanmar Dental Association, the Department of Oral Medicine at the University of Dental Medicine in Yangon and Mandalay, the People's Health Foundation, and the NPO Myanmar-Japan Collaboration Project for Fostering Medical Human Resources. We also thank Dr. T. Maruyama from the Center for Innovative Clinical Medicine, Okayama University Hospital, Japan, for supporting our statistical analysis. This work was supported by the Grant in Aid for 'Strengthening of Function' from Okayama University in the 2015 fiscal year.

## References

1. Warnakulasuriya S: Global epidemiology of oral and oropharyngeal cancer. *Oral Oncol* (2009) 45: 309-316.
2. Kao SY, Chu YW, Chen YW, Chang KW and Liu TY: Detection and screening of oral cancer and pre-cancerous lesions. *J Chin Med Assoc* (2009) 72: 227-233.
3. Reichart PA and Way TH: Oral cancer and pre-cancer in Myanmar: a short review. *J Oral Pathol Med* (2006) 35: 193-196.
4. Dikshit R, Gupta PC, Ramasundarahettige C, Gajalakshmi V, Aleksandrowicz L, Badwe R, Kumar R, Roy S, Suraweera W,

- Bray F, Mallath M, Singh PK, Sinha DN, Shet AS, Gelband H, Jha P and Million Death Study Collaborators: Cancer mortality in India: a nationally representative survey. *Lancet* (2012) 379: 1807–1816.
5. Sein K, Maung KK and Aung TH: An epidemiologic study of 70 oral cancer cases at the Institute of Dental Medicine, Yangon, Myanmar 1985–1988. *Odontostomatol Trop* (1992) 15: 5–8.
  6. Oo HN, Myint YY, Maung CN, Oo PS, Cheng J, Maruyama S, Yamazaki M, Yagi M, Sawair FA and Saku T: Oral cancer in Myanmar: a preliminary survey based on hospital-based cancer registries. *J Oral Pathol Med* (2011) 40: 20–26.
  7. Singhanian V, Jayade BV, Anehosur V, Gopalkrishnan K and Kumar N: Carcinoma of buccal mucosa: A site specific clinical audit. *Indian J Cancer* (2015) 52: 605–610.
  8. Sargeran K, Murtomaa H, Safavi SM, Vehkalahti MM and Teronen O: Survival after diagnosis of cancer of the oral cavity. *Br J Oral Maxillofac Surg* (2008) 46: 187–191.
  9. Pfeifer GP, Denissenko MF, Olivier M, Tretyakova N, Hecht SS and Hainaut P: Tobacco smoke carcinogens, DNA damage and p53 mutations in smoking-associated cancers. *Oncogene* (2002) 21: 7435–7451.
  10. Ng KH, Siar CH, Ramanathan K, Murgasu P and Chelvanayagam PI: Squamous Cell Carcinoma of the oral mucosa in Malasia—Any Change? *Southeast Asian J Trop Med Public Health* (1985) 16: 602–606.
  11. Chattopadhyay A: Epidemiologic study of oral cancer in eastern India. *Indian J Dermatol* (1989) 34: 59–65.
  12. Reichart PA and Nguyen XH: Betel quid chewing, oral cancer and other oral mucosal diseases in Vietnam: a review. *J Oral Pathol Med* (2008) 37: 511–514.
  13. Reichart PA: Oral cancer and precancer related to betel and miang chewing in Thailand. a review. *J Oral Pathol Med* (1995) 24: 241–243.
  14. Stoopler ET, Parisi E and Sollecito TP: Betel quid-induced oral lichen planus: a case report. *Cutis* (2003) 71: 307–311.
  15. Reichart PA and Warnakulasuriya S: Oral lichenoid contact lesions induced by areca nut and betel quid chewing: a mini review. *J Investig Clin Dent* (2012) 3: 163–166.
  16. Yano H, Matsuzaka K, Sakamoto M, Murakami S, Hata N, Hashimoto K, Yakushiji T, Kaneko M, Hanazawa Y, Tanzawa H, Katakura A, Shibahara T and Inoue T: Clinical statistical study of exfoliative cytology performed during oral cancer screening in Chiba city in the past 11 years. *JJSEDP* (2016) 8: 33–38.
  17. Nagao T, Warnakulasuriya S, Ikeda N, Fukano H, Fujiwara K and Miyazaki H: Oral cancer screening as an integral part of general health screening in Tokoname City, Japan. *J Med Screen* (2000) 7: 203–208.
  18. Kirita T, Zheng Y, Kurumatani N, Shimooka H, Kamikaido N, Okamoto M, Ohgi K, Yamamoto K, Yamanaka Y, Yonemasu K and Sugimura M: Descriptive epidemiology of oral cancer in Japan—Trends and predictions of mortality and incidence—. *Jpn J Oral Maxillofac Surg* (1997) 43: 140–147 (in Japanese).