Special Section

Tobacco Use and Stomach Cancer in Mizoram, India

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Abstract

The incidence of stomach cancer in India is lower than that of any other country around the world. However, in Mizoram, one of the north-eastern state of India, a very high age-adjusted incidence of stomach cancer is recorded. A hospital-based case-control study was carried out to identify the influence of tobacco use on the risk of developing stomach cancer in Mizoram. Among the cases, the risk of stomach cancer was significantly elevated among current smokers [odds ratio (OR), 2.3; 95% confidence interval (95% CI), 1.4-8.4] but not among ex-smokers. Higher risks were seen for *meiziol* (a local cigarette) smokers (OR, 2.2; 95% CI, 1.3-9.3). The increased risk was apparent among subjects who had smoked for ≥30 years. The increased risk was significant with 2-fold increase in risk among the subjects who smoked for ≥11 pack-years. The risk increased with increasing cumulative dose of tobacco smoked (mg). *Tuibur* (tobacco smoke–infused water), used mainly in Mizoram, was seemed to increased the risk of stomach cancer among current users in both univariate and multivariate models (OR, 2.1; 95% CI, 1.3-3.1). Tobacco chewer alone (OR, 2.6; 95% CI, 1.1-4.2) showed significant risk. Tobacco use in any form [smoking and smokeless (*tuibur* and chewing)] increased the risk of stomach cancer in Mizoram independently after adjusting for confounding variables. (Cancer Epidemiol Biomarkers Prev 2005;14(8):1892–6)

Introduction

Stomach cancer is one of the most common cancers in the world with an estimated 876,000 new cases reported in 2000 (1). Stomach cancer is highest among male in the population of Changle in China (age-adjusted rate = 145.0 per 10^5; ref. 2). Among females, it is highest in the population of Yamagata in Japan (age-adjusted rate = 38.9 per 10^5; ref. 2). However, the rates of stomach cancer in India are lower in comparison with other countries around the world (3). In India, earlier studies showed relatively higher incidence of stomach cancer among males in Chennai during 1997 to 1998 (age-adjusted rate = 13.2 per 10^5) and among women it is next to cancer of the breast (age-adjusted rate = 7.0 per 10^5; ref. 4). However, recent studies in Mizoram, showed very high incidence of stomach cancer (5).

Mizoram is situated between 92.15′ to 93.29′ E longitude and 21.58′ to 24.35′ N latitude and virtually land locked and situated between Myanmar in the east and Bangladesh in the west. The Mizo people have their ancestral origin in China (6). Tobacco smoking rate in Mizoram is very high among adults (7). A peculiar habit of using ''tuibur'' (tobacco smoke–infused water) has also been observed in Mizoram. The habit of chewing betel quid, containing fresh betel nut, slaked lime wrapped in betel leaf is also widespread in Mizoram. Tobacco is often used. Dried tobacco mixed with lime processed with tips of thumb on the palm of other hand into a powder that is place near the gum known locally as ''Khaini'' also chewed in Mizoram.

Tobacco use in the form of smoking is highly associated with stomach cancer. The people of Mizoram are culturally and ethnically distinct from the other tribes and communities of India. Due to their peculiar smoking habits and use of other tobacco products and high prevalence of stomach cancer in Mizoram, a matched case-control study was carried out at the Aizawl Civil Hospital, Aizawl to investigate influence of tobacco use on cancer stomach.

***Tuibur*.** A number of smoking and smokeless tobacco products are in use all over the world. But unlike other smokeless tobacco products, a unique tobacco smoke–infused water is used in Mizoram and is locally known as *tuibur*. This product is made locally by passing smoke, generated by burning tobacco, through water until the preparation turns cognac in color and has a pungent smell. *In vitro* studies using the allium root test show the toxic nature of *tuibur* (8). Indigenous crude devices are used for the production of *tuibur* on small scale. Users take about 5 to 10 mL *tuibur* orally and keep it in the mouth for some time and then spit it out. Most of the users take it several times a day.

***Meiziol*.** It is a local cigarette made from vaihlo (*Nicotiana dadacum*) tobacco. After plucking, the tobacco leaves are thrashed by feet until the leaves become soft and most of the juices flow out. Then they are dried in the sun or sometimes in a warm place like over the fireplace without applying direct heat. Then they are cut into small pieces and rolled directly using a thin paper. The tobacco content of each *meiziol* is about 0.8 to 1 g. The length of each *meiziol* is 6 to 7 cm.

Materials and Methods

This study was a hospital-based matched case-control study carried out at Aizawl Civil Hospital situated at Aizawl, Mizoram. This hospital serves as a tertiary health care facility and is the only hospital having facility to treat cancer in the state with a population of 891,058 (2001 census). The study was conducted from August 2001 to August 2004 during which 372 new cases (all Mizos) of the stomach cancer were registered. This represented 35.1% of all cancer cases registered in this hospital during the study period (n = 1,060).

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The inclusion criteria of cases were:

1. Newly diagnosed stomach cancer cases confirmed by histopathology,
2. Mizo ethnicity, and
3. Cases diagnosed between August 2001 to August 2004.

The exclusion criteria of cases were:

1. Patients with advanced disease (n = 19), where the tumor had spread so as to obscure the primary site,
2. Patients with recurrent cancer (n = 13),
3. Patients too old to be interviewed elaborately (n = 8), and
4. Patients who refused to be interviewed (n = 3).

A total of 329 patients were finally included (253 men and 76 women) with male-to-female ratio of 3.3:1. Controls were selected from hospital patients suffering from non-malignant disease admitted with either injury, minor eye ailments, or infections of any other type or with osteomuscular diseases. The controls were matched for age (±5 years), sex, and ethnicity. For each case, two controls were selected (n = 665). All the confirmed stomach cancer cases were directed to the social investigator(s) of the project for interview and simultaneously information was also collected from the controls. Trained social investigators were employed for interviewing both cases and controls at hospitals used a pretested questionnaire. The main items included in the questionnaire were age, sex, ethnicity, present and past occupation, income, family history, and details of habits about tobacco use.

Subjects who reported that they were regularly smoking/using tuibur/chewing during the index year were defined as current users, those who reported that they had stopped regular using any habits the year before the index year or before were defined as ex-smokers/ex-users/ex-chewers, and people who reported that they never had smoked before or during the index year were defined as never-smokers or never-users or never-chewers. The cumulative dose of smoking was expressed as pack-years. One pack-year was regarded as the equivalent of 20 cigarettes smoked per day for 1 year. The duration from the year of the cessation to the index year was calculated and categorized into the following intervals: 1 to 9, 10 to 19, and 20 years.

Statistical Analysis. Univariate and multivariate logistic regression were used to analyze data. Conditional maximum-likelihood method (9) was used to estimate the variables of regression models due to matched design and significance was taken at $P \leq 0.05$ (two tailed). Initially, a univariate analysis was done. The crude measure of association between single putative risk factors and stomach cancer was expressed as odds ratio (OR) and its 95% confidence interval (95% CI) was calculated from the SE of the regression coefficient. For controlling confounding variables and other covariables like alcohol drinking, level of education, occupation, income, etc., the data were analyzed by conditional multiple logistic regressions to evaluate the extent to which risk factors are associated independently with stomach cancer in Mizoram. The categories used for each adjusting variable in the logistic regression are frequency per day, age began (years), duration (years), cumulative dose, and years since stopped. The statistical packages used for the analysis were Epi-Info-2002 and SPSS version 12.

Ethical Clearance. The study has been cleared by Institutional Ethical Committee of Regional Medical Research Centre, Dibrugarh.

Results

All the stomach cancer patients (n = 329) were confirmed by histology. Of the 329 cases, 95.7% (n = 315) were having adenocarcinoma of which 75.9% (n = 250) were diffuse type. Antrum and pylorus were the major sites of cancer.

The age and sex profile of the cases and controls is shown in Table 1. The mean age of the cases and controls was 56.8 and 57.1 years, respectively. There were no statistically significant differences between the age of the cases and controls, suggesting that age matching was effective. Of the cases, 76.9% were male and majorities (65.3%) of the stomach cancer were in the age group of 45 to 64 years at the time of diagnosis of stomach cancer. Level of education, income groups, and occupation, which were not matching factors in the study, were also included in all models to control for their confounding effect.

ORs were calculated using non-smokers as reference group to see the association with smoking (Table 2). The ORs of current smokers (OR, 2.3; 95% CI, 1.4-8.4) was found to be statistically significant compared with ex-smokers. Although the 50% reduction in risk had been observed after controlling the other habits and co-factors in the multivariate model, a significant risk had been observed, indicating independent effect on the development of stomach cancer. Statistically significant higher risks were seen for smokers of combined users of tobacco (cigarette and *meiziol*) with OR, 3.1 (95% CI, 2.0-11.1) but among the single type of tobacco users, higher risks were seen for *meiziol* smokers, a local cigarette (OR, 2.2; 95% CI, 1.3-9.3) in the multivariate model in comparison to cigarette smokers. Overall, the excess risk was limited to smokers of >10 *meiziol* per day. Risk also tended to increase with duration and with pack-years, with an OR of ~3 among smokers of ≥30 years and those who smoked ≥20 pack-years. Increasing risk was also observed with the amount of tobacco (mg) smoked increases. Risk tended to decline with years since quitting and with age started smoking and these linear trend were statistically significant ($P < 0.01$).

The risk associated with *tuibur* is mainly seen in Mizoram. Non-users were kept as the reference group to compute the risk estimates. The OR of current *tuibur* user was higher than former *tuibur* users. The likelihood ratio test showed that the risk associated with current *tuibur* users was significantly different from that seen among former *tuibur* users and OR

Table 1. Age distribution and social characteristics of cases and controls

Variables	Cases, n (%)	Controls, n (%)
Age group (y)		
<45	24 (7.3)	52 (7.8)
45-54	97 (29.5)	195 (29.3)
55-64	118 (35.9)	238 (35.8)
65-74	62 (18.8)	124 (18.6)
75≤	28 (8.5)	56 (8.4)
Mean ± SD	56.8 ± 8.4	57.1 ± 8.9
Sex		
Male	253 (76.9)	512 (77.0)
Female	76 (23.1)	153 (23.0)
Male/Female	3.3:1	
Education		
Illiterate	165 (50.1)	195 (29.3)
Up to class XII	122 (37.1)	364 (54.7)
College level or more	42 (12.8)	106 (15.9)
Income		
Low	48 (14.6)	70 (10.5)
Middle	123 (37.4)	288 (43.3)
High	158 (48.0)	307 (46.2)
Occupation		
Office worker	65 (19.8)	180 (27.1)
Skilled worker	26 (7.9)	41 (6.2)
Unskilled worker	49 (14.9)	36 (5.4)
Cultivator	95 (28.9)	200 (30.1)
Others	94 (28.6)	208 (31.2)

Table 2. Tobacco smoking and risk of stomach cancer

Habits	Cases	Controls	Univariate*, OR (95% CI)	Multivariate †, adjusted OR (95% CI)
Smoking status				
Non-smokers	85	389	1.0 (reference)	1.0 (reference)
Ex-smokers	75	104	3.1 (1.6-11.3)	1.8 (0.4-7.7)
Current smokers	169	157	4.6 (2.7-14.7)	2.3 (1.4-8.4)
Smoking types				
Non-smokers	85	389	1.0 (reference)	1.0 (reference)
Cigarette	13	39	1.8 (0.8-7.2)	1.2 (0.5-14.2)
Meiziol	167	170	4.0 (1.7-10.4)	2.2 (1.3-9.3)
Cigarette + *Meiziol*	64	50	5.9 (2.5-12.1)	3.1 (2.0-11.1)
Smoking frequency/d				
Non-smokers	85	389	1.0 (reference)	1.0 (reference)
<5	15	28	2.3 (0.7-7.2)	1.1 (0.6-5.8)
5-10	114	122	3.6 (1.3-10.4)	1.7 (0.3-8.2)
>10	115	101	4.9 (2.7-13.6)	2.8 (1.3-9.3)
$P_{trend} < 0.0001$				
Age began (y)				
Non-smokers	85	389	1.0 (reference)	1.0 (reference)
≤10	44	46	4.1 (1.4-10.4)	2.1 (0.5-7.1)
11-20	153	142	2.7 (0.7-8.2)	1.3 (0.1-6.2)
>20	47	68	1.9 (0.04-9.1)	1.1 (0.01-8.0)
$P_{trend} < 0.001$				
Smoking duration (y)				
Non-smokers	85	389	1.0 (reference)	1.0 (reference)
≤15	21	45	1.9 (0.4-13.4)	1.1 (0.03-9.4)
16-30	99	111	4.1 (0.8-12.6)	1.8 (0.8-9.5)
>30	124	105	5.4 (2.5-11.5)	2.9 (1.3-11.6)
$P_{trend} < 0.001$				
Pack-years of smoking				
Non-smokers	85	389	1.0 (reference)	1.0 (reference)
<5	20	25	2.1 (1.1-8.3)	1.1 (0.02-6.68)
5-10	73	90	3.1 (1.8-10.4)	1.4 (0.18-6.91)
11-19	60	68	4.0 (1.9-13.8)	2.0 (1.3-10.6)
≥20	91	93	4.5 (2.1-15.5)	2.7 (1.5-15.4)
$P_{trend} < 0.001$				
Tobacco smoked (mg)				
Non-smokers	85	389	1.0 (reference)	1.0 (reference)
<25,000	53	70	2.7 (0.11-5.19)	1.2 (0.05-9.53)
25,000-50,000	61	64	3.6 (0.76-9.17)	1.8 (0.22-8.63)
>50,000	130	142	4.2 (1.21-11.5)	2.1 (1.28-13.9)
$P_{trend} < 0.001$				
Years since stopped smoking				
Non-smokers	85	389	1.0 (reference)	1.0 (reference)
<10	36	36	4.5 (1.5-17.4)	2.3 (1.1-14.2)
10-19	27	33	3.2 (1.2-13.2)	2.1 (1.1-12.9)
≥20	12	35	1.7 (0.54-6.2)	1.1 (0.5-8.4)
$P_{trend} < 0.01$				

*Matched (cases and controls were matched for age and sex) univariate OR estimated by conditional logistic regression analysis.
† Adjusted ORs (adjusted for alcohol drinking, chewing, *tuibur*, level of education, occupation, and income group) obtained by matched conditional multiple logistic regression analysis using maximum likelihood approach.

of former *tuibur* users was not statistically significant in the multivariate model (OR, 1.3; 95% CI, 0.4-2.1). Significant dose-response effects were observed as the intensity of *tuibur* use per day and duration in years increases and decreasing trend was observed for the increase of age of start in the multivariate model with the statistically significant trend ($P < 0.001$) indicating independent effect of the habit. The risk remains for 1 to 10 years after cessation of the habit, although the trend test was not statistically significant. Increased risks were also observed as the use of cumulative dose to amount of *tuibur* (ml) increases with significant trend ($P < 0.001$; Table 3).

Association of different type of chewing habit with stomach cancer has been shown in Table 4. In univariate analysis, both ex-chewers and current chewers had higher risk (2.0-2.2 times) of stomach cancer compared with non-chewers. But in multivariate analysis, after controlling for other habits, statistically non-significant risk was observed compared with non-chewers. On the other hand, the risk of stomach cancer significantly higher (OR, 2.6) even after adjustment in persons who chewing tobacco (smokeless tobacco) only. In addition, there appeared an increase in risk for stomach cancer in late chewers. Increased risks were also observed among the tobacco chewers as the amount of tobacco (in mg; OR, 2.6; 95% CI, 1.2-5.6) increases in a dose-dependent manner.

The risk among persons who practice different tobacco-related habits are given in Table 5. The highest risk showed who practice both *meiziol* and *tuibur* (OR, 2.3; 95% CI, 1.8-3.6). The risk associated with the practice of just one of the habit showed *meiziol* users (OR, 2.2; 95% CI, 1.6-3.1) with a higher risk than *tuibur* (OR, 2.0; 95% CI, 1.5-3.2), betel with tobacco only (OR, 1.7; 95% CI, 0.6-2.9), and betel without tobacco only (OR, 1.3; 95% CI, 0.4-2.0).

Discussion

Tobacco smoking and use of smokeless tobacco, chewing of tobacco and *tuibur*, are common in both the sexes in Mizoram. We found tobacco smoking to be a significant risk factor. The excess risk was largely confined to long-term heavy smokers. Relatively high prevalence of tobacco smoking in Mizoram (7) may have contributed to the high rates of stomach cancer.

Table 3. *Tuibur* (tobacco smoke–infused water) and risk of stomach cancer

Habits	Cases	Controls	Univariate*, OR (95% CI)	Multivariate†, adjusted OR (95% CI)
Tuibur status				
Non-user	236	557	1.0 (reference)	1.0 (reference)
Former user	37	46	1.9 (1.1-2.8)	1.3 (0.4-2.1)
Current user	56	55	2.4 (1.5-3.4)	2.1 (1.3-3.1)
Frequency/d				
Non-user	236	557	1.0 (reference)	1.0 (reference)
<5	17	28	1.3 (0.4-4.0)	1.1 (0.2-7.2)
5-10	48	55	1.7 (0.3-7.4)	1.3 (0.4-8.2)
>10	28	18	3.3 (1.6-10.7)	2.8 (1.1-11.7)
$P_{trend} < 0.001$				
Age began (y)				
Non-user	236	557	1.0 (reference)	1.0 (reference)
≤19	23	19	3.4 (1.8-16.5)	2.7 (1.3-15.6)
20-29	25	21	2.2 (0.6-12.7)	1.5 (0.6-6.4)
≥30	45	61	1.7 (0.3-8.6)	1.2 (0.8-7.3)
$P_{trend} < 0.0001$				
Duration (y)				
Non-user	236	557	1.0 (reference)	1.0 (reference)
≤15	20	26	1.8 (0.6-4.8)	1.4 (0.05-7.9)
16-30	45	50	2.7 (1.4-6.6)	1.7 (0.3-8.4)
>30	28	25	3.6 (1.7-11.2)	2.4 (1.1-10.5)
$P_{trend} < 0.0001$				
Years since stopped				
Non-user	236	557	1.0 (reference)	1.0 (reference)
<10	15	12	2.4 (1.24-8.54)	1.9 (1.1-6.2)
10-20	18	27	1.6 (0.4-5.27)	0.5 (0.02-6.1)
>20	9	21	1.1 (0.1-4.98)	0.2 (0.07-7.2)
Trend test not significant				
Cumulative dose to amount of tuibur (ml)				
Non-user	236	557	1.0 (reference)	1.0 (reference)
<1,000	45	57	1.8 (0.7-5.2)	0.7 (0.05-8.2)
1,000-2,000	24	27	2.1 (1.1-9.2)	1.3 (0.5-7.5)
>2000	24	17	3.3 (1.7-9.2)	2.1 (1.7-8.6)
$P_{trend} < 0.001$				

*Matched (cases and controls were matched for age and sex) univariate OR estimated by conditional logistic regression analysis.
† Adjusted ORs (adjusted for alcohol drinking, chewing, smoking, level of education, occupation, and income group) obtained by matched conditional multiple logistic regression analysis using maximum likelihood approach.

An increased risk of stomach cancer among smokers has been observed in numerous case-control and cohort studies (10-16) and is consistent with our study too. However, studies from Europe have reported no association between stomach cancer and smoking (17-23). Smoking as a variable risk factor for stomach cancer has also been reported from India (24, 25). However, the present study indicated statistically significant higher risk among current smokers compared with ex-smokers, which is consistent with previous findings (10, 12, 13, 16, 26). Furthermore, we are also reporting smoking of crude tobacco, *meiziol* (local cigarette) in this study, and its association with higher risk. Our study has shown significant dose response relationship with the quantity of smoked like other studies (10, 19, 27-31). Tobacco smoke contains a variety of carcinogen including *N*-nitroso compounds and nitrogen oxides that may promote endogenous formation of *N*-nitroso compounds (32), which have been linked to gastric carcinogenesis (33). IARC has revealed that smoking is causally associated with cancer of the stomach (34). A potential causal role of tobacco in causation of pre-cancerous lesions, in a high-risk area of China, where smoking was found to nearly double the risk of transition to gastric dysplasia (35). Another study (36) carried out in the United States revealed that current smokers had 2.3 times increased risk of dying from stomach cancer compared with non-smokers.

The Third National Cancer Survey of the United States (37) and studies elsewhere reported a non-significant risk of stomach cancer with smokeless tobacco use (31, 38, 39). Our study revealed significant elevated risk among the chewers of tobacco only (smokeless tobacco) and *tuibur* users than the nonusers, which supported the findings of toxicity of *tuibur* (8). There is sufficient evidence that smokeless tobacco causes oral and pancreatic cancer in humans and sufficient evidence of carcinogenicity from animal studies (40). The working group of the IARC monograph concluded that smokeless tobacco is ''carcinogenic to humans.'' It is pertinent to mention here that while keeping *tuibur* in the mouth for sometime, some portion of it also swallowed. Therefore, association of *tuibur* with stomach cancer in Mizoram cannot be ruled out. Of course, further experimental studies are required to confirm the risks of *tuibur* use in Mizoram.

Although our study revealed no significant association between betel quid chewers and stomach cancer like other study (25), a risk (OR, 2.8) had been observed in persons who consumed betel quid along with tobacco and those who were late chewers. However, there are sufficient evidence of betel

Table 4. Chewing of betel nut with or without tobacco and risk of stomach cancer

Habits	Cases	Controls	Univariate*, OR (95% CI)	Multivariate†, adjusted OR (95% CI)
Chewing status				
Non-chewers	131	388	1.0 (reference)	1.0 (reference)
Ex-chewers	83	120	2.0 (1.4-2.9)	1.6 (0.7-2.6)
Current chewers	115	150	2.2 (1.6-3.1)	1.5 (0.5-2.2)
Chewing ingredients				
Non-chewers	131	388	1.0 (reference)	1.0 (reference)
Betel nut + betel leaf	110	189	1.7 (1.2-2.3)	1.2 (0.7-2.1)
Tobacco alone	25	20	3.7 (1.9-7.2)	2.6 (1.1-4.2)
Betel nut + Betel leaf + tobacco	54	56	2.8 (1.8-4.4)	2.0 (1.3-5.3)
Chewing frequency/d				
Non-chewers	131	388	1.0 (reference)	1.0 (reference)
≤3	82	110	1.03 (0.7-1.5)	0.6 (0.1-4.4)
>3	116	160	2.2 (1.5-2.9)	1.4 (1.0-4.3)
$P_{trend} < 0.001$				
Age began (y)				
Non-chewers	131	388	1.0 (reference)	1.0 (reference)
≤10	27	39	2.0 (1.2-3.5)	1.3 (0. 3-1.4)
11-15	53	102	1.5 (0.8-1.9)	0.9 (0.4-1.9)
16-20	68	79	1.5 (1.0-2.3)	0.7 (0.06-3.3)
21-30	30	34	2.6 (1.4-4.5)	1.9 (1.1-3.1)
≥31	20	16	3.7 (1.7-7.7)	2.6 (1.6-5.5)
Trend test not significant				
Years of chewing				
Non-chewers	131	388	1.0 (reference)	1.0 (reference)
≤15	66	96	2.0 (1.3-3.0)	1.2 (0.06-4.4)
16-30	48	64	2.2 (1.4-3.4)	1.3 (0.65-5.4)
>30	72	103	2.0 (1.4-3.0)	1.1 (0.03-6.4)
Trend test not significant				
Years since stopped chewing				
Non-chewers	131	388	1.0 (reference)	1.0 (reference)
<10	44	52	2.5 (1.5-4.0)	1.1 (0.01-6.4)
10-20	25	40	1.8 (1.04-3.2)	0.74 (0.02-4.2)
20<	14	24	1.7 (0.8-3.6)	0.61 (0.03-5.6)
Trend test not significant				
Cumulative dose to chewing of betel nut + betel leaf				
Non-chewers	131	388	1.0 (reference)	1.0 (reference)
<50,000	42	76	1.6 (1.0-2.5)	0.63 (0.05-3.2)
50,000-100,000	60	88	2.0 (1.3-3.0)	1.3 (0.08-5.3)
>100,000	84	68	3.6 (2.4-5.4)	2.3 (1.2-4.5)
$P_{trend} < 0.01$				
Cumulative dose to amount of tobacco chewing (mg)				
Non-chewers	131	388	1.0 (reference)	1.0 (reference)
<20,000	13	18	2.1 (0.9-4.7)	1.5 (0.04-4.8)
>20,000	24	22	3.2 (1.6-6.2)	2.6 (1.2-5.6)

*Matched (cases and controls were matched for age and sex) univariate OR estimated by conditional logistic regression analysis.
†Adjusted ORs (adjusted for alcohol drinking, smoking, using of *tuibur*, level of education, occupation, and income group) obtained by matched conditional multiple logistic regression analysis using maximum likelihood approach.

Table 5. Different tobacco-related behaviors and risk of stomach cancer

Habits	Cases	Controls	Univariate*, OR (95% CI)	Multivariate †, adjusted OR (95% CI)
Never tobacco/betel user	135	288	1.0 (reference)	1.0 (reference)
Betel with tobacco only	45	50	1.9 (0.8-3.1)	1.7 (0.6-2.9)
Betel without tobacco only	89	126	1.5 (0.6-2.1)	1.3 (0.4-2.0)
Meiziol only	143	130	2.4 (1.7-3.2)	2.2 (1.6-3.1)
Tuibur only	56	53	2.2 (1.4-3.5)	2.0 (1.5-3.2)
Meiziol and *tuibur* only	90	80	2.6 (1.6-3.9)	2.3 (1.8-3.6)
Meiziol and betel with tobacco	67	73	2.0 (1.3-2.9)	1.9 (0.9-4.1)
Meiziol and betel without tobacco	48	58	1.7 (1.1-2.7)	1.6 (0.5-3.2)
Meiziol, tuibur, and betel with tobacco	64	66	2.4 (1.3-3.2)	2.1 (1.2-4.1)
Meiziol, tuibur, and betel without tobacco	57	60	2.0 (1.3-3.1)	1.8 (0.8-5.1)

*Matched (cases and controls were matched for age and sex) univariate OR estimated by conditional logistic regression analysis.
†Adjusted ORs (adjusted for alcohol drinking, corresponding tobacco user, level of education, occupation, and income group) obtained by matched conditional multiple logistic regression analysis using maximum likelihood approach.

quid with tobacco is carcinogenic to humans in sites other than stomach like oropharynx, hypopharynx, larynx, and esophagus, but betel quid without tobacco is not classifiable as to its carcinogenicity to humans (41).

In conclusion, tobacco users in the form of smoking or smokeless (chewing of tobacco only and *tuibur*) were found risk factor for stomach cancer in our study. The findings add to the growing consensus that tobacco is risk factors for stomach cancer and that efforts aimed at tobacco cessation may eventually help to reduce the burden of stomach cancer, still one of the world's most common malignancies.

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