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The impact of oral hygiene on head and neck cancer risk in a Chinese Population

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Conflict of interest statement

The authors declare no potential conflicts of interest.

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Abstract

Background—Although the impact of oral hygiene on head and neck cancer (HNC) risk has been investigated, few studies have been conducted among Asians.

Mehods—We conducted a multicenter case-control study to investigate this potential association. We performed unconditional multiple logistic regression models adjusted by potential confounders.

Results—We observed an inverse association of frequency of dental visits with HNC risk, with an adjusted OR of 3.70 (2.51-5.45) for never dental visits compared with ≥1 time/year (p_{trend}<0.001). We also observed a positive association between the number of missing teeth and HNC risk, with an adjusted OR for ≥ 5 missing teeth compared with < 5 missing teeth of 1.49 (1.08-2.04). Combining multiple oral hygiene indicators, poor oral hygiene scores increased HNC risk.

Conclusions—Poor oral hygiene may increase HNC risk in a Chinese population. Improving oral hygiene may contribute to reducing HNC risk in the Chinese population.

Keywords

Oral Hygiene; Dental Care; Risk; Head and Neck cancer; Chinese

Introduction

Head and neck cancer (HNC) is the sixth most common cancer in the world, with more than 600,000 cases diagnosed each year[(1)]. The anatomical sites of HNC typically include oral

cavity, oropharynx, hypopharynx and larynx, and it has been noted that these sites are strongly associated with environmental exposures. The established risk factors are predominantly tobacco smoking and alcohol drinking, and these factors cause approximately 80% of HNCs independently or synergistically[2, 3]. Recently, human papilloma virus (HPV) infection has become an established risk factor for oropharyngeal cancer[4].

Although it has been proposed that oral hygiene and dental care indicators may modify HNC risk, it remains inconsistent. Higher proportions of missing teeth[5–13], denture use[6, 11, 14–17] and gum bleeding[9, 13, 18] might increase HNC risk, and frequent teeth cleaning[5, 9, 10, 13, 19–21] and regular visit dentist[9–13, 16, 21, 22] might decrease HNC risk. Recently, the International Head and Neck Cancer Epidemiology Consortium (INHANCE), in a large-scale pooled case-control study, reported significant associations between oral hygiene indicators and HNC risk after adjustment of potential confounders[23]. Although this paper reported on a high impact of oral hygiene on HNC risk, only one Asian study was included in this study. Therefore, we conducted a large scale multi-center case-control study to investigate the association of oral hygiene and dental care with HNC risk in a Chinese population.

Materials and Methods

Design and subjects

We conducted a multicenter case-control study to elucidate the etiology of HNC in an East Asian population. The study center consists of eight centers from China (Beijing, Fujian, Henan, Jiangsu, Liaoning, Shanghai, Sichuan) and Taiwan, and the recruitment of subjects from December 2010 to February 2015. Detailed information from the face-to-face interview of both cases and controls included items on smoking and drinking habits, dietary habits, height and weight, individual and family medical history, occupational status, education level, and other lifestyle factors including oral hygiene and dental care. The study was approved by the ethical board of study centers and centrally at the University of Utah, and all subjects signed an informed consent form.

The inclusion criteria for cases were (1) age more than 18 years old, (2) confirmed invasive tumor of head and neck region (3) histologically confirmed squamous cell carcinoma, and (4) interviews performed within six months of cancer diagnosis. Tumors were assigned to one of the five categories as follows: (i) oral cavity (ICD-O-3 topography: C00.3 to C00.9, C02.0 to C02.3, C03.0, C03.1, C03.9, C04.0, C04.1, C04.8, C04.9, C05.0, C06.0 to C06.2, C06.8, and C06.9); (ii) oropharynx (C01.9, C02.4, C05.1, C05.2, C09.0, C09.1, C09.8, C09.9, C10.0, C10.2-C10.4, C10.8, and C10.9) (iii) hypopharynx (C12.9, C13.0 to C13.2, C13.8, and C13.9) (iv) oral cavity, pharynx unspecified or overlapping (C02.8, C02.9, C05.8, C05.9, C14.0, C14.2, and C14.8), and (v) larynx (C10.1, C32.0 to C32.3 and C32.8 to C32.9). Controls were frequency matched by sex, 5-year age group, ethnicity, and residence area from each of the study centers. Controls were selected from a defined list of non-chronic diseases not related to tobacco smoking or alcohol drinking. The proportion of hospital controls within a particular diagnostic group did not exceed 33%; These groups were (1) benign disorders, (2) endocrine and metabolic, (3) skin, subcutaneous tissue, and musculoskeletal disorders, (4) trauma, (5) circulatory disorders, (6) ear and eye disorders,

(7) diseases of upper-respiratory tract, (8) diseases of the oral cavity, jaw and salivary gland, (9) gastro-intestinal, (10) nervous system, (11) other diseases, and (12) no diagnosis (healthy population). Hospital controls were randomly chosen from subjects admitted as in-patients or out-patients in the same study center as the cases, and they were in the hospital for less than one month when recruited.

Finally, our study included 921 cases (424 oral cavity, 106 oropharynx, 81 hypopharynx, 85 larynx, and 225 unspecified or overlapping) and 806 controls.

Definition of the exposure variable

Our questionnaire included four oral hygiene and dental care indicators: frequency of teeth cleaning, number of missing teeth, denture use, and frequency of dental visits. We divided subjects into each category according to oral hygiene and dental care indicators: 2 categories for frequency of teeth cleaning (> 1 time/day and ≤1 time/day), 2 categories for number of missing teeth (<5 and ≥5), 2 categories for denture use (No or Yes), and 4 categories for frequency of dental visits (≥ 1 time/year, 1 time/2-4years, 1 time/≥ 5 years, and never),. In addition, we calculated oral hygiene scores using all oral hygiene and dental care indicators in this study. We summed the following variables: frequency of teeth cleaning: > 1 time/day=0, ≤ 1 time/day=1; number of missing teeth: '<5'=0, '≥5'=1; denture use: no=0, yes=1; regular dental visits: yes=0, no=1. This score ranged from 0 to 4 from best to worst oral hygiene condition.

Statistical analysis

We estimated the odds ratios (ORs) and the 95% confidence intervals (CIs) using unconditional multiple logistic regression models. Models included adjustment for ethnicity (Han vs Taiwanese vs others), age (18-44 vs 45-54 vs 55-64 vs 65-85 years), sex (male vs female), education levels (illiterate vs primary school vs junior/middle school vs senior/high school vs college/university above), center (China mainland vs Taiwan), cigarette smoking intensity (never vs <20 cigarettes/day vs ≥20 cigarettes/day), cigarette smoking duration (never vs <20 years vs ≥20 and <40 years vs ≥40 years), betel quid chewing intensity (never vs <20 pieces/day vs ≥20 pieces/day), betel quid chewing duration (never vs <20 years vs ≥20 years), alcohol drinking intensity (never vs <2 drinks/day vs ≥2 drinks/day), alcohol drinking duration (never vs <20 years vs ≥20 and <40 years vs ≥40 years), and body mass index (BMI) at interview period (<22 kg/m^2 vs ≥22 and <25 kg/m^2 vs ≥25 kg/m^2). Betel quid chewing intensity and duration were adjusted in cases with oral cavity and oropharynx, and with oral cavity, pharynx unspecified or overlapping. Differences in categorical variables across groups were assessed by the chi^2-test or Fisher's exact test as appropriate. To evaluate potential interactions of oral hygiene and dental care indicators with potential confounders, we performed likelihood-ratio tests, which compared models with and without the interaction term (p for heterogeneity).

All statistical analyses were performed using the software STATA ver. 14 (Stata Corp, College Station, TX, USA). All tests were two-sided, and p-values of <0.05 were considered statistically significant.

Results

Table 1 shows the distributions of cases and controls by subject characteristics. Among cases, the proportion of older subjects, male, cigarette smokers, betel quid consumers, alcohol drinkers, lower education level, or Han population was significantly higher than controls.

We observed a significant inverse association of frequency of dental visits with HNC risk, with adjusted ORs of 1.72 (95% CI, 1.10-2.67) for 1 time/2-4 years, 2.09 (95% CI, 1.40-3.14) for 1 time/≥ 5 years, and 3.70 (95% CI, 2.51-5.45) for never dental visits compared with ≥ 1 time/yearwith a statistically significant trend (p_{trend}<0.001; Table 2). In addition, the number of missing teeth was significantly associated with an increased HNC risk, with an adjusted OR for ≥ 5 missing teeth compared with < 5 missing teeth of 1.49 (95% CI, 1.08-2.04). Although lower frequency of teeth cleaning and denture use were positively associated with HNC risk, these associations were inconsistent after adjustment by potential confounders. Additionally, poor oral hygiene scores increased the risk of HNC, with adjusted ORs of 1.99 (95% CI, 1.41-2.82) for a score of 1, 1.88 (95% CI, 1.30-2.71) for a score of 2 and 4.76 (95% CI, 2.88-7.85) for a score of ≥3 compared with 0, with a significant trend (p_{trend}<0.001).

The inverse association with frequency of dental visits was significantly observed with all subsites (Table 3). The impact of frequency of teeth cleaning and number of missing teeth was stronger in oral cavity and oropharynx than in other subsites. Regarding denture use, we did not find major differences by subsite. Although poor oral hygiene scores increased the risk of all subsites, we found no significant trends for cancers risk of the hypopharynx and larynx.

We further investigated the impact of oral hygiene and dental care indicators on HNC risk stratified by potential confounders (Table 4). We observed that the impact of lower frequency of dental visits was stronger among males, smokers, drinkers and Taiwanese. Additionally, a significant inverse association with frequency of teeth cleaning was observed among Taiwanese, and we observed a significant positive association with denture use among drinkers. Regarding number of missing teeth, we observed significant associations with HNC risk among older subjects, females, never smokers, drinkers, and Taiwanese.

Discussion

In this study, we observed that lower frequency of dental visits and greater number of missing teeth were significantly associated with an increased HNC risk in a Chinese population. In addition, we found that poor oral hygiene scores increased the risk of HNC with a significant dose-response trend.

Regarding the frequency of dental visits, to date, 12 studies have been reported[8–13, 16, 18, 21–24]. Among them, nine of them reported that lower frequency of dental visits is associated with an increased HNC risk[9–13, 16, 21–23], and our results were consistent with them.

Next, there were 13 studies and 2 meta-analysis that evaluated the association between number of missing teeth and HNC risk[5–13, 18, 22, 23, 25–27]. Ten case-control studies and both meta-analyses supported that higher proportion of missing teeth increase HNC risk similar to our study results[5–13, 23, 26, 27]. Previous studies on missing teeth and the increased risk of HNC have been fairly consistent. The mechanism behind this association is plausible considering that periodontal disease is associated with tooth loss[28]. Zeng et al. reported on a positive association of periodontal disease with HNC risk using meta-analysis[29]. Additionally, it has been known that tooth loss is associated with smoking behavior[30], and may be a surrogate marker of socioeconomic status (SES)[31]. Although we did not have information about the income of subjects, education level was adjusted for SES in this study.

Following the methodology from studies in Taiwan, ARCAGE, and INHANCE, we evaluated the impact of an oral hygiene score on HNC risk[13, 16, 23]. All of the previous studies, and our current study indicated a significant dose-positive relationship between oral hygiene scores and HNC risk after adjustment by smoking and drinking.

The strengths of this study includes the number of HNC cases, which is one of the largest in an Asian population. Second, we adjusted for a considerable number of potential confounders carefully including tobacco smoking, alcohol drinking and betel quid use. We were able to conduct various stratified analyses. Some limitations of our study include the hospital-based case-control design. We tried to minimize the effect of selection bias, and we selected controls with diseases unrelated to smoking and drinking. Our results could potentially be affected by overestimation of odds ratios due to recall bias, since subjects with cancer may recall poor oral hygiene with more effort. Though we would not expect that HNC patients would necessarily think of poor oral hygiene as a strong risk factor for HNC, in which case, the recall bias may be minimized. Third, residual confounding of smoking and drinking could not be ruled out completely, but we did conduct analysis among never-smokers and never-drinkers. Additionally, we adjusted on betel quid chewing intensity and duration, which is a common habit in some East Asian populations. Fourth, we did not have information on HPV infection. Although we evaluated the impact of oral hygiene and dental care indicators in oropharyngeal cases only, these results were consistent (data not shown).

In conclusion, we observed that poor oral hygiene increased the risk of HNC and its subsites in a Chinese population. Improving oral hygiene in terms of frequent dental visits may contribute to reducing HNC risk in the Chinese population.

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Table 1

Characteristics of head and neck cancer cases and controls

Characteristics	Cases (N=921)		Controls (N=806)		*p*-value
	N	%	N	%	
Age					
18-44	146	16	257	32	<0.001
45-54	273	30	215	27	
55-64	297	32	222	27	
65-85	205	22	112	14	
Sex					
Male	726	79	556	69	<0.001
Female	195	21	250	31	
Cigarette smoking intensity (cigarettes/day)					
Never	319	34	462	57	<0.001
<20	148	16	136	17	
≥20	448	49	205	25	
Missing	6	1	3	1	
Duration of cigarette smoking (years)					
Never	319	35	462	57	<0.001
<20	70	8	101	13	
20≤ and <40	391	42	192	24	
≥40	138	15	49	6	
Missing	3	0	2	0	
Betel quid chewing intensity (betel pieces/day)					
Never	624	68	761	94	<0.001
<20	113	12	28	4	
≥20	166	18	14	2	
Missing	18	2	3	0	
Duration of betel quid chewing (years)					
Never	624	68	761	95	<0.001
<20	117	13	31	4	

Characteristics	Cases (N=921)		Controls (N=806)		*p*-value
	N	**%**	**N**	**%**	
≥20	175	19	11	1	
Missing	5	0	3	0	
Alcohol drinking intensity (drinks/day)					
Never	433	47	582	72	<0.001
<2	149	16	133	17	
≥2	297	32	72	9	
Missing	42	5	19	2	
Duration of drinking (years)					
Never	433	47	582	72	<0.001
<20	106	11	93	11	
≥20 and <40	272	30	104	13	
≥40	77	8	22	3	
Missing	33	4	5	1	
BMI (kg/m2)					
<22	306	33	241	30	0.332
≥22 and <25	329	36	300	37	
>25	285	31	264	33	
Missing	1	0	1	0	
Education					
Illiterate	59	6	24	3	<0.001
Primary school	228	25	129	16	
Junior/middle school	261	28	150	19	
Senior/high school	244	27	170	21	
College/university and above	129	14	333	41	
Center					
Mainland	439	48	405	50	0.284
Taiwan	482	52	401	50	
Ethnicity					
Han	556	60	407	51	<0.001
Taiwanese	348	38	390	48	

Characteristics	Cases (N=921)		Controls (N=806)		*p*-value
	N	**%**	**N**	**%**	
Others	17	2	9	1	
Subsite					
Oral cavity	424	46			
Oropharynx	106	12			
Hypopharynx	81	9			
Larynx	85	9			
Unspecified or overlapping	225	24			

Abbreviation; BMI; body mass index.

Table 2

Impact of oral hygiene and dental care on head and neck cancer risk

Variables	Case	Control	OR	95% CI	OR**	95% CI
Frequency of teeth cleaning						
>1 time/day	429	491	1.00	-	1.00	-
≤1 time/day	484	313	1.77	1.46-2.15	1.13	0.89-1.44
Missing	8	2	-	-	-	-
Number of missing teeth						
<5	635	696	1.00	-	1.00	-
≥5	264	108	2.68	2.09-3.43	1.49	1.08-2.04
Missing	22	2	-	-	-	-
Denture use						
No	719	689	1.00	-	1.00	-
Yes	197	114	1.66	1.29-2.13	1.29	0.94-1.75
Missing	5	3	-	-	-	-
Frequency of dental visits						
≥1 time/year	89	271	1.00	-	1.00	-
1 time/2–4 years	88	115	2.33	1.61-3.36	1.72	1.10-2.67
1 time/≥5 years	205	132	4.73	3.42-6.54	2.09	1.40-3.14
Never	526	261	6.14	4.63-8.13	3.70	2.51-5.45
Missing	13	27	-	-	-	-
P_{trend}				<0.001		<0.001
Oral hygiene score (best to worst oral hygiene)						
0	124	288	1.00	-	1.00	-
1	290	249	2.71	2.06-3.54	1.99	1.41-2.82
2	305	202	3.51	2.66-4.62	1.88	1.30-2.71
≥3	163	37	10.23	6.76-15.49	4.76	2.88-7.85
Missing	39	30				
P_{trend}				<0.001		<0.001

Abbreviation; OR, odds ratio; CI, confidence interval.

* Oral hygiene score is the sum of the four following variables: frequency of teeth cleaning: >1 time/day=0, ≤1 time/day=1; number of missing teeth: '<5'=0, '≥5'=1; denture use: no=0, yes=1; regular dental visits: yes=0, no=1.

** Adjusted by age, sex, cigarette smoking intensity, cigarette smoking duration, betel quid chewing intensity, betel quid chewing duration, drinking intensity, drinking duration, body mass index, study center, ethnicity, education level.

Table 3

Impact of oral hygiene and dental care on head ane neck cancer risk according to subsites and study center

	Oral cavity and Oropharynx		***Hypopharynx and Larynx***		***Unspecified or Overlapping***	
Variables	**OR****	**95% CI**	**OR****	**95% CI**	**OR****	**95% CI**
Frequency of teeth cleaning						
>1 time/day	1.00	-	1.00	-	1.00	-
≤1 time/day	1.49	1.11-1.99	0.66	0.42-1.05	1.14	0.80-1.64
Number of missing teeth						
<5	1.00	-	1.00	-	1.00	-
≥5	1.83	1.27-2.64	1.30	0.74-2.27	1.35	0.84-2.18
Denture use						
No	1.00	-	1.00	-	1.00	-
Yes	1.34	0.94-1.91	1.12	0.62-2.02	1.35	0.83-2.17
Frequency of dental visits						
≥1 time/year	1.00	-	1.00	-	1.00	-
1 time/2-4 years	2.13	1.21-3.74	1.06	0.34-3.28	1.68	0.89-3.18
1 time/≥5 years	1.75	1.03-2.97	2.82	1.19-6.70	2.45	1.38-4.33
Never	3.68	2.24-6.05	6.42	2.77-14.88	4.34	2.43-7.76
P_{trend}		<0.001		<0.001		<0.001
Oral hygiene score (best to worst oral hygiene)						
0	1.00	-	1.00	-	1.00	-
1	1.79	1.14-2.82	4.96	2.19-11.25	2.48	1.52-4.02
2	2.29	1.44-3.63	2.65	1.14-6.14	1.94	1.13-3.33
≥3	6.30	3.51-11.29	6.23	2.30-16.90	5.06	2.43-10.54
P_{trend}		<0.001		0.106		<0.001

Abbreviation; OR, odds ratio; CI, confidence interval.

* Oral hygiene score is the sum of the four following variables: frequency of teeth cleaning: >1 time/day=0, ≤1 time/day=1; number of missing teeth: '<5'=0, '≥5'=1; denture use: no=0, yes=1; regular dental visits: yes=0, no=1.

** Adjusted by age, sex, cigarette smoking intensity, cigarette smoking duration, betel quid chewing intensity, betel quid chewing duration, drinking intensity, drinking duration, body mass index, study center, ethnicity, education level. Betel quid chewing intensity and betel quid chewing duration was not adjusted in hypopharynx and larynx.

Table 4

Impact of oral hygiene and dental care on head and neck cancer risk according to potential confounders

	Age				***Sex***				***Smoking status***				***Drinking status***				***Study center***			
	18-54 years		***55-85 years***		***Male***		***Female***		***Never***		***Ever***		***Never***		***Ever***		***Main land***		***Taiwan***	
Variables	**OR**	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**
Frequency of teeth cleaning																				
>1 time/day	1.00	–	1.00	–	1.00	–	1.00	–	1.00	–	1.00	–	1.00	–	1.00	–	1.00	–	1.00	–
≤1 time/day	1.48	1.05-2.09	0.92	0.65-1.31	1.17	0.88-1.57	1.20	0.76-1.91	1.05	0.74-1.49	1.24	0.88-1.75	1.34	0.99-1.82	0.87	0.58-1.31	0.94	0.69-1.29	1.79	1.18-2.71
$P_{\text{for heterogeneity}}$		0.129				0.650				0.420				0.046				0.029		
Number of missing teeth																				
<5	1.00	–	1.00	–	1.00	–	1.00	–	1.00	–	1.00	–	1.00	–	1.00	–	1.00	–	1.00	–
≥ 5	1.39	0.72-2.72	1.66	1.16-2.37	1.36	0.93-1.99	1.91	1.04-3.52	2.05	1.28-3.28	1.09	0.70-1.68	1.30	0.88-1.93	2.09	1.18-3.72	1.41	0.90-2.21	1.68	1.03-2.71
$P_{\text{for heterogeneity}}$		0.792				0.107				0.009				0.207				0.726		
Denture use																				
No	1.00	–	1.00	–	1.00	–	1.00	–	1.00	–	1.00	–	1.00	–	1.00	–	1.00	–	1.00	–
Yes	1.49	0.80-2.79	1.30	0.91-1.86	1.18	0.81-1.73	1.42	0.82-2.45	1.37	0.89-2.11	1.18	0.75-1.84	0.97	0.66-1.44	2.14	1.23-3.71	1.36	0.93-1.99	1.19	0.67-2.14
$P_{\text{for heterogeneity}}$		0.708				0.338				0.372				0.017				0.244		
Frequency of dental visits																				
≥1 time/year	1.00	–	1.00	–	1.00	–	1.00	–	1.00	–	1.00	–	1.00	–	1.00	–	1.00	–	1.00	–
1 time/2-4 years	2.23	1.18-4.23	1.57	0.85-2.91	2.70	1.55-4.70	0.78	0.36-1.71	1.15	0.62-2.11	2.80	1.45-5.39	1.63	0.98-2.71	1.93	0.80-4.67	0.65	0.30-1.41	2.57	1.43-4.62
1 time/≥5 years	2.91	1.59-5.35	1.87	1.07-3.26	3.69	2.23-6.11	0.76	0.36-1.60	1.48	0.83-2.62	3.04	1.68-5.51	1.62	0.98-2.69	3.10	1.47-6.52	0.62	0.30-1.29	4.10	2.43-6.94
Never	4.41	2.43-8.02	3.80	2.23-6.46	6.85	4.16-11.26	1.27	0.65-2.46	2.11	1.24-3.60	6.70	3.73-12.03	3.02	1.90-4.81	5.58	2.67-11.65	1.05	0.55-2.01	13.30	7.11-24.89
$P_{\text{for heterogeneity}}$		0.434				<0.001				0.003				0.130				<0.001		
Oral hygiene score (best to worst oral hygiene)																				
0	1.00	–	1.00	–	1.00	–	1.00	–	1.00	–	1.00	–	1.00	–	1.00	–	1.00	–	1.00	–
1	2.48	1.56-3.94	1.66	0.96-2.85	2.93	1.89-4.54	1.00	0.54-1.84	1.27	0.79-2.05	3.36	1.99-5.65	1.70	1.13-2.57	3.32	1.69-6.50	1.43	0.80-2.56	2.95	1.84-4.75
2	2.67	1.57-4.53	1.56	0.91-2.66	2.86	1.80-4.54	0.90	0.47-1.73	1.28	0.76-2.13	2.89	1.68-4.97	1.74	1.12-2.73	2.72	1.38-5.37	1.33	0.75-2.37	3.05	1.71-5.42
≥3	5.68	2.22-14.51	4.30	2.28-8.13	5.06	2.75-9.30	6.14	2.28-16.49	3.92	1.96-7.83	5.97	2.86-12.48	3.69	2.01-6.77	####	4.02-27.77	3.01	1.47-6.15	11.06	4.47-27.39
$P_{\text{for heterogeneity}}$		0.579				0.185				0.367				0.323				0.159		

Abbreviation; OR, odds ratio; CI, confidence interval.

* Oral hygiene score is the sum of the four following variables: frequency of teeth cleaning: ≥1 time/day=0, <1 time/day=1; number of missing teeth: '<5'=0, '≥5'=1; denture use: no=0, yes=1; regular dental visits: yes=0, no=1. Adjusted by age, sex, cigarette smoking intensity, cigarette smoking duration, betel quid chewing intensity, betel quid chewing duration, drinking intensity, drinking duration, body mass index, study center, ethnicity, education level.