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Hookah smoking, nass chewing, and oesophageal squamous cell carcinoma in Kashmir, India

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BACKGROUND: Although cigarette smoking is an established risk factor for oesophageal squamous cell carcinoma (ESCC), there is little information about the association between other smoking and smokeless tobacco products, including hookah and nass, and ESCC risk. We conducted a case–control study in Kashmir Valley, India, where hookah smoking, nass chewing, and ESCC are common, to investigate the association of hookah smoking, nass use, and several other habits with ESCC.

METHODS: We recruited 702 histologically confirmed ESCC cases and 1663 hospital-based controls, individually matched to the cases for age, sex, and district of residence from September 2008 to January 2012. Conditional logistic regression models were used to calculate odds ratios (ORs) and 95% confidence intervals (95% CIs).

RESULTS: Ever-hookah smoking (OR = 1.85; 95% CI, 1.41–2.44) and nass chewing (OR = 2.88; 95% CI, 2.06–4.04) were associated with ESCC risk. These associations were consistent across different measures of use, including intensity, duration, and cumulative amount of use, and after excluding ever users of the other product and cigarette smokers. Our results also suggest an increased risk of ESCC associated with ever-gutka chewing and -bidi smoking. However, the latter associations were based on small number of participants.

CONCLUSION: This study shows that hookah and nass use are associated with ESCC risk. As prevalence of hookah use seems to be increasing among young people worldwide, these results may have relevance not only for the regions in which hookah use has been a traditional habit, but also for other regions, including western countries.

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Oesophageal cancer is the sixth most common cause of cancer deaths worldwide (Ferlay *et al*, 2010). Although the proportion of incident cases of oesophageal squamous cell carcinoma (ESCC) to oesophageal adenocarcinoma is decreasing in many western countries (Trivers *et al*, 2008; Steevens *et al*, 2010), ESCC still is the most common histological type of oesophageal cancer globally (Jemal *et al*, 2011). Cigarette smoking is a known risk factor for ESCC (IARC Working Group, 2012). However, there is little information about the association between another method of smoking tobacco, hookah (also known as waterpipe, narghile, qalyan), and ESCC risk. Smoke from hookah and cigarette have many common harmful constituents (Eissenberg and Shihadeh, 2009). Historically, hookah smoking has been a tradition mainly limited to the Eastern Mediterranean region, some parts of Asia, including India, and North Africa (IARC Working Group, 2012). Several recent studies have reported an increasing trend of hookah smoking among young people in these regions and also in several countries in Europe and North America (Jackson and Aveyard, 2008; Jawaid *et al*, 2008; Jordan and Delnevo, 2010; Maziak, 2011; Smith *et al*, 2011). It has been estimated that approximately 100 million individuals worldwide are currently regular hookah users (Ward *et al*, 2005). This indicates the need for epidemiologic studies of potential adverse health outcomes of hookah smoking, including ESCC. The use of smokeless tobacco, which is also increasing among young people in many countries, have been associated with ESCC risk (Boffetta *et al*, 2008; IARC Working Group, 2012). Nevertheless, chewing nass, a smokeless tobacco product, which is a mixture of tobacco, ash, lime, oil, and flavouring and colouring agents (IARC Working Group, 2007), and is used in some parts of Iran, India, and Central Asia (Evstifeeva and Zaridze, 1992; Nasrollahzadeh *et al*, 2008), has been less studied in relation to ESCC.

Although epidemiologic data on ESCC from the Kashmir Valley in Jammu and Kashmir State, the northernmost state of India, are sparse, the region is considered as a moderate to high incidence area for oesophageal cancer. According to the only available cancer registry report from the region, the age standardised incidence rate of oesophageal cancer was 42.6 and 27.5 per 10^5 person-year for

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men and women, respectively, in the 1980s (Khuroo *et al*, 1992). Oesophageal cancer constitutes more than 20% of all cancers (Mattoo and Kaul, 1974; Dhar *et al*, 1993), and ESCC is the most common type of oesophageal cancer in the region (Malik *et al*, 2011). Although a few earlier studies have pointed to potential associations between some lifestyle, dietary and genetic factors, and ESCC in the Kashmir Valley (Maqbool and Ahad, 1976; Khan *et al*, 2011; Malik *et al*, 2011), little is established about the risk factors of ESCC in the region. Relatively high prevalence of hookah smoking and nass chewing (Siddiqi and Preussmann, 1989; Mir and Dar, 2009) suggests that these habits may be among the important risk factors for ESCC in the valley.

To investigate risk factors of ESCC in the Kashmir Valley, we conducted a case–control study in the region, and collected detailed information on multiple lifestyle factors. In this article, we report the association between several habits, including hookah smoking, gutka (also known as gutkha and chutka, a mixture of tobacco, areca nut, lime, and several other substances, such as flavourings and sweeteners; Javed *et al*, 2010) and nass chewing, and cigarette and bidi (temburni leaf and tobacco; IARC Working Group, 2004) smoking, and ESCC risk. Any association between tobacco use and ESCC in this population is unlikely to be biased by a confounding effect of alcohol, a major risk factor of ESCC in western populations (IARC Working Group, 2012), as alcohol drinking is negligible in Kashmir Valley (Mir and Dar, 2009).

METHODS

Case and control selection

This study was conducted from September 2008 to January 2012. All cancer cases were recruited at the Regional Cancer Centre and Department of Radiation Oncology of Sher-i-Kashmir Institute of Medical Sciences (SKIMS), located in Srinagar, the largest and central city in Kashmir Valley. SKIMS is the only tertiary care hospital in the whole Kashmir Valley, and all patients with cancer and some patients with other diseases are referred to from Srinagar and from 10 hospitals in the surrounding districts. All newly diagnosed cases of oesophageal cancer with histopatologically confirmed ESCC, who were above the age of 18 years and did not have any previous cancer, were invited to participate in this study.

For each case subject, we attempted to recruit at least one hospital-based control, individually matched to the case for sex, age (± 5 years), and district of residence. For all cases from Srinagar and 30% of cases from other areas, we were able to recruit controls from the patients that resided in the same districts as the cases from in-patient wards of SKIMS and the Government Medical College Hospital, Srinagar. For the remaining cases (i.e., 70% of cases from areas other than Srinagar), controls were enroled from in-patient wards of the district hospitals in the districts from where their respective cases were referred. Therefore, matching for district of residence was complete. The major reasons for hospitalisations of the enroled controls are listed in Supplementary Table 1. The maximum interval between recruitment of cases and controls was 6 months. The participation rate for cases and control was 96% (732 invited, 30 refusals) and 98% (1697 invited, 34 refusals), respectively. The majority of those who refused were too ill to participate in the study. This study was reviewed and approved by the Institutional Ethics Committee of SKIMS.

Data collection

Structured questionnaires were administered in face-to-face interviews by trained interviewers at hospitals. Data on socio-demographic factors, including age, sex, ethnicity, religion, place of residence, and education and lifestyle factors were collected. Detailed information on life-long history of use, with starting and stopping ages, and daily amount of use, was obtained for several tobacco products and cannabis. Any change in the type of tobacco products and amount of use was also recorded. Ever use of gutka, nass, hookah, cigarette, bidi, and cannabis was defined as the use of the respective product at least weekly for a period of 6 months or more. For chewing tobacco products, the usual site of placement of nass/gutka in the mouth, and for hookah smoking, the usual frequency of changing water in the hookah apparatus was recorded. In hookah smoking, the smoke from charcoal-heated tobacco passes through a water basin before inhalation (Maziak, 2011). Therefore, some harmful constituents of tobacco may accumulate in the water with every session of smoking. Information on ever-alcohol use (alcohol drinking at least weekly for 6 months or more) was also collected. To minimise the inter-individual variation, a limited number of staff conducted the interviews and no proxies were used.

Statistical analysis

Numbers and percentages by case status were calculated and presented for categorical variables. Only small numbers of participants had used gutka, bidi, and alcohol; therefore, data for these variables are presented as ever- *vs* never-use only. Results for cannabis use are not shown, as only two ESCC cases and one control reported ever use of cannabis. For cigarette and hookah smoking, and nass chewing, data on intensity, duration, and cumulative amount (average intensity multiplied by duration) of use are also presented. In these variables, the never users were considered as the reference category; we attempted to classify ever users in three groups with equal number of controls in each group.

Conditional logistic regression models were used to calculate unadjusted and adjusted odds ratios (ORs) and 95% confidence intervals (95% CIs). The adjusted risk estimates were obtained from multivariate models in which age, ethnicity, religion, place of residence (rural/urban), education level, daily fruit and fresh vegetable intake, ever use of bidi, cannabis, gutka and alcohol, and cumulative use of cigarette, hookah, and nass were included. Fruit and vegetable intake data (grams per day) were transformed to logarithmic values following addition of 0.1 to the original values. The ORs (95% CIs) for intensity and duration of nass, hookah, and cigarette use were not adjusted for cumulative use of the respective tobacco product. By design, case and control subjects were matched by age, sex, and place of residence. Age was included in the multivariate models, because the matching for age was not perfect (± 5 years). Adjustments were done for place of residence and education level as indicators of socioeconomic status and for religion, because earlier studies in this region suggested dissimilar incidence of ESCC among people with different religions (Maqbool and Ahad, 1976).

We also estimated population-attributable fraction for several tobacco products in relation to ESCC using adjusted ORs and the following formula: $[P_e\ (OR-1)]/[1+P_e\ (OR-1)]$, where P_e was the proportion of exposed controls (Coughlin *et al*, 1994). All statistical analysis were done using Stata software, version 11 (StataCorp., College Station, TX, USA). Two-sided P-values <0.05 were considered as statistically significant.

RESULTS

A total of 702 ESCC cases and 1663 controls were enroled in this study. All cases had at least one matched control. Table 1 shows the distribution of demographic variables in case and control subjects. The majority of study participants were older than 50 years. Among both cases and controls, approximately 55% were male and 97% were of Kashmiri ethnic group. More ESCC cases than controls resided in rural areas ($P<0.001$). Formal education

Epidemiology

Table 1 Demographic characteristics of ESCC cases and matched controls

Characteristics	ESCC cases, *N* (%)	Matched controls, *N* (%)	*P*-value
Total	702 (100)	1663 (100)	
Age group, years			0.002
<40	19 (2.7)	54 (3.2)	
40–49	53 (7.5)	197 (11.9)	
50–59	157 (22.4)	424 (25.5)	
60–69	264 (37.6)	568 (34.2)	
⩾70	209 (29.8)	420 (25.2)	
Mean age (s.d.), years	61.6 (11.1)	59.8 (11.1)	<0.001
Sex			0.80
Men	392 (55.8)	919 (55.3)	
Women	310 (44.2)	744 (44.7)	
Ethnicity			0.58
Kashmiri	681 (97.0)	1618 (97.3)	
Gogri	11 (1.6)	16 (1.0)	
Pahadi	9 (1.3)	27 (1.6)	
Other	1 (0.1)	2 (0.1)	
Religion			0.03
Muslim	694 (98.9)	1647 (99.0)	
Hindu	5 (0.7)	2 (0.1)	
Sikh	3 (0.4)	14 (0.8)	
Place of residence			<0.001
Rural	674 (96.0)	1516 (91.2)	
Urban	28 (4.0)	147 (8.8)	
Education			<0.001
No formal school	625 (89.0)	1074 (64.6)	
1–4 grade	33 (4.7)	202 (12.1)	
5–8 grade	24 (3.4)	123 (7.4)	
High school	16 (2.3)	149 (9.0)	
College graduation	4 (0.6)	95 (5.7)	
Post-graduation	0 (0.0)	20 (1.2)	
Fruit and vegetable intake, median grams per day (interquartile range)	1.3 (0.8–2.0)	6.1 (2.1–72.1)	<0.001

Abbreviation: ESCC = oesophageal squamous cell carcinoma. Although cases and controls were individually matched, the percentages of cases and controls are not necessarily equal in each sex category, because some cases have one matched control and others have more controls. *P*-values calculated using χ^2-tests for categorical variables and Wilcoxon Rank Sum tests for continuous variables.

level and daily fruit and fresh vegetable intake were higher in controls than in ESCC cases ($P<0.001$).

Table 2 shows the ORs (95% CIs) for the association between tobacco and alcohol use and ESCC. The proportion of ever users of these products among controls were as following: hookah, 42.0%; gutka, 0.8%; nass, 11.5%; cigarette, 13.6%; bidi, 0.2%; and alcohol, 0.0%. Ever-hookah smoking was associated with an increased risk of ESCC (OR = 1.85; 95% CI, 1.41–2.44). Intensity, duration, and cumulative amount of hookah smoking were also associated with ESCC. Compared with changing the water of hookah basin in a daily basis, the OR (95% CI) doing this practice once a week or less frequently was 1.32; 95% CI, 0.57–3.02).

Ever-gutka and -nass chewing showed an increased risk of ESCC; however, only the association for nass was statistically significant (OR = 2.88; 95% CI, 2.06–4.04). Only a small number of participants had ever chewed gutka. Intensity, duration, and cumulative amount of nass use were also associated with an increased risk of ESCC. Among nass chewers, the ORs (95% CIs) for placement of nass under the tongue *vs* in gingival rim were 3.00 (1.21–7.41) in unadjusted and 0.65 (0.14–3.09) in adjusted models. The association between hookah and nass use and ESCC persisted after excluding ever users of the other product and cigarette smokers (Supplementary Table 2).

Cigarette smoking was not associated with the risk of ESCC in this study. Longer durations of cigarette smoking were inversely associated with ESCC in unadjusted analysis, but neither duration nor intensity of smoking had an association with the risk in adjusted models. Although the risk estimates suggest an association between ever-bidi smoking and ESCC, the number of ever users of these products was small, and consequently, 95% CIs were wide. Also, only 1.1% of ESCC cases had ever drunk alcohol. As none of the controls was an ever drinker, risk estimates for alcohol drinking could not be calculated.

Population attributable fraction for the tobacco products that showed significant associations with ESCC in multivariate models in our study was as follows: hookah smoking, 26%; nass chewing, 18%; and bidi smoking, 3%.

DISCUSSION

In this study, hookah smoking and nass chewing were associated with approximately two- and three-fold increase, respectively, in the risk of ESCC. The associations between hookah and nass use and ESCC were consistent across different measures of use, including intensity, duration, and cumulative amount of use, and after excluding ever users of the other product and cigarette smokers. This study suggests an increased risk of ESCC associated with ever use of gutka and bidi. However, these associations were based on small number of participants.

A recent meta-analysis has summarised the relatively small number of studies available on long-term effects of hookah use, and has suggested associations between hookah smoking and several health outcomes, including lung cancer and low birth weight (Akl *et al*, 2010). To our knowledge, there are only three earlier observational studies on the association between hookah smoking and ESCC: two hospital-based case–controls studies from Kashmir Valley and one population-based case–control study from an area with high incidence of ESCC in Iran. One of the studies from Kashmir, with 100 cases and 100 controls, reported prevalence of 36% of hookah use among controls, whereas this prevalence was 92% in cases ($P<0.001$, based on χ^2-tests; Khan *et al*, 2011). The other study provided an age- and sex-adjusted OR (95% CI) of 21.4 (11.6–39.5) for ever use of hookah, based on 135 cases and 195 controls with hookah-use prevalence of 21% among controls (Malik *et al*, 2011). In the Iranian study, with 300 ESCC cases and 571 controls, the OR (95% CI) for ever use of hookah was 1.85 (0.95–3.58), adjusted for several socio-demographic factors, but not for other tobacco products use (Nasrollahzadeh *et al*, 2008). When users of other tobacco products were excluded from the analyses, the OR (95% CI) for hookah use only was 1.69 (0.76–3.77), based on small number of hookah smokers (12 and 18 among ESCC cases and controls, respectively). The higher risk estimates in previous studies from Kashmir Valley may be because these results, unlike ours, were not adjusted for several potential confounding socio-demographic factors and the use of other tobacco products. Also, in one of those studies, controls were medical staff or those who referred for routine check-ups to SKIMS, many of whom were probably from Srinagar (Malik *et al*, 2011), which is the only major urban area in the valley. As hookah use is much more common in rural than in urban areas of the valley (Siddiqi and Preussmann, 1989), enrolment of cases who are referred from whole valley, but recruitment of controls mainly from urban areas (selection bias), can be another reason for the above difference in the magnitude of risk estimates.

Table 2 Association between tobacco and alcohol use and ESCC

Tobacco use	ESCC cases, *N* (%)	Matched controls, *N* (%)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Hookah smoking				
Never	282 (40.2)	964 (58.0)	Referent	Referent
Ever	420 (59.8)	699 (42.0)	2.36 (1.92–2.89)	1.85 (1.41–2.44)
Intensity				
Never use	282 (40.2)	964 (58.0)	Referent	Referent
<4 times per day	76 (10.8)	179 (10.8)	1.73 (1.26–2.37)	1.37 (0.91–2.07)
4–5 times per day	98 (14.0)	268 (16.1)	1.39 (1.04–1.86)	1.10 (0.69–1.47)
⩾6 times per day	246 (35.0)	252 (15.1)	4.35 (3.45–5.66)	4.02 (2.79–5.78)
P for trend			<0.001	<0.001
Duration				
Never use	282 (40.2)	964 (58.0)	Referent	Referent
1–33 years	120 (17.1)	198 (11.9)	2.23 (1.68–2.96)	1.77 (1.21–2.60)
34–45 years	147 (20.9)	276 (16.6)	2.06 (1.57–2.69)	1.77 (1.24–2.52)
⩾46 years	153 (21.8)	223 (13.4)	2.99 (2.23–4.01)	2.06 (1.42–3.01)
P for trend			<0.001	<0.001
Cumulative use				
Never use	282 (40.2)	964 (58.0)	Referent	Referent
1–139 hookah-years	97 (13.8)	228 (13.7)	1.66 (1.24–2.21)	1.12 (0.77–1.64)
140–240 hookah-years	110 (15.7)	245 (14.8)	1.77 (1.33–2.36)	1.54 (1.05–2.26)
⩾241 hookah-years	213 (30.3)	224 (13.5)	4.29 (3.26–5.65)	3.62 (2.50–5.23)
P for trend			<0.001	<0.001
Frequency of changing water				
Daily	388 (92.4)	656 (94.5)	Referent	Referent
⩽Weekly	32 (7.6)	38 (5.5)	1.48 (0.84–2.60)	1.32 (0.57–3.02)
Gutka chewing				
Never	692 (99.6)	1650 (99.2)	Referent	Referent
Ever	10 (1.42)	13 (0.8)	1.84 (0.80–4.23)	2.87 (0.87–9.46)
Nass chewing				
Never	501 (71.4)	1471 (88.5)	Referent	Referent
Ever	201 (28.6)	192 (11.5)	3.41 (2.67–4.37)	2.88 (2.06–4.04)
Intensity				
Never use	501 (71.4)	1471 (88.5)	Referent	Referent
<4 times per day	40 (5.7)	71 (4.3)	2.04 (1.34–3.12)	1.61 (0.93–2.77)
4–5 times per day	54 (7.7)	74 (4.4)	2.28 (1.56–3.34)	2.25 (1.34–3.80)
⩾6 times per day	107 (15.2)	47 (2.8)	6.87 (4.70–10.03)	5.34 (3.24–8.83)
P for trend			<0.001	<0.001
Duration				
Never use	501 (71.6)	1471 (88.4)	Referent	Referent
1–34 years	63 (9.0)	62 (3.7)	3.41 (2.28–5.09)	2.42 (1.41–4.17)
35–44 years	39 (5.6)	50 (3.0)	2.41 (1.52–3.80)	2.19 (1.17–4.08)
⩾45 years	97 (13.8)	80 (4.8)	4.02 (2.83–5.71)	3.58 (2.20–5.82)
P for trend			<0.001	<0.001
Cumulative use				
Never use	501 (71.6)	1471 (88.5)	Referent	Referent
1–119 nass-years	46 (5.6)	52 (3.1)	2.93 (1.91–4.50)	2.14 (1.20–3.82)
120–199 nass-years	36 (5.1)	71 (4.3)	1.70 (1.10–2.61)	1.44 (0.80–2.60)
⩾200 nass-years	117 (16.7)	69 (4.1)	5.31 (3.78–7.45)	4.56 (2.89–7.22)
P for trend			<0.001	<0.001
Site of placement of nass/gutka in the mouth				
Gingival rim	149 (74.1)	166 (86.5)	Referent	Referent
Under the tongue	52 (25.9)	26 (13.5)	3.00 (1.21–7.41)	0.65 (0.14–3.09)
Cigarette smoking				
Never	632 (90.0)	1437 (86.4)	Referent	Referent
Ever	70 (10.0)	226 (13.6)	0.67 (0.49–0.91)	0.97 (0.60–1.55)
Intensity				
Never use	632 (90.0)	1437 (86.4)	Referent	Referent
<5 cigarettes per day	28 (4.0)	84 (5.1)	0.73 (0.46–1.16)	0.99 (0.50–1.97)
5–6 cigarettes per day	17 (2.4)	72 (4.3)	0.48 (0.28–0.85)	0.75 (0.34–1.68)
⩾7 cigarettes per day	25 (3.6)	70 (4.2)	0.80 (0.49–1.31)	1.27 (0.55–2.92)
P for trend			0.03	0.95
Duration				
Never use	632 (90.0)	1437 (86.4)	Referent	Referent
1–29 years	18 (2.6)	69 (4.1)	0.56 (0.32–0.98)	1.20 (0.51–2.82)
30–39 years	21 (3.0)	66 (4.0)	0.67 (0.39–1.13)	1.08 (0.47–2.45)
⩾40 years	312 (4.4)	91 (5.5)	0.74 (0.47–1.14)	0.81 (0.42–1.58)
P for trend			0.01	0.69

Table 2 *(Continued)*

Tobacco use	ESCC cases, *N* (%)	Matched controls, *N* (%)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Cumulative use				
Never use	632 (90.0)	1437 (86.4)	Referent	Referent
1–6.2 pack-years	23 (3.3)	77 (4.6)	0.63 (0.39–1.04)	1.30 (0.62–2.71)
6.3–13.1 pack-years	21 (3.0)	73 (4.4)	0.61 (0.37–1.02)	0.59 (0.28–1.25)
⩾13.2 pack-years	26 (3.7)	76 (4.6)	0.75 (0.47–1.21)	1.27 (0.56–2.86)
P for trend			0.04	0.85
Bidi smoking				
Never	687 (97.9)	1660 (99.8)	Referent	Referent
Ever	15 (2.1)	3 (0.2)	11.82 (3.40–41.06)	16.30 (2.46–108.20)
Alcohol drinking				
Never	694 (98.9)	1663 (100)	Referent	Referent
Ever	8 (1.1)	0 (0.0)	—	—

Abbreviations: CI = confidence interval; ESCC = oesophageal squamous cell carcinoma; OR = odds ratio. ORs (95% CIs) were obtained from conditional logistic regression models. *P* for trend was obtained from the same models by assigning consecutive numbers to categories within each categorical variable. Cumulative use was calculated by multiplying intensity of use (per day) by duration of use (in years). Numbers may not add up to the total numbers due to missing data in some variables. Adjusted ORs (95% CIs) were obtained from models in which age, ethnicity, religion, place of residence, education level, cumulative use of cigarette, hookah and nass, and ever use of bidi, cannabis, gutka, and alcohol, and daily fruit and fresh vegetable consumption were included. The ORs (95% CIs) for intensity and duration of nass, hookah, and cigarette use were not adjusted for cumulative use of the respective tobacco product.

Hookah smokers seem to be exposed to many toxic compounds as cigarette smokers, such as nicotine, nitric oxide, carbon monoxide, polycyclic aromatic hydrocarbons, and nitrosamines (Monzer *et al*, 2008; Eissenberg and Shihadeh, 2009; Ghasemi *et al*, 2010; Jacob *et al*, 2011). Furthermore, hookah smokers may be exposed to harmful smoke from the burning charcoal (Monzer *et al*, 2008). The exposure to smoke per puff with hookah smoking may even be higher than with cigarette smoking; each puff from the hookah has reported to deliver 12 times as much smoke as a single cigarette puff (Eissenberg and Shihadeh, 2009). The similarity of biological consequences of waterpipe and cigarette smoking reported in other studies supports the association between hookah smoking and ESCC. The relatively high prevalence of hookah use among the young people in a number of populations worldwide, which is reported to be increasing (Jackson and Aveyard, 2008; Jawaid *et al*, 2008; Jordan and Delnevo, 2010; Maziak, 2011; Smith *et al*, 2011; Jarrett *et al*, 2012), indicates public health implication of this association and other hookah-related adverse health consequences. In our study, less frequent changing of water in hookah apparatus was not associated with ESCC risk. However, the number of hookah smokers who changed the water less frequently than daily was small.

An association between nass use and precancerous oral and oesophageal lesions (Zaridze *et al*, 1986; Evstifeeva and Zaridze, 1992) and ESCC (Nasrollahzadeh *et al*, 2008) has been reported in a few studies. The latter study reported a two-fold increased risk of ESCC in ever- *vs* never-nass users (Nasrollahzadeh *et al*, 2008). The association between nass chewing and ESCC is plausible, because several experimental and epidemiological studies have shown the role of chewing tobacco in oesophageal carcinogenesis (IARC Working Group, 2007, 2012). Furthermore, other constituents of nass, such as polycyclic aromatic hydrocarbons from ash, may have additional carcinogenic effects on the oesophageal epithelium (Roth *et al*, 1998; Islami *et al*, 2009; Abedi-Ardekani *et al*, 2010). We did not find any association between placement location of nass in the mouth and ESCC risk in adjusted models.

Although cigarette smoking increases ESCC risk by 3- to 5-fold in western countries (Tuyns, 1983; Brown *et al*, 2001), it has been associated with only 1.3- to 1.5-fold increased risk in high-incidence areas of China and Iran (Tran *et al*, 2005; Nasrollahzadeh *et al*, 2008), suggesting that the majority of ESCC cases in those high-incidence areas are due to other factors. In our study, the highest category of cumulative use showed a non-significant OR of 1.27. This may partly be related to low cumulative cigarette use in our study; only 2.2% of participants had smoked 20 or more pack-years of cigarette. The association between bidi smoking and ESCC has been reported by several other studies from areas where this habit is more common (IARC Working Group, 2012); our study provides only modest supporting evidence.

This study is the largest study from Kashmir Valley that has investigated risk factors of ESCC in this relatively high-risk region, using analytical methods and with adjustments for several potential confounding factors, and the largest study that has ever studied the association between hookah and nass use and ESCC. Other strengths of this study include matching controls to all cases for the district of residence, to reduce possibility of confounding by area of residence, using several measures of exposure for common tobacco products, and histological confirmation of all ESCC diagnoses. Because of its case–control design, recall bias can be a limitation of this study. As the majority of participants had little formal education, and because there was little earlier information on the association between hookah and nass use and risk of ESCC, participants were unlikely to be aware of study hypotheses, particularly with regard to hookah and nass. Therefore, it is unlikely that the use of these products were reported differentially by controls and ESCC cases. Also, the evidence for recall bias in retrospective *vs* prospective epidemiologic studies is generally weaker for tobacco products than for other cancer risk factors (Gandini *et al*, 2008).

In conclusion, this study shows that hookah and nass use are associated with an increased risk of ESCC. These associations, as well as the associations between these products and several other health outcomes, indicate that the tobacco control programmes should more strictly include tobacco products other than cigarette. Because of the increasing trend of using hookah reported worldwide, results of this study can have public health implications not only for the regions in which hookah use has been a tradition, but also for many other regions, including the western countries.

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Conflict of interest

The authors declare no conflict of interest.

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