

ORIGINAL ARTICLE

Smoking water-pipe, chewing nass and prevalence of heart disease: a cross-sectional analysis of baseline data from the Golestan Cohort Study, Iran

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ABSTRACT

Objective Water-pipe and smokeless tobacco use have been associated with several adverse health outcomes. However, little information is available on the association between water-pipe use and heart disease (HD). Therefore, we investigated the association of smoking water-pipe and chewing nass (a mixture of tobacco, lime and ash) with prevalent HD.

Design Cross-sectional study.

Setting Baseline data (collected in 2004–2008) from a prospective population-based study in Golestan Province, Iran.

Participants 50 045 residents of Golestan (40–75 years old; 42.4% men).

Main outcome measures ORs and 95% CIs from multivariate logistic regression models for the association of water-pipe and nass use with HD prevalence.

Results A total of 3051 (6.1%) participants reported a history of HD, and 525 (1.1%) and 3726 (7.5%) reported ever water-pipe or nass use, respectively. Heavy water-pipe smoking was significantly associated with HD prevalence (highest level of cumulative use vs never use, OR=3.75; 95% CI 1.52 to 9.22; *p* for trend=0.04). This association persisted when using different cut-off points, when restricting HD to those taking nitrate compound medications, and among never cigarette smokers. There was no significant association between nass use and HD prevalence (highest category of use vs never use, OR=0.91; 95% CI 0.69 to 1.20).

Conclusions Our study suggests a significant association between HD and heavy water-pipe smoking. Although the existing evidence suggesting similar biological consequences of water-pipe and cigarette smoking make this association plausible, results of our study were based on a modest number of water-pipe users and need to be replicated in further studies.

INTRODUCTION

Heart disease (HD), including ischaemic HD (IHD) and heart failure (HF), is a major cause of morbidity and mortality worldwide, in both high-income and low- and middle-income countries.^{1,2} Tobacco use in the form of cigarette smoking is an established IHD risk factor.^{3,4} An association between cigarette smoking and HF has also been reported in several studies,^{5–8} perhaps mediated partly through

the effect of smoking on IHD, a major risk factor for HF,⁹ and partly through other mechanisms.^{5,6,8} Smoke from another method of smoking tobacco, water-pipe (also known as hookah, shisha, nargileh and qalyan)¹⁰ also contains many of the same toxic compounds as cigarettes^{11–13} and therefore may increase HD risk. However, as water-pipe use has historically been limited to rarely studied populations, such as those in the East Mediterranean, little data on the relationship of water-pipe use with HD is available. Of considerable potential public health concern, the use of water-pipe is rapidly increasing globally,¹⁰ and it is estimated that 100 million people now use water-pipe worldwide.¹⁴ This increase is seen most rapidly among the youth of the East Mediterranean and Western countries in Europe and North America.^{10,15–17} This calls for epidemiological studies of health effects of water-pipe, including its association with HD.¹⁸

An association between smokeless tobacco use, another type of tobacco product, and IHD incidence^{19,20} and mortality^{19,21} has also been suggested. However, this association has not been consistent across studies.²¹ Smokeless tobacco also seems to be positively associated with HF,²² although studies are sparse.

The Golestan Cohort Study (GCS), a large-scale prospective study in Golestan Province, northern Iran, has collected detailed information on life-long use of water-pipe, nass (a chewing tobacco product, mixed with lime and ash, which is used locally and mostly by men),²³ risk factors of IHD, and history of previous diagnosis of HD. The aim of this paper is to present results for the association of smoking water-pipe and chewing nass with prevalent HD using baseline data collected in the GCS.

MATERIALS AND METHODS

The design of the GCS has been described elsewhere.²³ Briefly, the GCS is a prospective population-based cohort, primarily designed to investigate risk factors of upper gastrointestinal cancers, with the primary goal of recruiting 50 000 healthy individuals (40–75 years old), with equal numbers of men and women, 20% from urban areas and 80% of Turkmen ethnicity from eastern

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parts of Golestan Province. A total of 50 045 adults were enrolled between 2004 and 2008. Eligibility criteria included permanent residence in the study area and no history of upper gastrointestinal cancers.

At baseline, trained nurses and physicians conducted face-to-face interviews using structured questionnaires to collect data on a large number of variables including age, sex, ethnicity, education, place of residence, ownership of several appliances, life-long history of tobacco use (cigarette, water-pipe and nass, separately), physical activity and past medical history (including medications and history of hypertension, diabetes and HD, as well as age at diagnosis of these diseases). Data on tobacco use included starting and stopping ages and daily amount used in different time periods, which captured changes in use over time. Data on alcohol use were also collected, but as alcohol drinking was negligible among the study participants,²³ we did not include the data in further analyses.

In accord with our earlier publications,²⁴ we calculated a composite score for wealth by applying multiple correspondence analysis to appliance ownership data (including bath in the residence, personal car, motorbike, black and white TV, colour TV, refrigerator, freezer, vacuum and washing machine). The scores were categorised in quartiles. Recreational physical activity is uncommon in this population, particularly in the age range of the study participants. Therefore, occupational physical activity is the main source of physical activity. Two questions assessed occupational physical activity: if the person worked every month throughout the year, and if intense physical activity was a part of the daily work. Three levels of occupational physical activity were defined based on the answers to these questions: intense physical activity at work, non-intense but regular physical activity and non-intense irregular physical activity.

Individuals were considered ever tobacco users if they had used cigarettes, water-pipe, or nass at least once a week for a period of 6 months or more. We calculated cumulative amount of cigarette use (as pack-years) using data on duration and quantity of use. As there are no standard units for quantity of water-pipe or nass use, we considered the frequency and duration of water-pipe smoking and nass chewing, assuming relatively small variation in overall exposure per time of use, and calculated 'water-pipe-years' and 'nass-years' as units of cumulative use, respectively; 50 nass-years indicates, for example, the use of nass five-times per day for 10 years. Participants in our study could have begun using tobacco after HD diagnosis, at which point tobacco use could not have contributed to their risk of this disease. To estimate the potential effect of such 'irrelevant exposure' on our results, we analysed our data using two approaches. First, we analysed all available data on tobacco use, regardless of when participants began smoking. Second, we excluded HD cases who started using tobacco after disease diagnosis. As only a small proportion of participants began to use tobacco products after HD diagnosis and risk estimates were similar for each approach (see online supplementary table S1), we report results after excluding cases who began smoking after HD diagnosis in this manuscript.

Weight and height were measured by trained research staff. Body mass index (BMI) was calculated by dividing weight (kg) by the squared value of height (m). In this study, only physicians measured blood pressure and collected data on past medical history. Systolic and diastolic blood pressures were obtained twice from each arm in the sitting position. Participants were considered to be hypertensive if they used anti-hypertensive medication or fulfilled the criteria of the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation

and Treatment of High Blood Pressure (average systolic blood pressure ≥ 140 mm Hg, or average diastolic blood pressure above ≥ 90 mm Hg).²⁵ Diabetes mellitus was self-reported based on the following question 'Have you ever been diagnosed by a doctor as having diabetes mellitus?' Participants were also asked about past cardiac problems using two separate questions: one was on rheumatic HD; the other question was 'Have you ever been diagnosed by a doctor as having angina, infarction, or HF?' Our initial intent was to collect data on IHD. However, we decided to collect data on IHD and HF as a combined entity because we expected that a substantial proportion of patients with HD in the study area, particularly in rural areas, would not be able to distinguish between IHD, HF, and perhaps some other types of HD. Those with a positive reply to the latter question were considered to have HD. We also examined medications typically prescribed to patients with HD or its risk factors by self-reported HD status (see online supplementary table S2). To study the effect of misclassification due to personal reporting, in a sub-analysis, we restricted our endpoint to participants using nitrate compounds (including medications containing trinitroglycerin, isosorbide dinitrate and glyceryltrinitrate), which are typically prescribed as antianginal agents.

Statistical analysis

Numbers and percentages were calculated and presented for categorical variables, as well as means and SDs for continuous variables. We used logistic regression models to calculate ORs and 95% CIs for the association between water-pipe, cigarette, and nass use and HD prevalence. *p* values for trend were obtained from logistic regression models by assigning consecutive numbers to categories within each categorical variable. Multivariate models were adjusted for age, sex, ethnicity, place of residence (rural/urban), education level, wealth, physical activity, BMI, hypertension, self-reported diabetes and cumulative use of the other tobacco products. Results were adjusted for place of residence (rural/urban), education and wealth because these are important indicators of socioeconomic status, and perhaps access to healthcare, in our study region. We adjusted the results for ethnicity in order to reduce the potential confounding effect of lifestyle factors that may have dissimilar distributions in different ethnic groups, such as dietary habits. Age, low physical activity, high BMI, hypertension and diabetes are established risk factors of HD.^{26–28} All statistical analyses were performed using STATA statistical software V.11 (Stata Corporation, College Station, Texas, USA). All reported *p* values are two-sided, and *p* < 0.05 was considered to be statistically significant.

RESULTS

Of 50 045 participants, 3051 (6.1%) reported a history of HD. The average age of all participants was 52.1 (SD, 9.0) years (table 1). The distribution of prevalent HD was similar in men and women. The majority of participants (61.4%) had irregular non-intense physical activity, and mean BMI was 26.7 (SD, 5.5) kg/m². Slightly fewer than half of participants (42.5%) had hypertension, and 6.9% reported diabetes. Traditional risk factors of IHD, including age, low physical activity, high BMI, hypertension and diabetes, were all associated with higher HD prevalence (see online supplementary table S3).

Distribution of water-pipe, cigarette and nass use and their associations with HD prevalence are shown in table 2. Ever water-pipe, cigarette and nass use was reported by 1.1%, 17.1% and 7.5% of participants, respectively. Heavy water-pipe smoking was significantly associated with HD prevalence

Table 1 Distribution of some sociodemographic characteristics and risk factors of IHD in the Golestan Cohort Study, at the baseline by self-reported HD status*

Characteristics	All participants	HD cases	Participants without HD	p Value
Total	50045 (100)	3051 (100)	46993 (100)	
Age (years)	52.1 (9.0)	56.9 (9.1)	51.8 (8.9)	<0.001
Sex				0.03
Women	28811 (57.6)	1787 (58.6)	27024 (57.5)	
Men	21234 (42.4)	1264 (41.4)	19970 (42.5)	
Ethnicity				<0.001
Non-Turkmen	12792 (25.6)	1022 (33.5)	11770 (25.0)	
Turkmen	37253 (74.4)	2029 (66.5)	35224 (75.0)	
Place of residence				<0.001
Rural	40013 (80.0)	2272 (74.5)	37741 (80.3)	
Urban	10032 (20.0)	779 (25.5)	9253 (19.7)	
Education				<0.001
No School	35118 (70.2)	2298 (75.3)	32820 (69.8)	
Primary/middle school	10708 (21.4)	569 (18.6)	10139 (21.6)	
High school	3155 (6.3)	133 (4.4)	3022 (6.4)	
University	1064 (2.1)	51 (1.7)	1013 (2.2)	
Wealth				<0.001
Low	14587 (29.1)	814 (26.7)	13773 (29.3)	
Low-Medium	10097 (20.2)	599 (19.6)	9498 (20.2)	
Medium-High	12348 (24.7)	749 (24.6)	11599 (24.7)	
High	13010 (26.0)	889 (29.1)	12121 (25.8)	
Physical activity				<0.001
Irregular non-intense	30647 (61.4)	2198 (72.2)	28449 (60.7)	
Regular non-intense	13536 (27.1)	654 (21.5)	12882 (27.5)	
Regular or irregular intense	5695 (11.4)	192 (6.3)	5503 (11.8)	
BMI (kg/m ²)	26.7 (5.5)	27.7 (5.7)	26.6 (5.4)	<0.001
Hypertension†				<0.001
Normotensive	28628 (57.5)	1032 (33.9)	27596 (59.0)	
Hypertensive	21197 (42.5)	2012 (66.1)	19185 (41.0)	
Self-reported diabetes				<0.001
Non-diabetic	46591 (93.1)	2481 (81.3)	44110 (93.9)	
Diabetic	3454 (6.9)	570 (18.7)	2884 (6.1)	

*Figures are the number of participants (percentage), except for age and BMI, for which mean (SD) is presented. Numbers may not add up to the total numbers due to missing data in some variables. p Values calculated using χ^2 tests for categorical variables and Wilcoxon Rank Sum tests for continuous variables.

†Including self-reported hypertension and individuals with high blood pressure at the baseline examination.

BMI, body mass index; HD, heart disease; IHD, ischaemic heart disease.

(highest level of cumulative use vs never use, OR=3.75; 95% CI 1.5 to 9.22; p for trend=0.04 in multivariate adjusted models). As many water-pipe users in this study were light water-pipe smokers, ever versus never water-pipe use was not associated with HD prevalence (OR=1.09; 95% CI 0.80 to 1.48), but moderate-high use (arbitrarily defined as cumulative use of >50 water-pipe-years) versus never-low use was associated with HD prevalence (OR=1.83; 95% CI 1.10 to 3.07). We examined this association with several other cutpoints for the cumulative use; with any cutpoint ≥ 39 water-pipe-years for the highest use category, the category was associated with HD (examples are shown in online supplementary table S4). When we restricted our HD case definition to participants who used HD medications containing nitrate compounds at the time of enrolment, the OR for the highest category of water-pipe use became slightly stronger in magnitude (4.50; 95% CI 1.24 to 16.36). As cigarette smoking was also associated with HD prevalence (p for trend <0.001), we further examined water-pipe use among never cigarette smokers. There was little overlap between water-pipe and cigarette smoking in our cohort and the above associations remained similar in these sensitivity analyses (see online supplementary table S5).

Nass use did not show a statistically significant association with HD prevalence in the overall analysis (highest category of use vs never-use, OR=0.91; 95% CI 0.69 to 1.20; p for trend=0.24) (table 2) or among never cigarette smokers (see online supplementary table S5). The distributions of water-pipe, cigarette and nass use by covariates are shown in online supplementary tables S6–S8, respectively.

DISCUSSION

This study provides evidence for a statistically significant positive association between water-pipe smoking and HD prevalence, while nass use showed no association. As expected, traditional risk factors for IHD, including age, cigarette smoking, low physical activity, high BMI, hypertension and a history of diabetes were also associated with HD.

The majority of studies on water-pipe smoking have evaluated the prevalence of use and the correlates of initiation and continuation of use. To our knowledge, the only previously published investigation of water-pipe smoking and HD is an abstract from a case-control study in Lebanon with 292 incident cases of IHD and 233 controls, which suggested an association between water-pipe use and IHD, with an OR (95% CI) of 1.9 (1.2– 2.8) in

Table 2 Association between tobacco use and self-reported HD in the Golestan Cohort Study

Tobacco use*	All participants (%)	HD cases (%)	Participants without HD (%)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)†
Water-pipe smoking					
Ever versus never use					
Never	49489 (98.9)	2990 (98.1)	46499 (99.0)	Reference	Reference
Ever	525 (1.1)	51 (1.9)	474 (1.0)	1.67 (1.25 to 2.24)	1.09 (0.80 to 1.48)
Moderate-high versus never-low use					
≤50 water-pipe-years	49894 (99.8)	3022 (99.4)	46872 (99.8)	Reference	Reference
>50 water-pipe-years	120 (0.2)	19 (0.6)	101 (0.2)	2.92 (1.78 to 4.77)	1.83 (1.10 to 3.07)
Cumulative use					
Never	49489 (98.9)	2990 (98.3)	46499 (99.0)	Reference	Reference
≤50 water-pipe-years	405 (0.8)	32 (1.0)	373 (0.8)	1.33 (0.93 to 1.91)	0.87 (0.60 to 1.28)
50.1–100	52 (0.1)	6 (0.2)	46 (0.1)	2.03 (0.86 to 4.74)	1.25 (0.52 to 3.03)
100.1–180	43 (0.1)	5 (0.2)	38 (0.1)	2.05 (1.03 to 2.80)	1.49 (0.57 to 3.87)
>180	25 (0.1)	8 (0.3)	17 (0.04)	6.39 (2.65 to 15.41)	3.75 (1.52 to 9.22)
				p trend: <0.001	p trend: 0.04
Cigarette smoking					
Ever versus never use					
Never	41445 (82.9)	2405 (79.7)	39040 (83.1)	Reference	Reference
Ever	8555 (17.1)	614 (20.3)	7941 (16.9)	1.26 (1.14 to 1.38)	1.63 (1.45 to 1.83)
Moderate-high versus never-low use					
≤5 pack-years	44187 (88.4)	2559 (85.3)	41628 (88.6)	Reference	Reference
>5 pack-years	5813 (11.6)	460 (14.7)	5353 (11.4)	1.40 (1.26 to 1.55)	1.76 (1.55 to 1.99)
Cumulative use					
Never	41445 (82.9)	2405 (79.7)	39040 (83.1)	Reference	Reference
≤5 pack-years	2742 (5.5)	154 (5.1)	2588 (5.5)	0.97 (0.82 to 1.14)	1.26 (1.05 to 1.52)
5.1–10	1260 (2.5)	73 (2.4)	1187 (2.5)	1.00 (0.79 to 1.27)	1.43 (1.11 to 1.84)
10.1–20.0	1798 (3.6)	121 (4.0)	1677 (3.6)	1.17 (0.97 to 1.41)	1.73 (1.41 to 2.13)
>20	2755 (5.5)	266 (8.8)	2489 (5.3)	1.73 (1.52 to 1.98)	2.04 (1.74 to 2.38)
				p trend: <0.001	p trend: <0.001
Nass chewing					
Ever versus never use					
Never	46264 (92.5)	2775 (92.5)	43489 (92.5)	Reference	Reference
Ever	3726 (7.5)	225 (7.5)	3501 (7.5)	1.01 (0.88 to 1.16)	0.85 (0.73 to 1.00)
Moderate-high versus never-low use					
≤50 nass-years	48026 (96.1)	2859 (95.3)	45167 (96.1)	Reference	Reference
>50 nass-years	1964 (3.9)	141 (4.7)	1823 (3.9)	1.22 (1.03 to 1.46)	0.95 (0.79 to 1.15)
Cumulative use					
Never	46264 (92.5)	2775 (92.5)	43489 (92.5)	Reference	Reference
≤50 nass-years	1762 (3.5)	84 (2.8)	1678 (3.6)	0.78 (0.63 to 0.98)	0.75 (0.60 to 0.95)
50.1–100	635 (1.3)	43 (1.4)	592 (1.3)	1.14 (0.83 to 1.56)	0.98 (0.71 to 1.36)
100.1–180	532 (1.1)	35 (1.2)	497 (1.0)	1.10 (0.78 to 1.56)	0.90 (0.62 to 1.28)
>180	797 (1.6)	63 (2.1)	734 (1.6)	1.35 (1.04 to 1.74)	0.91 (0.69 to 1.20)
				p trend: 0.09	p trend: 0.24

Numbers may not add up to the total numbers due to missing data in some variables.

*Among HD cases, those who started the use of the tobacco product after receiving a diagnosis of HD were excluded from the analyses related to the respective product; 100 water-pipe-years, for example, indicates water-pipe use equivalent to use 10 times per day for 10 years (or use 5 times per day for 20 years).

†All results for each tobacco product were adjusted for cumulative use of the other products listed in this table, as well as for age, sex, ethnicity, place of residence, education level, wealth, physical activity, body mass index, hypertension, and self-reported diabetes (these variables were as shown in Table 1).
HD, heart disease.

unadjusted and 2.2 (0.9 to 5.4) in adjusted models for ever-water-pipe smokers versus never-smokers.²⁹ This dearth of information may be partly because the ‘epidemic’ of water-pipe use is now mainly among young people:^{10 16} due to the usual long latency of the health effects of tobacco use, such effects are not yet common among the majority of people who use water-pipe. However, there is biological evidence that water-pipe could cause HD via mechanisms similar to those of cigarette smoking. Water-pipe smokers are exposed to many of the same toxic compounds as cigarette smokers, and perhaps at higher levels per puff: each puff from the water-pipe has been reported to deliver

12-times as much smoke as a single cigarette puff.¹¹ Similar nicotine levels have been reported in plasma following water-pipe and cigarette smoking, and carboxyhaemoglobin levels are three-fold higher after water-pipe than after cigarette use.¹¹ Carbon monoxide levels following water-pipe smoking are also higher as compared with cigarette smoking and the majority of the excess carbon monoxide appears to come from the burning charcoal used to heat the tobacco.¹² Both cigarette and water-pipe smoking increase nitric oxide concentration in serum.¹³

A limited number of studies on other health outcomes of water-pipe smoking have been published;^{30 31} they also indicate

harmful health effects. Current evidence suggests an association between water-pipe use and respiratory illness, lung cancer, low birth-weight and periodontal disease.^{30–31} A more limited number of studies have also suggested associations between water-pipe smoking and risk of upper aerodigestive tract neoplasia^{32–33} and bladder cancer.^{34–35}

Several methodological considerations are of potential concern. Cross-sectional analyses may be subject to bias due to reverse causality. For example, one might argue that after receiving a diagnosis of HD, patients may replace cigarette smoking with water-pipe use. To avoid this problem, we excluded from analysis HD patients who started using water-pipe after receiving a diagnosis of HD. Diagnosis of HD was based on participants' reports, which could be misclassified. Such misclassification, if non-differential with respect to water-pipe use, would lead to results that are biased toward null,³⁶ not away from null. Therefore, non-differential misclassification cannot explain our finding of an increased risk of HD in relation to water-pipe use. In fact, when we limited our case definition to cases using nitrate compounds, the risk estimates strengthened, supporting our hypothesis. Differential misclassification is also possible if there was residual confounding after adjustments, as water-pipe users—people with lower wealth and education—may be less aware of their HD. Such misclassification, however, would also shift our findings towards a null or an inverse association, and as such would have resulted in the attenuation of our risk estimates. Using prevalence ratios, rather than incidence ratios, may lead to what has been called incidence-prevalence bias,³⁷ but since water-pipe use is unlikely to expand longevity, prevalence ratios would be either equal to or underestimations of incidence ratios. Finally, analyses using different cutpoints for the highest category of water-pipe use all showed an increased risk of HD.

One limitation of our study is a lack of specificity in our assessment of HD. Prior history of angina, infarction, or HF was asked as a single question, because we did not expect participants in our study would be able to distinguish between IHD, HF, or other types of HD. As these data were collected by interactive face-to-face interviews conducted by trained researcher physicians, it is unlikely that many cases of HDs other than IHD and HF were categorised as HD cases in this study. Although little information is available on the relative prevalence of IHD and HF in Iran, we would nevertheless expect that a majority of cases are IHD. In the most recent available national mortality data from Iran (2004), IHD (The International Classification of Diseases (ICD10 codes I20 to I25)) was the cause of 21.8% of all mortality cases in Iran, approximately 7-times more than hypertensive HD (ICD 10 codes I10 to I13, which included heart failure), which was the cause of death in 3.2% of cases.³⁸ Similarly, in the few available reports on incidence in Iran, HF was associated with IHD in 60–65% of admitted patients,^{39–40} with similar proportions observed in studies from adjacent countries (40–60%),^{41–45} and those from the West.^{5–46} Furthermore, we analysed medication use in our study and observed that only 5% of our cases used digoxin, a medication commonly prescribed for symptomatic HF,^{47–48} and even among those using digoxin, one-third also used nitrate compounds, indicated for IHD. Therefore, we believe that IHD is far more common than HF in this study, and that a considerable proportion of HF patients also had IHD. However, further studies on the association of water-pipe use with IHD, HF, and other forms of HD are needed.

Regardless of the exact diagnosis (IHD, HF, or other), our results suggest potentially harmful effects of water-pipe smoking on cardiac structure and function. The prevalence of water-pipe

use in our study was 1%, substantially lower than rates of use among young people globally.¹⁰ In the USA, for example, 5–20% of college students have reported water-pipe use over the past month.¹⁷ Therefore, if associations are causal, water-pipe use may cause many cases of HD and other tobacco-related diseases in the coming decades, should use continue at current or higher levels.

In our study, we observed no evidence for an association between nass use and HD. Whereas studies from Sweden generally have not shown an association between smokeless tobacco (mainly snus) use and IHD incidence, some US studies and a multicentre study in 52 countries (the INTERHEART Study, with various smokeless tobacco products) have shown positive associations.^{19–20} Variations across studies may be related to the type of smokeless tobacco product used (eg, snuff, snus and many chewing products), differences in use across populations and methodological differences between studies.²¹

The null association between nass chewing and prevalent HD in our study may be true, but residual confounding cannot be ruled out. Nass chewing is far more common in rural than in urban areas of Golestan, and due to lower access to advanced medical care centres, the rate of undiagnosed subclinical cases of HD in rural areas of Golestan may be higher than in urban areas. However, we adjusted for rural/urban residence, and patterns of residence in the age range of our study participants are relatively stable and easily measurable. Therefore, substantial residual confounding due to residence is unlikely. Nass chewing was also more common among those with lower wealth and education, people who may be less likely to be aware of their HD. If residual confounding exists, the estimated risk ratios would be falsely low. It should also be noted that nass is not a pure tobacco product, and lime and ash, with probably varied constituents, are also mixed with tobacco. Further studies on the association between nass chewing—and its constituents—and HD are warranted.

In our study, similar to previous literature, traditional IHD risk factors, including age, cigarette smoking, low physical activity, high BMI, hypertension and diabetes were associated with HD prevalence. As these associations have been reviewed in a number of publications,^{26–28} we do not elaborate on them here.

The strengths of this study include relatively high participation rates, collection of detailed lifetime information on different types of tobacco products using a validated questionnaire,⁴⁹ and adjustments for several potential confounders. We were also able to investigate the association between water-pipe use and HD among never cigarette smokers. On the other hand, although this study, with approximately 3000 HD cases and 47 000 controls, represents the largest published study on the association between water-pipe smoking and HD, the number of water-pipe users among HD cases was relatively small, thus limiting the precision of the estimates. We also lacked information on blood cholesterol levels. Cigarette smoking may cause IHD by lowering high density lipoprotein cholesterol or by exacerbating the effects of low density lipoprotein cholesterol.^{50–52} However, cholesterol level would be a mediator not a confounder; as blood cholesterol levels are unlikely to modulate the prevalence of water-pipe smoking, any spurious association between water-pipe use and HD as a result of confounding effect of cholesterol levels is not expected. Other potential limitations, including the cross-sectional nature of the study, self-report of outcomes, and inability to distinguish between different types of HD, have been discussed above.

In conclusion, we found a statistically significant association between heavy water-pipe smoking and HD. Although this

association was based on a modest number of water-pipe users, similarity in the constituents and biological consequences of water-pipe and cigarette smoke provide plausibility. However, the observed association needs to be replicated in other populations. Future studies are also needed to evaluate the associations of water-pipe use, cancer, and other diseases. The growing body of evidence linking water-pipe smoking to chronic disease, coupled with a worldwide increase in prevalence of water-pipe use in young people, is of particular public health concern and may warrant prevention and control measures.

Key messages

We found a statistically significant association between water-pipe smoking and ischaemic heart disease. Future studies are also needed to evaluate the associations of water-pipe use, cancer and other diseases. The growing body of evidence linking water-pipe smoking with chronic disease and increasing prevalence of water-pipe use among young people are of particular public health concern and may warrant prevention and control measures.

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