

Original Article



Smoking Water-Pipe, Opium Use and Prevalence of Heart Disease: A Cross-sectional Analysis of Baseline Data from the Pars Cohort Study, Southern Iran

Ali Adib, MD¹; Seyed Masoom Masoompour, MD²; Hossein Molavi Vardanjani, PhD, MD³; Abdullah Gondomkar, MD²; Hossein Poustchi, MD⁴; Alireza Salehi, MD²; Farhad Islami, MD⁵; Reza Malekzadeh, MD^{2,4}

¹Student Research Committee, Shiraz University of Medical Sciences, Shiraz, Iran

²Non-Communicable Diseases Research Center, Shiraz University of Medical Sciences, Shiraz, Iran

³School of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran

⁴Liver, Pancreatic, and Biliary Diseases Research Center, Digestive Disease Research Institute, Tehran University of Medical Sciences, Tehran, Iran

⁵Surveillance and Health Services Research, American Cancer Society, Atlanta, GA, USA

Abstract

Background: Associations between hookah and opium use and an increased risk of ischemic heart disease (IHD) have been suggested in a few studies, but more research is needed on the nature of these associations. We aimed to investigate the association between hookah and opium use and the prevalence of IHD in a population with relatively high prevalence of these exposures in Iran.

Methods: Using baseline data from the Pars Cohort Study (PCS), a prospective study of individuals aged 40-75 years in Fars province, southern Iran, we calculated adjusted and crude odds ratios (ORs) and corresponding 95% confidence intervals (CIs) for the independent association of hookah and opium use with prevalence of IHD.

Results: Of 9248 participants, 10.2% (95% CI: 9.5, 10.9) had self-reported IHD. Prevalence of ever use of hookah and opium was 48.9% (95% CI: 44.6, 53.6) and 10.2% (95% CI: 8.3, 12.5) among those with IHD, and 37.0% (95% CI: 35.7, 38.3) and 8.1% (95% CI: 7.5, 8.7) among those without IHD, respectively. Adjusted OR for the association with prevalence of IHD was 1.26 (95% CI: 1.08, 1.46) for hookah use and 1.71 (95% CI: 1.30, 2.24) for opium abuse. No dose-response association was found between hookah and prevalence of IHD.

Conclusion: Hookah and opium abuse were associated with prevalent IHD in this study. Although more research is needed on these associations, particularly in prospective settings, reducing hookah and opium use could potentially reduce IHD risk.

Keywords: Hookah smoking, Ischemic heart disease, Opium use

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Introduction

Ischemic heart disease (IHD) is one of the leading causes of years of life lost worldwide.^{1,2} According to the Global Burden of Disease 2016, total deaths from IHD have increased by 19.0% during the recent years (rising from 7.96 million deaths in 2006 to 9.48 million deaths in 2016).³ Although IHD deaths rates have been declining during the past three decades in most parts of the world, especially in high-income countries, they remain high in some other regions, including the Middle East.⁴ As such, IHD is the first cause of years of life lost in Iran.⁵

Hookah, also known as water-pipe, *shisha* and *ghalyan*, is a tobacco consumption device⁶ that has been historically common in Asia (particularly in the Middle East) and North Africa, but recently, its use has been increasing among youth worldwide.⁷⁻⁹ Hookah users are exposed to many carcinogenic compounds that cigarette smokers

are¹⁰; thus, similar to cigarette smokers, they may be at higher risk of IHD.^{6,11} Opium is one of the most commonly used illicit substances in Iran.^{12,13} A few earlier studies have suggested that opium use could be a risk factor for heart disease.^{14,15}

However, still more research is needed on the nature of the associations between hookah and opium use and IHD. The aim of this cross-sectional study is to investigate the association between these habits and prevalent IHD in Iran.

Materials and Methods

Study Design and Setting

For this analysis, we used baseline data from the Pars Cohort Study (PCS). The study design and protocol of PCS are described elsewhere.¹⁶ In brief, PCS is a prospective study launched in 2012 to investigate the epidemiology and

risk factors of non-communicable diseases in Valashahr district, a mostly rural setting located in Fars province, southern Iran. A total of 9721 (or almost all) Valashahr inhabitants aged 40–75 were invited and 9264 agreed to participate in PCS.¹⁶ The number of participants included in this analysis was 9248, as we omitted 16 participants due to missing data.

Data Collection

Using a structured questionnaire, trained staff interviewed participants at the PCS center located in Valashahr to collect data on demographic characteristics, several indicator of socioeconomic status (SES), tobacco and opium use, and medical history. Participants had been asked to bring their medication to the PCS center; information on the medications was collected during interviews. Anthropometric indices and blood pressure were measured using calibrated equipment, and fasting blood samples were obtained from all participants.

Self-reported history of IHD was the outcome of interest in this study. The participants were considered to have IHD if they answered yes to the question “have you been diagnosed by a physician to have angina, infarction, or heart failure?” Participants who reported only a history of congenital heart disease were not included in the group of individuals with a history of IHD.

Data on hookah use were collected for “average number of episodes of use per day”, “number of days (per week) in which hookah was use”, and “overall duration of exposure to hookah (from the first use to the time of interview or the date of cessation; in months/years)”. Hookah users were defined as participants who reported using hookah at least once a week for a period of 6 months or more. Cumulative amount of hookah use was calculated in hookah-years by multiplying the average number of episodes of hookah use per day by total years of use.

Methods for reliable measurement of opium use and patterns of use in this populations have been described elsewhere.¹⁷ In this study, we analyzed the overall amount of opium used in *nokhods* (a local unit for opium use that equals 0.195 g) and overall duration of opium use (from the first use to the date of interview or the date of cessation; in months/years). Cigarette smokers were those who had used cigarette for a period of six months or more. Cumulative use of cigarettes was calculated in pack-years.

Body mass index (BMI, in kg/m²) was calculated and categorized according to the World Health Organization (WHO) recommendation: underweight (<18.5), normal (18.5–24.9), overweight (25–29.9), obese I (30–34.9), obese II (35–39.9), and obese III (>40). Waist to hip ratios (WHR), as an indicator of abdominal obesity, were calculated and categorized into its tertiles. Data on physical activity were collected and metabolic equivalent of task (MET) scores were calculated for each participant (18). Participants were categorized into tertiles of the

MET score.

Participants were considered hypertensive if they reported previously diagnosed hypertension by a physician, or were on anti-hypertensive drugs, or had a systolic blood pressure of ≥ 140 mm Hg or diastolic blood pressure of ≥ 90 mm Hg at the interview. Participants with diabetes mellitus in this study were those previously diagnosed with diabetes by a physician, or those who were on diabetes mellitus medicines, or had fasting blood sugar levels of ≥ 126 mg/dL in samples obtained at the interview. The following cutoffs (in mg/dL) were used to define abnormal laboratory tests: triglyceride, ≥ 200 ; low-density lipoprotein (LDL), ≥ 160 ; high-density lipoprotein (HDL), ≤ 40 ; and total cholesterol, ≥ 240 .¹⁹

Using multiple correspondence analysis, we calculated asset-based wealth index, a composite score indicating relative SES of each participant based on self-reported assets and appliances owned by participants including house, car, motorcycle, color or black/white TV, bath in home, vacuum, washing machine, refrigerator, freezer, computer, and microwave device. Participants were categorized into three SES subgroups including low SES, moderate SES, and high SES, according to the tertiles of the wealth index.

Statistical Analysis

We provided mean and standard deviation (SD) for quantitative variables and frequencies and relative frequencies for qualitative variables by IHD status. For reported prevalence, we estimated 95% confidence intervals (CIs) applying binomial distributions. To compare the distribution of the included variables between participants with and without IHD, we used Chi-square and Fisher's exact tests for categorical variables and t-test and Mann-Whitney U test for continuous variables. We used logistic regression to estimate odds ratios (ORs) and corresponding 95% CIs. In multivariable analyses, we included variables with a *P* value of ≤ 0.2 in univariate analysis. At first, a saturated model was fitted, and then all candidate variables except main exposures were selected in the model by applying a backward elimination procedure. Accordingly, the model was reduced to the best of available models according to the Akaike information criterion (AIC) and the Bayesian information criterion (BIC) goodness-of-fit indices. We also checked for any statistically significant interaction between hookah use and cigarette smoking, but no significant interaction was observed. Two-sided *P*-values ≤ 0.05 were considered statistically significant. All statistical analyses were done using Stata software, version 11 (Stata Corporation, College Station, TX, USA).

Results

Of 9248 individuals included in this study, 946 (10.2%, 95% CI 9.6%–10.9%) had self-reported IHD. The mean

age of participants with IHD (58.7; SD, 9.7 years) was higher than those without IHD (51.9; SD, 9.4 years) ($P < 0.001$). Approximately 46% of total participants and 42% of IHD participants were male (Table 1). The participants were mostly from two major ethnic groups, Fars and Turk. The majority of IHD participants (66.1%, 95% CI 61.0%–71.5%) were illiterate while this prevalence rate was 47.1% (95% CI 45.6%–48.6%) for non-IHD participants.

Overall, 38.3% and 8.3% of the participants reported ever use of hookah and opium, respectively. DM (23.1%, 95% CI: 20.1–26.4), depression (32.03%, 95% CI: 28.5–35.8), and anxiety (44.8, 95% CI: 40.6–49.2) were significantly more prevalent among IHD patients than non-IHD participants (Table 2).

There was no significant difference between prevalence of abnormal LDL in IHD (7.3 %, 95% CI: 5.6–9.2) and non-IHD participants (6.04%, 95% CI: 5.5–6.5). Abnormal TG (25.6%, 95% CI: 22.5–29.1) and HDL (8.5 %, 95% CI: 6.8-10.6) were more prevalent among IHD patients compared with non-IHD participants (Table 3).

In multivariate analysis, both ever hookah use (OR 1.26; 95% CI 1.08–1.46 vs. never hookah use) and ever opium use (OR 1.71; 95% CI 1.30–2.24 vs. never use) were associated with IHD (Table 4).

No association was found between cumulative use of hookah and prevalence of IHD in multivariate analysis (OR 1; 95% CI 0.99-1.001 for hookah year among ever users and OR 0.99; 95% CI 0.98–1.006 for years of

hookah use among ever users).

Discussion

We found a statistically significant association between hookah and opium use and prevalence of IHD.

Ever use of hookah in our study was associated with 1.3-fold higher odds of having IHD. In a case-control study on the association between hookah use and coronary artery disease confirmed by coronary angiography, the risk of having severe stenosis (>70%) in coronary arteries was 3-times higher in those with a lifetime exposure exceeding 40 hookah-years than non-users.²⁰ In a cross-sectional study in Golestan Province in northern Iran, heavy hookah users (100–180 hookah-year) were at about 4-fold higher odds of having prevalent IHD compared to non-smokers.²¹ However, they found no association between ever use of hookah and IHD, probably due to low prevalence of hookah use (1.1% vs. 38.2% in our study) and moderate intensity of use in that population. We did not find any association between cumulative use of hookah and prevalence of IHD in the multivariable analysis. This might be due to various factors. Heavy hookah users may be more likely to die prematurely from respiratory diseases or other conditions related to tobacco smoking, including IHD, and those cases would be unaccounted for in cross-sectional studies. Moreover, heavy hookah users may underreport the amount or duration of hookah use. However, lack of dose-response analysis may also suggest that the association between ever hookah use and IHD in this study is spurious, although given the similarities

Table 1. Demographic and Background Data of Participants

Characteristics	Total Participants	Participants without IHD	Participants with IHD	P Value
Total	9248 (100)	8302 (100)	946 (100)	
Age, mean (SD) in years	52.6 (9.7)	52.0 (9.4)	58.7 (9.8)	<0.001
Gender				0.008
Male	4269 (46.2)	3871 (46.6)	398 (42.1)	
Female	4979 (53.8)	4431 (53.4)	548 (57.9)	
Marital status				<0.001
Not-married	1048 (11.34)	904 (10.9)	144 (15.2)	
Married	8197 (88.66)	7396 (89.1)	801 (84.8)	
Ethnicity				0.035
Fars	5210 (56.3)	4650 (56.0)	560 (59.2)	
Turk	3587 (38.8)	3255 (39.2)	332 (35.1)	
Other minorities	451 (4.9)	397 (4.8)	54 (5.7)	
Education level				<0.001
No formal education	4532 (49.0)	3907 (47.1)	625 (66.1)	
≤5 years	2723 (29.5)	2541 (30.6)	182 (19.3)	
6–8 years	973 (10.5)	912 (11.0)	61 (6.5)	
High school	732 (7.9)	674 (8.1)	58 (6.1)	
University	281 (3.0)	262 (3.2)	19 (2.0)	
Socioeconomic status				0.33
Low	3230 (34.9)	2906 (35.0)	324 (34.3)	
Medium	2936 (31.8)	2616 (31.5)	320 (33.8)	
High	3082 (33.3)	2780 (33.5)	302 (31.9)	

SD, standard deviation; IHD, ischemic heart disease.

Numbers in parentheses represents column percentages except for age.

Table 2. Non-demographic Characteristics of the Study Participants by IHD Status

Characteristics	Total Participants	Non-IHD	IHD	P Value
Total	9248	8302 (100)	946 (100)	
Hookah use				<0.001
Ever use (%)	3534 (38.3, 37.0–39.6)	3072 (37.1, 35.7–38.3)	462 (49.0, 44.5–53.5)	
Never use (%)	5698 (61.7)	5217 (62.9)	484 (51.0)	
Hookah year (among ever users, Mean ± SD)	52.9 ± 89.4	51.5 ± 90.1	62.4 ± 84.2	0.01
Duration of hookah use (years among ever users, Mean ± SD)	19.7 ± 14.9	19.3 ± 14.8	22.4 ± 15.4	<0.001
Opium use				0.02
Ever use (%)	773 (8.4, 7.8–9.0)	676 (8.1, 7.5–8.7)	97 (10.3, 8.3–12.5)	
Never use (%)	8475 (91.6)	7626 (91.9)	849 (89.7)	
Total used <i>nokhod</i> (among ever users, Mean ± SD)	24894.4 ± 42083.4	23946.6 ± 39285	31468.3 ± 57740.3	0.1
Duration of opium use (years among ever users, Mean ± SD)	14.1 ± 11.3	14.0 ± 11.3	14.7 ± 11.2	0.5
Cigarette smoking				0.7
Ever use (%)	1912 (20.7, 19.8–21.6)	1712 (20.6, 19.6–21.6)	200 (21.1, 18.3–24.2)	
Never use (%)	7336 (79.3)	6590 (79.4)	746 (78.9)	
Pack-year (among ever users, Mean ± SD)	23.6 ± 21	23.3 ± 21.1	26.2 ± 20	0.07
Duration of cigarette use (years among ever users, Mean ± SD)	25.4 ± 13.6	25.1 ± 13.4	28.0 ± 14.8	0.004
Physical activity status				<0.001
Low (%)	3056 (33.0, 31.9–34.2)	2627 (31.6, 30.4–32.8)	429 (45.3, 41.1–49.8)	
Medium (%)	3049 (33.0, 31.8–34.2)	2751 (33.1, 31.9–34.3)	298 (31.5, 28.0–35.2)	
High (%)	3143 (34.0, 32.8–35.2)	2924 (35.2, 33.9–36.5)	219 (23.2, 20.1–26.4)	
History of OCP use				0.03
Yes (%)	2681 (53.9, 51.8–55.9)	2435 (54.9, 52.7–57.1)	246 (44.9, 39.4–50.8)	
No (%)	2298 (46.1)	1996 (45.1)	302 (55.1)	
Hypertension				<0.001
Yes (%)	2763 (29.9, 28.8–31.0)	2130 (25.7, 24.5–26.7)	633 (66.9, 61.8–72.3)	
No (%)	6485 (70.1)	6172 (74.3)	313 (33.1)	
Diabetes				<0.001
Yes (%)	1199 (13.0, 12.2–13.7)	980 (11.8, 11.1–12.5)	219 (23.2, 20.1–26.4)	
No (%)	8049 (87.0)	7322 (88.2)	727 (76.8)	
History of depression				<0.001
Yes (%)	1791 (19.4, 18.5–20.3)	1488 (17.9, 17.0–18.8)	303 (32.0, 28.5–35.8)	
No (%)	7457 (80.6)	6814 (82.1)	643 (68.0)	
History of anxiety				<0.001
Yes (%)	2738 (29.6, 28.5–30.7)	2314 (27.9, 26.7–29.0)	424 (44.8, 40.6–49.2)	
No (%)	6510 (70.4)	5988 (72.1)	552 (55.2)	

SD, standard deviation; IHD, ischemic heart disease; OCP, oral contraceptives; DM, diabetes mellitus; HTN, hypertension. Numbers in parentheses represents column percentages and CIs.

between exposure to harmful compounds during hookah and cigarette use, the observed association is more likely to be real.

The mechanism of association between hookah use and IHD is likely to be similar to that for cigarette smoking, as the toxicant profiles of smoke from hookah and cigarettes have many similarities.²² Both hookah and cigarette smoke contain polycyclic aromatic hydrocarbons, volatile aldehydes, and heavy metals which have been implicated to play a role in atherosclerosis.²³ They both contain carbon monoxide that can exacerbate angina and reduce arrhythmias threshold through impairment of oxygenation.^{23,24} However, hookah may expose users to much more smoke compared to cigarettes, resulting in more toxicant exposure.¹⁰ Burning charcoal (for heating tobacco) in hookah pipe results in much greater generation of the mentioned toxicants.²⁵

We found that opium use was associated with 1.7-fold higher odds of having IHD. Opium use has been

associated with increased risk of cancers of the esophagus, stomach, larynx, lung, and urinary bladder.²⁶ In the Golestan Cohort Study, a prospective study in northern Iran, the risk of death from IHD was about twice higher among opium users than non-users.¹³ However, few other well-designed studies have investigated the association between opium use and IHD.

The mechanism of the association between opium use and IHD is unclear. In a case-control study, those with opium addiction had a decreased serum level of adiponectin level, which could result in insulin resistance and increased risk of CVD.²⁷ In a population-based cross-sectional study, opium addiction was a predictor for hyperhomocysteinemia, which may accelerate the atherosclerosis process.²⁸

In this population, those with higher SES had higher odds of having prevalent IHD, consistent with the 'third stage' of epidemiologic transition of cardiovascular diseases.²⁹ Improvement in socioeconomic status and

Table 3. Anthropometric and Laboratory Characteristics of the Participants by IHD Status

Characteristics	Total Participants (% , 95% CI)	Non-IHD (% , 95% CI)	IHD (% , 95% CI)	P Value
Total	9248	8302 (100)	946 (100)	
Body mass index				0.001
<18.5 kg/m ²	384 (4.2, 3.7–4.6)	346 (4.2, 3.7–4.6)	38 (4.0, 2.8–5.5)	
18.5–24.9	3712 (40.1, 38.9–41.4)	3390 (40.8, 39.4–42.2)	322 (34.0, 30.4–37.9)	
25–29.9	3436 (37.1, 35.9–38.4)	3064 (36.9, 35.6–38.2)	372 (39.3, 35.4–43.5)	
30–34.9	1367 (14.8, 14.0–15.6)	1200 (14.5, 13.6–15.2)	167 (17.7, 15.1–20.5)	
35–39.9	251 (2.7, 2.4–3.1)	217 (2.6, 2.2–2.9)	34 (3.6, 2.4–5.0)	
≥40	98 (1.0, 0.9–1.3)	85 (1.0, 0.8–1.2)	13 (1.4, 0.7–2.3)	
Waist to hip ratio				<0.001
Low	3068 (33.3, 32.2–34.5)	2880 (34.9, 33.6–36.1)	188 (20.0, 17.2–23.0)	
Moderate	3067 (33.3, 32.2–34.5)	2791 (33.8, 32.5–35.1)	276 (29.3, 25.9–33)	
High	3067 (33.3, 32.2–34.5)	2590 (31.3, 30.1–32.5)	477 (50.7, 46.2–55.4)	
Weight to height ratio				<0.001
Low	3069 (33.3, 32.2–34.5)	2864 (34.7, 33.4–35.9)	205 (21.8, 18.9–24.9)	
Moderate	3070 (33.4, 32.2–34.5)	2739 (33.1, 31.9–34.4)	331 (35.2, 31.4–39.1)	
High	3063 (33.3, 32.1–34.5)	2658 (32.2, 30.9–33.4)	405 (43.0, 38.9–47.4)	
Triglycerides				<0.001
≥200 mg/dL	1950 (21.1, 20.2–22.1)	1708 (20.6, 19.6–21.6)	242 (25.7, 22.5–29.1)	
<200	7284 (78.9)	6583 (79.4)	701 (74.3)	
Total cholesterol				0.053
≥240 mg/dL	1214 (13.1, 12.4–13.9)	1071 (12.9, 12.1–13.7)	143 (15.2, 12.7–17.8)	
<240	8020 (86.9)	7220 (87.1)	800 (84.8)	
LDL				0.1
≥160 mg/dL	570 (6.2, 5.7–6.7)	501 (6.0, 5.5–6.5)	69 (7.3, 5.6–9.2)	
<160	8664 (93.8)	7790 (94.0)	874 (92.7)	
HDL				0.04
≤40 mg/dL	646 (7.0, 6.5–7.6)	565 (6.81)	81 (8.6, 6.8–10.6)	
>40	8588 (93.0)	7726 (93.19)	862 (91.4)	
Fasting blood sugar				<0.001
≥126 mg/dL	804 (8.7, 8.1–9.3)	655 (7.89)	149 (15.8, 13.3–18.4)	
<126	8444 (91.3)	7647 (92.11)	797 (84.2)	

IHD, ischemic heart disease; LDL, low density lipoprotein; HDL, high density lipoprotein. Numbers in parentheses represents column percentages and CIs.

urbanization in certain stages can result in reduced physical activity and an increase in unhealthy diet (e.g., fast foods) and social stress. As all people in our study population were covered by universal health insurance, the higher prevalence of IHD in higher SES groups is unlikely to be entirely related to longer survival due to having better access to care. As expected, IHD was associated with well-established IHD risk factors in our study. The observed association between anxiety and depression and IHD may not be causal, as people may be more likely to have stress after being diagnosed with IHD. More research is needed on the nature of these associations.

Collection of detailed data on hookah and opium use and other risk factors of IHD, measurement of anthropometric indices and blood pressure by trained staff, and of fasting

blood sugar and lipids by laboratory tests are among the strengths of this study. On the other hand, the diagnosis of IHD and data on hookah and opium use were based on self-reports. However, an earlier study showed acceptable reliability and validity for self-reports of opium by comparing self-reports with urine codeine and morphine in a similar setting in northern Iran.³⁰ Further, cross-sectional studies may provide preliminary evidence for a causal association but they cannot prove it. Observing a non-significant dose-response association between cigarette smoking and the IHD prevalence may be also due to the cross-sectional nature of our data. Accordingly, we may interpret that there is no dose-response association between cigarette smoking and being an IHD patient. In other words, it is probable that IHD patients who smoke

Table 4. Associations between Evaluated Factors and Ischemic Heart Disease Prevalence

Characteristics	Unadjusted OR (95% CIs)	Adjusted OR (95% CIs)*
Ever use of Hookah	1.63 (1.42–1.86)	1.26 (1.08–1.46)
Ever use of Opium	1.28 (1.02–1.61)	1.71 (1.30–2.24)
Age, 10-year increments	1.89 (1.77–2.01)	1.51 (1.39–1.64)
Educational level		
No formal education	Reference	Reference
Up to 8 years	0.43 (0.37–0.51)	0.74 (0.61–0.89)
High school or university	0.51 (0.40–0.65)	0.86 (0.63–1.10)
Socioeconomic status		
Low	Reference	Reference
Medium	1.09 (0.93–1.29)	1.24 (1.03–1.48)
High	0.97 (0.82–1.14)	1.29 (1.06–1.57)
Physical activity		
Low	Reference	Reference
Medium	0.66 (0.56–0.77)	0.87 (0.74–1.04)
High	0.45 (0.38–0.54)	0.78 (0.65–0.95)
Ever use of cigarette	1.04 (0.88–1.2)	1.44 (1.17–1.77)
Waist to hip ratio		
Low	Reference	Reference
Medium	1.51 (1.24–1.83)	1.20 (0.97–1.47)
High	2.82 (2.36–3.36)	1.54 (1.27–1.88)
History of hypertension	5.86 (5.07–6.76)	4.09 (3.49–4.78)
History of diabetes mellitus	2.25 (1.90–2.65)	1.29 (1.07–1.56)
History of Anxiety	2.10 (1.83–2.41)	1.63 (1.38–1.94)
History of depression	2.15 (1.86–2.50)	1.48 (1.23–1.78)
HDL (≤ 40 vs. >40 mg/dL)	1.28 (1.007–1.63)	1.33 (1.01–1.74)

CIs, confidence intervals; OR, odds ratio; HTN, hypertension; HDL, high density lipoprotein.

* Adjusted for all variables included in this table.

cigarette more than others did not survive or the patients quit or reduced their cigarette use after being diagnosed with the disease.

In conclusion, hookah and opium use were associated with prevalence of IHD in our study. It seems more research is needed on the nature of these associations, and whether reducing hookah and opium use can potentially improve population health.

Authors' Contribution

Study concept and design: SMM, HMV, RM; acquisition of data: AG, HP; analysis and interpretation of data: AA, SMM, HMV; drafting of the manuscript: AA, SMM, HMV, AS, FI; critical revision of the manuscript for important intellectual content: AA, SMM, HMV, AG, HP, AS, FI, RM; statistical analysis: AA, SMM, HMV; administrative, technical, and material support: AG, HP, RM; study supervision: RM, FI, SMM.

Conflict of Interest Disclosures

The authors declare that they do not have any conflict of interest.

Ethical Statement

This study was approved by the ethics committees of Shiraz University of Medical Sciences (Approval code# IR.sums.med.rec.1397.s35) and was performed in accordance with Declaration of Helsinki. All participants signed written informed consent.

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