RESEARCH COMMUNICATION

Hookah Smoking and Lung Cancer in the Kashmir Valley of the Indian Subcontinent

Parvaiz A Koul[1*], Mubashir R Hajni[1], Mushtaq A Sheikh[1], Umar H Khan[1], Azra Shah[2], Yasmin Khan[3], A G Ahangar[4], Reyaz A Tasleem[5]

Abstract

Background: The literature about the causal relationship between lung cancer and tobacco smoking mostly concerns cigarettes. Hookah smoking is popular in the Kashmir valley of the Indian subcontinent, and is generally believed to be innocuous because of the passage of the smoke through water before inhalation. Objective: To determine the relationship of hookah smoking to lung cancer in Kashmir. Materials and Methods: In a case-control design, 251 cases of lung cancer and 500 age-matched controls were studied. A predefined questionnaire was administered through a personal interview regarding various smoking and dietary patterns and the results compared through statistical analyses. Results: There were 194 (178 current) ever-smokers amongst the cases and 223 (134 current) amongst controls. Smokers had a 4.2 times risk of lung cancer compared to non smokers (OR 4.23, 95% CI 3.0-5.96, p<0.0001). There were 120 hookah smokers amongst the cases and 100 amongst the controls and hookah smokers were nearly six times at risk for lung cancer as compared to nonsmokers (OR 5.83, (95% CI 3.95-8.60, p< 0.0001). Cigarette smokers were commoner amongst cases (46 vs 64 in controls; OR 3.49, 95% CI 2.18-5.60, p=0.000). The severity of smoking was associated with a higher risk of lung cancer (Chi-square 72.09, p 0.000).The practice of changing water of the hookah after each session proved non-existent. Conclusion: Hookah smoking is associated with a significantly higher risk for lung cancer in Kashmiri population, with about 6 fold elevated risk as compared to non-smoking controls.

Keywords: Tobacco - smoking - cancer - lung - Hookah - water-pipe

Asian Pacific J Cancer Prev, **12**, 519-524

Introduction

Hookah (water pipes) has been used by the indigenous African and Asians for smoking tobacco for nearly 400 years (Chattopadhyay, 2000). In other areas it is also known as as 'shisha', and 'narghile' and on account of their pertinence and relevance a South African, Ethiopian, Persian or even a European origin has been ascribed to the water pipe. It has been claimed that >100 million people worldwide smoke water pipes daily (Wolfram et al., 2003; Anonymous, 2010). It is a common practice in the Arabian Peninsula, Turkey, India, Pakistan, Bangladesh, and some regions of China, being more prevalent than cigarette smoking in certain areas. Among Arab women in many countries, there is less of a stigma associated with narghile than with cigarette smoking and therefore less of a gender differential (Kandela 2000; Tamim et al., 2003; Maziak et al., 2004; Maziak et al., 2004). Hookah parlors have gained popularity in recent years in the West and the Eastern Mediterranean region, (Kulwicki et al., 2003; Maziak et al., 2004) and India (Ray, 2009), especially amongst the youth and university students (Harel et al., 2004; Rastam et al., 2004; Taha et al., 2010). Hookah tobacco is available in a variety of flavors, such as apple, mint, and cappuccino, and is typically practiced in groups with the same mouthpiece passed from person to person.

Hookah smoking by a large majority is perceived to be a rather innocuous form of smoking tobacco (Shihadeh et al., 2004; Ward et al., 2006; Jackkson et al., 2008; Primack et al., 2008) because the smoke gets filtered through water before inhalation (Kandela 2000; Kiter et al., 2000). Scientific facts about the effects of hookah are controversial. Some investigators have reported that when compared to cigarette smoking, the number of puffs and volume from using hookahs are about ten times higher than cigarettes (Shihadeh et al., 2003; Shihadeh, 2004). Hookah smoke is reported to contain 36 times the amount of nicotine and a higher concentrations of heavy metals (Shihadeh et al., 2003; Shihadeh, 2004) and the burning temperature of tobacco for hookah use is about 900°, compared to 450° for cigarettes, which could produce different type and levels of harmful chemicals and tar (Shihadeh, 2004). Further, exhaled CO levels from hookah users were reported twice as high as cigarette smokers in cessation programs (Jackkson et al., 2008), and hookah smoke is purported to be a hazard to nonsmokers too

*[1]Internal & Pulmonary Medicine, [2]Clinical Pathology, [4]Cardiothracic & Vascular Surgery, SheriKashmir Institute of Medical Sciences, [3]Nutritional Sciences, Government College for Women, [5]Pathology, Government Medical College, Srinagar, India *For correspondence : parvaizk@gmail.com*

(Maziak et al., 2004; Steentoft et al., 2006; Maziak et al., 2008). However other investigators have underscored the fact that the smoke while it passes through the water is rendered less toxic and as such the health risks are lesser than in cigarette smoking. They also contend that the effect of the temperature and absence of side stream smoke in tobacco smoking makes it less harmful (Sajid et al., 2008).

While smoking has unequivocally been linked to the development of lung cancer, majority of the work has been relating to cigarette smoking. Epidemiologic evidence for an association between hookah smoking and lung cancer is limited. The valley of Kashmir has traditionally been a low incidence area for lung cancer but the trend is demonstrating a surge and a recent study conducted by us (Koul et al., 2010), showed that the age standardized incidence rates of lung cancer average 6.48 per 100,000 population, 10.23 amongst males and 2.14 among females with the summer capital district of Srinagar having the the highest age standardized incidence rate of 19.34 per 100,000 males in India. Hookah smoking is widely practiced in Kashmir and was found to be the commonest form of smoking amongst the patients with lung cancer. An earlier study from Kashmir also reported hookah smoking as the dominant form of smoking in a small cohort of 25 lung cancer patients (Nafae et al., 1973). The present study investigates the association between hookah smoking and lung cancer in Kashmir.

Materials and Methods

The study was conducted in the SheriKashmir Institute of Medical Sciences, Srinagar, Kashmir (India), a 650 bedded tertiary care university hospital that serves as the main referral center for the Pulmonary and Oncology cases of the Kashmir valley of the Indian subcontinent. The population is largely ethnic Muslim. Hookah smoking is the dominant form of smoking practiced by the people, even as cigarettes having gained popularity especially amongst the youth.

Hookah (locally called 'Jajeer') in Kashmir (Figure 1) is traditionally made of an earthern-ware water bowl or base (made in current times of tinned copper or brass with exquisite surface carvings) that is half filled with water and connects to a separable earthenware head (or Chillam) by a cane wood conduit or body, the lower end of which stays submerged in the water of the base. Another inverted J-shaped hose (termed as 'Nalcha' in local parlance) of cane wood comes out of the base and ends in the mouth piece; both pipes passing through a cloth stopper (Gatha) in the neck of the base to render the assembly air-tight. Sun dried tobacco used for smoking is mixed in a ratio of 50:50 with molasses and then sold in the form of paper cones called 'Phuttgies' of variable weight ranging from one to 2 chattakh (60-120 grams). The users store the tobacco in one of the compartments of a 2-compartment 'tobacco box', one compartment of which houses the tobacco thus procured and the other contains charcoal for use during the smoking session. The 'Chillam' is fed with this mixture and ignited with live charcoal; the smoke thus generated inhaled via the mouth piece after it has bubbled through the water in the base. The water of the main hookah base is changed at variable intervals.

The cases for the study included 251 newly diagnosed cases of histologically proved lung cancer seen during the period from June 2005 to December 2006 who were referred to SheriKashmir Institute of Medical Sciences for diagnosis, evaluation or treatment of lung cancer and agreed to be a part of the study . About 572 healthy age (± 5 years) matched controls with broad matching for the area of residence were identified as controls (generally relatives of the patients) and after exclusion of 72 subjects on various reasons, 500 controls were finally included for the study.

Predesigned questionnaire in locally understandable language was tested and validated in a cohort of 10 cases of lung cancer and 20 controls and subsequently administered to the study cases and controls. The questionnaire was administered through a personal interview with specific enquiry about social and demographic background, history of smoking, current smoking status, pack years of smoking, amount of smoking, specific history about the pattern (hookah, cigarettes, mixed), average amount of tobacco smoked, water change habit, etc. Additionally a food frequency questionnaire was administered to the study participants (modified National Cancer Institute Habits and History Questionnaire) to collect dietary data. The questionnaire contains semi-quantitative food frequency list made up of foods and beverages, ethnic foods commonly consumed in Kashmir, an open ended section and other dietary behaviors like dining at restaurants and food preparation methods. Study participants were interviewed about their diet during the year prior to diagnosis (cases) and the year prior to enrollment into the study (controls). The hookah smokers was classified into light (upto 30 gms of tobacco/molasses mixture per day, the equivalent of 15 gms of tobacco or 15 cigarettes of 1 gms), medium (30-60 g per day, equivalent of 15-30 gms of tobacco or 16-30 cigarettes) and heavy (>60 g per day). All analyses were performed using SPSS software. Categorical variables were analyzed by using Pearson's X^2 test whereas continuous variables were tested by student's t-test. Wilcoxon's rank test was used to test for differences in smoking. Odds ratio and 95% confidence intervals (CIs) were calculated as an estimate of the relative risk using logistic regression

The study was approved by the Institute Postgraduate and Ethics study and informed consent was obtained for all participants in the study. Results have been expressed as mean + SD, and a p-value of <0.05 was considered significant.

Results

The cases included 209 males and 42 females whereas the controls included 328 male and 72 female subjects. The mean age in males was 58.4 years and in females 56.51 years. Seventy seven percent of the cases and 44.6% of the controls were ever smokers. Table 1 shows distribution of the smoking patterns in the cases and the controls. Smoking was strongly associated with the presence of lung cancer, with 194 cases being ever smokers (178 current smokers, 16 ex smokers) as compared to 173 controls

Figure 1. Figure showing a traditional Kashmiri hookah. The small willow pot in the corner is a fire pot called 'Kangri' and the metal box is the tobacco box that houses the charcoal and the tobacco-molasses mixture for use in the session. Tongs generally dangle from the head [chillam] for picking the live charcoal

Table 1. Smoking Patterns Amongst the Cases and Controls and Odds Ratios for Lung Cancer

Smoking status	Cases N(%)	Controls N(%)	Odds Ratio	p-value
Ever Smoker	194 (77)	223 (45)	4.23 (3.0-5.96)	<0.0001
Current Smoker	178 (71)	134 (27)	6.45 (4.49-9.27)	<0.0001
Exclusive Cigarette Smoking	46 (18)	64 (13)	3.49 (2.18-5.6)	<0.0001
Exclusive Hookah Smoking	120 (48)	100 (20)	5.83 (3.95-8.60)	<0.001
Combined	28 (11)	59 (12)	2.31 (1.36-3.92)	0.003
Nonsmoker	57 (23)	277 (56)	-	-

Table 2. The Severity of Smoking Amongst the Cases and the Controls

Grades of smoking	Cases N(%)	Controls N(%)
Light	48 (19.1)	145 (29)
Medium	109 (43.4)	68 (13.6)
Heavy	37 (14.7)	10 (2.0)

Chi square, 72.09; p=0.0000

Table 3. Comparison of the Dietary Intake in the Study and Control Group

Food	Cases N(%) Mean + SD (range)	Controls N(%) Mean + SD (range)	p
Protein (g)	50.3±6.2 (37-66)	51.2±8.6 (33-68)	0.26
Fat (g)	22.5±3.5 (15-30)	23.1±4.3 (15-30)	0.23
Carbohydrate (g)	380.5±50.5 (260-510)	386±73.2 (250-520)	0.40
Total Caloric Intake (Kcal)	2300±266.2 (1600-2850)	2359.2±365.7 (1800-3200)	0.11
Vitamin A (IU)	2131.3±276.8 (1600-2610)	2172.2±193.2 (1850-2500)	0.09
Vitamin C (mg)	35.6±4.1 (27-45)	36.1±4.3 (23-45)	0.24

(94 current, 78 ex smokers); the lung cancer rate being 51.5% % in smokers and 17.1% in non smokers (OR 3.93, 95% confidence limits 2.70 to 5.73, p<0.0001). Current smokers thus had a 6.5 times risk of having lung cancer when compared to non smokers (Table 1).

When smoking patterns were specifically analyzed, hookah smoking was the commonest pattern of smoking either exclusively or with cigarettes. The lung cancer cases included 120 exclusive hookah smokers, 46 cigarette smokers whereas 28 smoked both cigarettes and hookah. One patient had a history of snuff abuse. Amongst the controls 100 were exclusive Hookah smokers, 64 smoked cigarettes exclusively whereas 59 (11.3% had a history of smoking both cigarettes as well as hookah). Exclusive hookah smokers were about 6 times more likely to have associated lung cancer as compared to non-smokers (OR 5.8, 95% confidence limits 3.9 to 8.6, p <0.0001). The duration of smoking was significantly associated with the risk of lung cancer (p < 0.0001), the mean duration of smoking being 31.2 ± 10.06 (0-46 years) years in cases and 20.3 ± 13.6 years (range 0-42 yrs) in controls. When graded according to the severity of smoking, heavy smokers had a higher risk of lung cancer (Table 2). Nearly 50% of the cases were moderate to heavy smokers compared to 15% of the controls (p=0.001). Sixty-three (50%) of the exclusive hookah smoking cases were heavy smokers as compared to 22% (n=22) controls with an OR of 13.7 (95%CI 7.8-23.98, p=0.000) of having associated lung cancer as compared to non smokers.

The water of the base was changed variously that ranged from every day to once a week (mean 2.71 ± 1.72 days in cases versus 2.81 ± 1.72 days, p=0.67). None of the participants changed the water after every session, with 89% of the cases and 76% of the controls changing water after more than 48 hours. There was no statistical difference in the water changing habit of cases and controls and the frequency of changing water was not associated with any increased risk of lung cancer. The various histological subtypes of lung cancer included squamous cell carcinoma (n=180), small cell type (n=53), adenocarcinoma (n=14) and others (n=4). Exposure to wood and fossil fuel (biomass fuels) was similar amongst the cases and the controls. All of the non smoking females had a history of exposure to biomass fuels.

Dietary intake in the cases and controls was similar with regard to total calorie, protein, fat, carbohydrate, vitamin A and vitamin C consumption as depicted in table 3. One patient and six control subjects had a history of lung cancer in the family (p = 0.3). No statistically significant difference was observed between the cases with regard to a past history of lung disease (p=0.16) and any nutrient deficiency (p=0.20, Table 3).

No statistically significant difference was observed in the distribution of the occupation of the patients and controls and the domicile was uniformly distributed amongst rural and urban.

Discussion

Our hospital based study provides evidence that hookah smoking is associated with an increased risk of lung cancer in ethnic Kashmiri population with the risk being 6 times more as compared to non smokers. The study reaffirms the previous report by by Nafae et al in the sixties who found hookah smoking as the commonest form of smoking in a cohort of 25 patients of lung cancer, seen in 20 of the 25, being exclusive in 17.

Hookah smoking has since the olden times been the major form of smoking in Kashmir and is nearly the exclusive form of smoking in women (all of our female smokers had a history of hookah smoking). However the smoking trends in teenage females is more of cigarettes which might post health effects over time. The health effects of hookah smoking have been conflicting with different researchers having varied points of view. While many investigators contend that waterpipe smoking may expose a smoker to a greater volume of smoke over a prolonged period of smoking simply because a typical session lasts much longer. It has been estimated that a hookah smoker in a typical session lasting 20 to 80 minutes may smoke as much smoke in one session as a cigarette smoker would inhale consuming 100 or more cigarettes (WHO 2005).

The composition of the tobacco used in water pipe smoking is variable and not well standardized. There is evidence that smoke emerging from water pipe contains numerous toxicants known to cause cancer, heart and other diseases (Knishkowy and Amitai, 2005), and has addictive potential because of the delivery of nicotine (Maziak et al., 2004). The nicotine content of water-pipe tobacco has been reported to be 2% to 4%, in comparison with 1% to 3% for cigarettes (Kiter et al., 2000). A study of carbon monoxide in water-pipe and cigarette smoke found carbon monoxide concentrations of 0.34% to 1.40% for water-pipe smoke and 0.41% for cigarette smoke. The carbon monoxide concentration in water-pipe smoke was significantly greater for smaller water-pipe size and for commercial as opposed to domestic charcoal (Sajid et al., 1993). Still another study found elevated end-expiratory carbon monoxide levels in a group of 18 healthy Jordanian water-pipe smokers (Shafagoj et al., 2002). In a separate report, the carboxyhemoglobin concentration was measured in 1832 healthy Saudi Arabian male volunteers after smoking for 10 to 40 minutes. The mean carboxyhemoglobin concentrations were higher among water-pipe smokers (10.1%) than among cigarette smokers (6.5%) or nonsmokers (1.6%), and a linear relationship was found between smoking intensity and carboxyhemoglobin concentration (Zahran et al., 1985). The mean plasma concentration of nicotine in water-pipe smokers after a single 45-minute session of smoking rose from 1.11 to 60.31 ng/mL, and that of cotinine rose from 0.79 to 51.95 ng/mL. Salivary nicotine concentration also rose from 1.05 to 624.74 ng/mL, and salivary cotinine rose from 0.79 to 283.49 ng/mL (Shafagoj et al., 2004). The mean 24 excretion of nicotine and cotinine were 73.59 μg and 249 μg, respectively after the smoking session (Shafagoj et al., 2004). According to another report, urinary cotinine concentrations were similar for water-pipe smokers (median of 2 pipes per day) and for cigarette smokers (median of 30 cigarettes per day (Macaron et al., 1997). Additionally an analysis of mainstream smoke aerosol found that narghile smoke contains significant amounts of nicotine, "tar," and heavy metals. Using a standard smoking protocol of 100 puffs of 3 seconds' duration in a single smoking session, 2.25 mg of nicotine and 242 mg of nicotine-free dry particulate matter were obtained. In addition, high levels of arsenic, chromium, and lead were found, in comparison with smoke from a single cigarette. Increasing the puff frequency increased the nicotine-free dry particulate matter, whereas removing water from the bowl increased the amount of nicotine (Shihadeh, 2003). These studies provide limited data to suggest that water-pipe smoke is at least as toxic as cigarette smoke. Water-pipe smokers may absorb higher concentrations of these substances because of higher concentrations in the smoke itself or because of the mode of smoking, including frequency of puffing, depth of inhalation, and length of smoking session. Water-pipe smokers may smoke for several hours at a time and may breathe in more deeply because of the less irritating nature of the moisturized smoke. Carbon monoxide concentration, specifically, may also be elevated because of the charcoal used to burn the narghile tobacco (Knishkowy and Amitai, 2005).

On the other side of the spectrum other investigators have rubbished the claims of various studies regarding the adverse influences of water pipe smoking. There has been a serious debate over statistics about cigarette environmental tobbaco smoke (ETS) and their interpretation (Wolfram et al., 2003). However, and in striking contrast with cigarettes, hookah does generate almost no side-stream smoke because of its peculiarities (charcoal topping the bowl and less elevated temperatures). So, the only smoke that has been suggested to be taken into account is the one rejected by the smoker, i.e. the one filtered by the hookah at the level of the bowl, inside the water, along the hose and then by the smoker's lungs themselves. Consequently, the resulting smoke is expected to be less toxic for non-smokers than cigarette side-stream smoke (Sajid et al., 2008). Besides, a great proportion of irritants, mainly aldehydes and phenols, are removed. A French study reported that the combustion gases of cigarette smoke passed through water had no inhibitory effect on the respiratory epithelium cilia (Sajid et al., 2007). Similar results were reported earlier (Guillerm et al 1961, Wynder et al., 1965). Water has been believed to act as an antioxidant against some short half life free radicals (Wynder et al., 1965). A more recent study also showed that hookah smoke is up to 3 times less concentrated than cigarette smoke as regards the particles, especially the ultrafine ones: 74.4 x10^9 for a 1000 ml hookah (machine) puff and 9.24 x 10^9 for a 45 ml cigarette "puff" (Zaga et al., 2002). There is also debate about the addiction potential of nicotine in hookah smokers with some researchers reporting that mild or moderate hookah smokers are not dependant (Monn et al., 2007) and that nicotine intake not being as high as in cigarette smokers (Salameh et al., 2008). A study on the potential health hazards associated with radioactivity in the smoking mixtures used in narghile found no differences with cigarettes (Al Mutairi et al., 2006). In the first aetiological study on exclusive hookah smoking and cancer while using CEA as a cancer biomarker, a team from Asia found a weaker association than that in cigarette smoking (Sajid et al., 2008), with only the heavy hookah smokers exhibiting substantially high CEA levels. They attributed the lower carcinogenic potential of hookah smoke in the lower temperatures that tobacco-molasses mixture attains during smoking and a

presumable filtering effect of the water in the body of the hookah base. Such a study helped in clearing up a growing confusion caused, among others, by the dismissal of early biomedical and anthropological research on the subject (Tamim et al., 2003).

Additional to the longer duration of the smoking session and eventual higher volumes of smoking, the fuel used for lighting the tobacco, generally wood charcoal, is another source of the noxious substances that get inhaled along with the flavored tobacco smoke in hookah smoking. However various forms of water pipes differ in this regard and not all forms have similar contact of the embers with the tobacco. Hookah in Kashmir is peculiar as the glowing embers are in direct contact with the tobacco in the hookah head without an intervening separator tin or silver foil as practiced by water pipe smokers in many areas of the eastern Mediterranean region. The carcinogenic potential of the smoke has been directly related to the working temperatures achieved during the smoking session (Knishokowy and Amitai, 2005) and thus Kashmiri hookah smoke could have a higher carcinogenic potential.

The habit of water changing is rather unique in our hookah smokers with a regular change of water after every session being virtually non existent. Water is changed even every week by some users and many of them attribute this habit to a 'additional special flavor' that is imparted as a result of the water through which smoke has passed many a times earlier. It is incumbent that the composition of this water is analyzed to ascertain the presence of known carcinogens and a further study is thus warranted. Even as the hookah sessions in Kashmir last only 5-10 minutes per individual per session which would result in lesser amounts of smoke being inhaled, practices of direct ember contact with tobacco and the water- changing might as well be operative in higher toxic potential of the inhaled smoke.

Pertinently, however, tobacco smoke particularly associated with cigarette smoking has proved to be genotoxic but there is little data available on hookah smoking. Yadav and Thakur in 2000 analyzed mitotic index, chromosomal aberrations, sister chromatid exchanges (SCEs) and satellite associations in somatic chromosomes of 35 hookah smokers. They concluded that hookah smoke is both clastogenic as well as genotoxic for human beings (Yadav and Thakur, 2000). Another recent study to assess the genotoxic effect of tobacco by comparing the frequencies of SCEs in lymphocytes of hookah and cigarette smokers found that the frequency of SCEs were increased in both the groups as compared to non smoker. The frequencies of SCEs were in fact higher in water pipe smokers compared to cigarette smokers suggesting a higher genotoxic effect of water pipe smoking when compared to cigarette smoking (Khabour et al., 2010).

We conclude that hookah smoking in Kashmir is associated with increased risk of lung cancer and the commonly held belief that passage through water renders the smoke harmless seems ill founded and potentially dangerous. Further studies in this regard are warranted so as to fully analyze the various variables associated with the habit of hookah smoking and associated development of lung cancer.

References

Al-Mutairi SS, Shihab-Eldeen AA, Mojiminiyi OA, et al (2006). Comparative analysis of the effects of hubble-bubble (Sheesha) and cigarette smoking on respiratory and metabolic parameters in hubble-bubble and cigarette smokers. *Respirology,* **11**, 449-55.

Anonymous (2010). The Sacred Narghile. Available at: http://www.sacrednarghile.com/en/mystery.php Accessed October 31, 2010

Chattopadhyay A (2000). Emperor Akbar as a healer and his eminent physicians. *Bull Indian Inst Hist Med Hyderabad* **30**, 151-8.

Guillerm R, Badré R, Vignon B (1961). Effet inhibiteurs de la fumée de tabac sur l'activité ciliaire de l'épithélium respiratoire et nature des composants responsables (Inhibitory Effects of Tobacco Smoke on the Respiratory Epithelium Ciliary Activity). Académie Nationale de Médecine, 416-23.

Harel Y, Molcho M, Tillinger E (2004). Youth in Israel: Health, Well-Being and Risk Behavior. Summary of Findings from the Third National Study (2002) and Trend Analysis (1994-2002) (in Hebrew). Ramat Gan, Israel: Bar Ilan University.

Jackkson D, Aveyard P(2008). Waterpipe smoking in students: prevalence, risk factors, symptoms of addiction, and smoke intake. Evidence from one British university. *BMC Public Health,* **8**, 174-6.

Kandela P (2000). Nargile smoking keeps Arabs in Wonderland. *Lancet*, **356**,1175 .

Khabour OF, Alsatari ES, Azab M, et al (2010). Assessment of genotoxicity of waterpipe and cigarette smoking in lymphocytes using the sister-chromatid exchange assay: A comparative study. Environ Mol Mutagenesis Aug 25 (Epub ahead of print) DOI: 10.1002/em.20601

Kiter G, Ucan ES, Ceylan E, et al (2000). Water-pipe smoking and pulmonary functions. *Respiratory Med,* **94**, 891-4.

Knishkowy B, Amitai Y (2005). Water pipe (narghile) smoking:an emerging health risk behavior. *Pediatrics,* **116**, e113-9.

Koul PA, Koul SK, Sheikh MA, et al (2010). Lung cancer in the Kashmir Valley. *Lung India,* **12**, 131-7.

Kulwicki A, Rice VH (2003). Arab American adolescent perceptions and experiences with smoking. *Public Hlth Nurs*, **20**, 177-83.

Macaron C, Macaron Z, Maalouf MT, et al (1997). Urinary cotinine in narguila or chicha tobacco smokers. *J Med Liban,* **45**, 19-20.

Maziak W, Rastam S, Eissenberg T, et al (2004). Gender and smoking status-based analysis of views regarding waterpipe and cigarette smoking in Aleppo, Syria. *Prev Med,* **38**, 479-84.

Maziak W, Eissenberg T, Rastam S, et al (2004). Beliefs and attitudes related to narghile (waterpipe) smoking among university students in Syria. *Ann Epidemiol*, **14**, 646-54.

Maziak W, Ward KD, Afifi Soweid RA, et al (2004). Tobacco smoking using a waterpipe: a re-emerging strain in a global epidemic. *Tob Control,* **13**, 327-33.

Maziak W, Ward KD, Eissenberg T (2004). Factors related to frequency of narghile (waterpipe) use: First insights on tobacco dependence in narghile users. *Drug Alcohol Depend,* **76**, 101-6.

Maziak W, Rastam S, Ibrahim I, et al (2008). Waterpipe-associated particulate matter emissions. *Nicotine Tob Res,* **10**, 519-23.

Monn C, Kindler P, Meile A, et al (2007). Ultrafine particle emissions from waterpipes. *Tob Control,* **16**, 390-3.

Nafae A, Misra SP, Dhar SN, et al (1973). Bronchogenic

carcinoma in Kashmir Valley. *Indian J Chest Dis*, **15**, 285-95.
Primack BA, Sidani J, Agarwal AA, et al (2008). Prevalence of and associations with waterpipe tobacco smoking among U.S. university students. *Ann Behav Med*, **36**, 81-6.
Rastam S, Ward KD, Eissenberg T, et al (2004). Estimating the beginning of the waterpipe epidemic in Syria. *BMC Public Hlth*, **4,** 32-6.
Ray CS (2009). The hookah-the Indian waterpipe. *Current Science,* **96**, 1319-23.
Sajid KM, Kamal C, Mahmood R (2008). Hookah smoking and cancer: carcinoembryonic antigen (CEA) levels in exclusive/ever hookah smokers. *Harm Reduct J*, **5**, 198-201.
Sajid KM, Akhter M, Malik GQ (1993). Carbon monoxide fractions in cigarette and hookah (hubble bubble) smoke. *J Pak Med Assoc*, **43**, 179-82.
Sajid KM, Parveen R, Durr-e-Sabih, et al (2007). Carcino-embryonic antigen (CEA) levels in hookah smokers, cigarette smokers and non-mokers. *J Pak Med Assoc,* **57**, 595-9.
Salameh P, Waked M, Aoun Z (2008). Waterpipe smoking: Construction and validation of the Lebanon Waterpipe Dependence Scale (LWDS-11). *Nicotine Tob Res,* **10**, 149-58.
Shafagoj YA, Mohammed FI (2002). Levels of maximum end-expiratory carbon monoxide and certain cardiovascular parameters following hubble-bubble smoking. *Saudi Med J,* **23**, 953-8.
Shafagoj YA, Mohammed FI, Hadidi KA (2002). Hubble-bubble (water pipe) smoking: levels of nicotine and cotinine in plasma, saliva and urine. *Int J Clin Pharmacol Ther,* **40,** 249-55.
Shihadeh A, Azar S, Antonios C, et al (2004). Towards a topographical model of narghile water-pipe cafe smoking: a pilot study in a high socioeconomic status neighborhood of Beirut, Lebanon. *Pharmacol Biochem Behav,* **79**, 75-82.
Shihadeh A (2003). Investigation of mainstream smoke aerosol of the argileh water pipe. *Food Chem Toxicol,* **41**, 143-52.
Shihadeh A, Saleh R (2005). Polycyclic aromatic hydrocarbons, carbon monoxide, "tar", and nicotine in the mainstream smoke aerosol of the narghile water pipe. *Food Chem Toxicol,* **43**, 655-61.
Steentoft J, Wittendorf J, Andersen JR (2006). Tuberculosis and water pipes as source of infection. *Ugeskr Laeger,* **168**, 904-7.
Taha AZ, Sabra AA, Al-Mustafa ZZ, et al (2010). Water pipe (shisha) smoking among male students of medical colleges in the eastern region of Saudi Arabia. *Ann Saudi Med,* **30**, 222-6.
Tamim H, Terro A, Kassem H, et al (2003). Tobacco use by university students, Lebanon, 2001. *Addiction*, **98**, 933-9
Ward KD, Weg MW, Relyea G, et al (2006). Waterpipe smoking among American military recruits. *Prev Med,* **43**, 92-7.
Wolfram RM, Chehne F, Oguogho A, et al (2003). Narghile (water pipe) smoking influences platelet function and (iso-) eicosanoids. *Life Sci*, **74**, 47-53.
World Health Organization (2005). Waterpipe tobacco smoking: Health effects, Research needs and Recommended action by regulators. WHO study group on Tobacco Product Regulation (TobReg).
Wynder EL, Goodman DA, Hoffmann D (1965). Ciliatoxic components in cigarette smoke (Part) 3. In vitro comparison of different smoke components. *Cancer,* **18**, 1652-8.
Yadav JS, Thakur S (2000). Genetic risk assessment in hookah smokers. *Cytobios,* **101**, 101-13.
Zaga V, Gatta-vecchia E (2002). Radicali liberi e fumo di sigaretta (Free radicals and cigarette smoke). *Giorn It Mal Tor,* **56**, 375-91.
Zahran FM, Ardawi MSM, al-Fayez S (1985). Carboxyhaemoglobin concentrations in smokers of sheesha and cigarettes in Saudi Arabia. *Br Med J*, **291**, 1768-70.