Prevalence of cigarette smoking and smoking-related disease correlates in Iranian asymptomatic HBV carriers

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Abstract

Introduction: The possible hepatotoxic effect of cigarette smoking in HBV patients has been proposed by epidemiological and experimental studies, therefore we aimed to evaluate the prevalence of smoking and it's correlated factors in Iranian asymptomatic HBV carriers.

Material and methods: In a cross-sectional study, we included 1116 asymptomatic HBV carriers from patients admitted to the hepatitis clinic of the Tehran Blood Transfusion Organization between 2002 and 2006. Demographic data, health history including cigarette smoking (>100 cigarettes per lifetime) and para-clinical information were registered.

Results: The prevalence of smoking in asymptomatic carriers of HBV was 13.5%. The mean smoking index in asymptomatic carriers of HBV was 29.0±20.6 pack-years (for 151 smoker patients). Frequency of cigarette smoking was higher in men than women (16.3 vs. 4.3%, $p<0.05$) and in married subjects than singles (15.7 vs. 7.6%, $p=0.003$). The mean age of smokers was significantly higher than non-smokers (43±10 vs. 40±12, $p=0.001$). Self-reported ethanol consumption was more common in smokers than non-smokers (44.2 vs. 11%, $p<0.05$). Relative risk for developing fatty liver in smokers was 1.79 (95% CI: 1.16-2.75). Developing fatty liver was correlated with a higher smoking index (32.1±20.9 vs. 27.8±19.6 pack-years).

Conclusions: Although this study suffers from some limitations such as assessing smoking by a questionnaire rather than plasma nicotine or urinary nicotine levels, we recommend specific smoking cessation strategies for hepatitis patients. We also suggest smoker HBV carriers be monitored more closely for developing fatty liver disease.

Key words: HBV, asymptomatic carriers, cigarette smoking.

Introduction

Hepatitis B virus (HBV) is a serious public health problem worldwide and is considered a major cause of chronic hepatitis, cirrhosis, and hepatocellular carcinoma (HCC). Approximately two billion people have serological evidence of past or present HBV infection, and more than 350 million are asymptomatic chronic carriers of HBV [1]. Around 75% of these chronic carriers live in Asia and the Western Pacific [2]. The prevalence of hepatitis B in the general population of Iran has been reported to be between 1 (Shiraz) to 9% (Toyserkan) [3], with a total of two million asymptomatic HBV carriers living in the country [4].

With regard to chronic hepatitis C, several studies have reported the negative impact of smoking on the aggravation of liver cirrhosis and response to treatment, health-related quality of life, and also mortality [5-12]. These studies have documented significant associations between smoking and elevated alanine transaminase (ALT) level [5], increased fibrosis, activity scores and severity of hepatic lesions [10], the risk for developing liver fibrosis [8], aggravation of cirrhosis in hospitalized patients [9], low response rates to interferon-alpha [6], and the risk of developing HCC [11, 12].

Within studies regarding smoking and HBV infection [10, 13-16], most have focused on possible effects of smoking on chronic active hepatitis [10, 14, 15]. A possible hepatotoxicity of cigarette smoking in HBV patients has been proposed by epidemiological and experimental studies [10]. In China, the high mortality rate of smokers through liver cancer has been attributed to the high prevalence of chronic HBV infection [15]. Furthermore, cigarette smoking is related to an increased expression of neuoncogene [13] and has adverse effects on liver cirrhosis development [16].

The aim of this study was to determine the prevalence of self report smoking in asymptomatic HBV carriers and evaluate some of its demographic, clinical and laboratory correlates.

Material and methods

In a cross-sectional study, we evaluated 1116 asymptomatic HBV carriers from patients of the hepatitis clinic of Tehran Blood Transfusion Organization between 2002 and 2006.

The state of asymptomatic HBV carrier was defined as persistent HBV infection (steady positivity for HBsAg in the serum) for more than six months, and without any significant, ongoing necroinflammatory liver disease [17]. The diagnosis of asymptomatic HBV carrier state was established by a hepatologist (SMA) or two infectious disease specialists (MK, BB). Patients with any other chronic liver diseases, a symptomatic infection, or a co-infection with hepatitis C (HCV), hepatitis D, or human immunodeficiency virus (HIV) were excluded.

Participants completed a structured questionnaire, which was then checked by an interviewer. The questionnaire collected extensive data on demographic data (sex, age, marital status and level of education), and also medical history (cigarette smoking, alcohol consumption, and a history of liver disease in self or family members).

The self report cigarette smoking was assessed according to two questions in the questionnaire: 1) "Have you smoked at least 100 cigarettes in your entire life?" and 2) "Do you now smoke cigarettes every day?". Based on the first question, we divided our subjects into two groups: ever smokers (smoked at least 100 cigarettes), and never smokers (smoked less than 100 cigarettes per lifetime) [18]. The smoking index (cigarette pack-year), defined as the number of years of smoking twenty cigarettes a day.

The drinking pattern was assessed using the graduated frequency (GF) method: how often during the past 12 months did the subjects drink more than X amount of alcohol [19]. In the version of the GF used in this study, there were nine mutually exclusive categories of frequency, ranging from "never" to "every day", and seven mutually exclusive categories of alcohol dose (expressed in local units of beer, wine, and spirits), ranging from 10 g to >160 of pure alcohol (details available from authors). Alcohol intake measures were recalculated into grams of ethanol. We used several definitions of binge drinking: >120 g of ethanol at least once a month [20].

Paraclinical information, including complete blood count, liver function tests, ESR, PT, albumin, FBS and lipid profile (total cholesterol and triglyceride), were also collected. The presence of fatty liver, assessed by ultrasound imaging according to published literature, was also registered [21].

Data analysis was carried out using the statistical software of SPSS-13 for Windows. To study the correlates of ever cigarette smoking, we used chi-squared and to evaluate the correlates of smoking index, we used independent sample t-test. $P<0.05$ was considered significant.

Results

Patient population

The mean age of patients was 37.1±11.6 years. 857 (76.8%) subjects were male and 259 (23.2%) female. 895 (80.2%) subjects were married and 221 (19.8%) single. 331 (29.7%) patients had an educational level of below diploma and 785 (70.3%) had diploma or an academic degree.

Smoking and its correlates

The prevalence of cigarette smoking in asymptomatic carriers of HBV was 13.5% (151 cases of 1116). Table I compares demographic, clinical and paraclinical characteristics of smoker and non-smoker asymptomatic HBV carriers. The relative risk for developing fatty liver in smokers versus non-smokers was 1.79 (95% CI: 1.16-2.75). Frequency of fatty liver was not significantly different between smokers with and without alcohol use (10.5 vs. 16.8%; p=0.44).

There was no association between the presence of fatty liver and age, marital status, level of education, and self-reported ethanol consumption,

Table I. The comparison of smokers and non-smokers regarding demographic, clinical and paraclinical findings

	Ever smokers N=151	Never smokers N=965	P value
Age	43.70±10.32	40.53±12.23	p=0.001
Male sex (%)	140 (92.7%)	718 (74.4%)	p<0.05
Marital status (married)	135 (89.4%)	763 (79.0%)	p=0.003
Educational level (below diploma)	40 (24.5%)	290 (30.4%)	p=0.12
Ethanol consumption	38 (44.2%)	113 (11.0%)	p<0.05
Fatty liver	23 (15.2%)	82 (8.5%)	p=0.008
ALT	47.15±103.82	33.85±41.58	p=0.12

hypertension and diabetes mellitus. Also the comparison of complete blood count, liver function tests, ESR, PT, albumin, FBS and lipid profile (total cholesterol and triglyceride) between smokers and non-smokers were not significantly different.

Smoking index and its correlates

Mean smoking index in asymptomatic HBV carriers was 17.0±8.6 pack-years (for 151 smoker patients). Developing fatty liver was correlated with a higher smoking index (19.1±9.9 vs. 16.8±8.6 pack-years). Smoking index was correlated with age (p=0.001, r=0.302), and was not associated with marital status, level of education, self-reported ethanol consumption, complete blood count, liver function tests, ESR, PT, Albumin, FBS and lipid profile.

Discussion

In this study, we showed that the prevalence of cigarette smoking in Iranian asymptomatic HBV carriers was 13.5%. The prevalence of cigarette smoking in the general population is different between countries, and even different between provinces of a country. In Iran, for instance, this rate has been reported to be 16.8% in Shiraz [22] and 22.3% in Tehran [23].

Another important finding of this study was that men with chronic hepatitis had a higher rate of cigarette smoking compared with their female counterparts. Similar rates of smoking have been reported in the general population of Iran, with rates of 18.5-26% in men and 3.6-10.1% in women [22, 24, 25]. We also found that older patients tended to smoke more commonly compared with younger subjects, which is in line with a former report from our country [22]. With respect to the association between smoking and educational level, the results of this study contrast those of one report from Iran which has shown a significant link between these two items [26].

Our study showed an association between ethanol intake and cigarette smoking, in agreement with the results of Bierut et al. [27]. One study reported that up to 80% of persons who were alcohol dependent were also smokers [28]. This combination has been named as a deadly combination [29].

We could not draw any significant correlation between smoking and liver enzymes. In this respect, although smoking has been reported to be associated with elevated ALT levels among anti-HCV-seropositive individuals, such evidence is lacking in HBV infected persons [5] as well as in the general population [30].

From the numerous studies assessing the risk factors of fatty liver in the general population, some have neglected the possible effect of cigarette smoking [31, 32], some have shown smoking as an associated factor with metabolic disturbances [33] and risk factors of fatty liver [34], and some others have failed to demonstrate such links [35, 36]. Our results exhibited a link between fatty liver and cigarette smoking in asymptomatic HBV carriers. This may be considered a very important finding because fatty liver and asymptomatic HBV carrier state are shown to have a significant synergistic association with liver damage [37]. The findings that fatty liver sensitizes the host's immune response to HBV infection have been reported by some studies [38, 39]; however, according to previous epidemiological studies, the coexistence of fatty liver and HBV carrier state is not uncommon in clinical practice [40]. Unfortunately, even the studies conducted in 2007 focusing on fatty liver in asymptomatic carriers of HBV have neglected the possible importance of smoking [37, 41].

Surprisingly, we could not find any association between fatty liver and alcohol consumption, which clearly contrasts literature. One possible explanations for this finding may be the relatively small sample size of this study. It is also important to note that the questionnaire used did not inquire about the amount of alcohol consumption. Previous reports suggest that low amounts of alcohol consumption does not increase risk of developing fatty liver [42].

Different mechanisms have been applied to explain the negative impacts of smoking in HBV carriers. N-acetyltransferase (NAT2) activity may be particularly critical in smoking related hepatocarcinogenesis among chronic HBV carriers [43]; N-acetyltransferase (NAT) is involved in the metabolic activation and detoxification of aromatic amines [43]. Nicotine, a major component of tobacco smoke, is rapidly absorbed through the lungs and released into the circulation, and is mainly metabolized by the liver. The effects of nicotine, both alone and combined with carbon tetrachloride (CCl_4), have been studied on the liver of rats [44]. CCl_4 induced liver lesions are also aggravated by tobacco nicotine, which has been ascribed to oxidative stress associated with lipid peroxidation both in vitro and in vivo [45-48]. Also, experimental studies on rats have shown that nicotine can cause deleterious effects to the liver, notably by aggravating the hepatotoxic effects of CCl_4 [44].

Application of effective smoking cessation programs has been strongly encouraged for all populations. Self-help strategies for smoking cessation, individual and combined pharmacotherapy along with counseling, can help smokers quit smoking [49]. Although specific strategies for smoking cessation have been previously developed for pregnant women [50], patients with coronary artery disease [51], and subjects with chronic obstructive pulmonary disease [52]. It has been shown in one study that smoking cessation will provide a healthier lifestyle for HBV carriers, however, that study had not provide a smoking cessation strategy for this population [53].

The main limiting point of the current study was the minimal data regarding some risk factors of fatty liver such as body mass index. Another limiting point of the current study was that smoking habits were assessed by a questionnaire not with laboratory data on plasma nicotine or urinary nicotine levels to establish the levels of smoking or exposure to smoking.

Conclusions

Because of the link between cigarette smoking and fatty liver in asymptomatic HBV carriers, it is recommended that smoker HBV carriers be screened more closely for possible evidence of fatty liver. Furthermore, strategies for smoking cessation should be specifically designed for carriers of HBV.

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