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ORIGINAL ARTICLE

Seroepidemiological Study of Hepatitis E Virus in Drug Addicts in Ahvaz, Southern Iran: 2005-2006

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Background and Aims: **Poor personal health in drug addicts predisposes them to Hepatitis E virus (HEV) infection. The objective of this study was to determine the prevalence of antibody to HEV (HEV- IgG) and evaluate epidemiological features of HEV infection among drug addicts.**

Methods: **224 drug addicts were included in this analytic descriptive study in Ahvaz, southern Iran, from 2005 to 2006. After a through physical examination and completing a questionnaire, 5 mL blood was obtained from each case and tested for anti-HEV-IgG by an enzyme linked immunosorbent assay (ELISA) method using commercial kit (Dia-prob). Data were analyzed in SPSS 11.5 using chi-square test.**

Results: **Of 228 cases, 35 (13.5%) were HEV-IgG positive. The sero-prevalence of positive HEV-IgG in injecting, inhalant and oral drug abusers was 22.8%, 9.1%, and 6.2%, respectively ($p<0.05$). HEV-IgG was positive in heroin, crack, and opiate abusers with a rate of 20.2%, 10.9%, and 11.6%, respectively. The sero-prevalence of positive HEV-IgG in the prison and addiction treatment center was 15.8%, and 13.3%, respectively ($p>0.05$).**

Conclusions: **Drug addiction is associated with an increased risk of exposure to HEV and resulted in the high prevalence of anti-HEV-IgG in addicts.**

Keywords: **Hepatitis E Virus, Drug Addiction, Seroprevalence**

Introduction

Hepatitis E virus (HEV) is considered as one of the most common causes of particular hepatitis in developing countries [1]. HEV has been found to be the causative agent of enterically transmitted non-A, non-B hepatitis in tropical and subtropical countries [2, 3]. It is transmitted in a fecal-oral manner [1-3]. HEV causes sporadic infections and large epidemics [1-3]. Published reports suggest that a still-undefined intra-unit factor or other factors are associated with HEV transmission [3-6]. The incidence of HEV infection is very dependent on the overall level of public health sanitation and in particular the quality of potable water [1]. The geographical distribution of the HEV is largely confined to developing countries such as India, China, Middle and Far East [1, 3, 7]. Outbreaks of hepatitis E involving large numbers of adults are not uncommon in developing countries with inadequate public health sanitation [1-3]. Several investigators, however, have indicated that HEV is endemic in Iran [8-10].

There are some reports indicated a significantly higher risk of acute HEV infection among patients with underlying diseases or situations such as chronic hemodialysis or addiction [3, 11-16]. It is possible that these were nosocomial infections acquired by person-to-person transmission in the hemodialysis unit [3]. Poor personal health in injecting drug addicts predisposes them to HEV infection [11, 12, 15-17]. The present study was

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conducted to determine the prevalence of IgG antibody to HEV and evaluate epidemiological features of HEV infection among drug addicts .

Patients and Methods

A total of 224 drug addicts were included in this analytic descriptive study which was conducted in Ahvaz, southern Iran, from 2005 to 2006. This study was approved and funded by Jondishapour Infectious Diseases and Tropical Medicine Research Center affiliated to Jondishapour University of Medical Sciences.

The study population was randomly selected from available addicts in prisons and addiction treatment centers. After a through physical examination and completing a questionnaire including characteristics, epidemiological data, vaccination, cigarette smoking, alcohol consumption, imprisonment, duration of time spent in prison, past history of icter or hepatitis and viral infections (*e.g.*, hepatitis B virus [HBV], hepatitis C virus [HCV], human immune deficiency virus [HIV]) in patients and his family, and variables related to addiction such as kind of drug and route of administration, a blood sample was taken from each participant to be tested for antibodies against HEV. Inclusion criteria included residency in prison or drug treatment centers. Exclusion criteria were a history of blood or blood products transfusion or operative surgery. Antibodies to HEV (anti-HEV) were detected by an enzyme linked immunosorbent assay (ELISA) using a commercial kit (Dia-prob). According to the manufacture, the specimens with antibody concentration ≥1.1 μ/mL were considered positive; the values between 1.1 and 0.9 μ/mL were considered suspicious and those <0.9 μ/mL were considered negative. Data were analyzed by SPSS ver 11.5 using χ^2. A p value <0.05 was considered statistically significant.

Results

All studied cases were male and had a mean±SD age of 34.1±6.1 (range: 18-54) years. Of 228 cases, 35 (15.4%; 95% CI: 10.7%-20.0%) were HEV-IgG positive. The prevalence of HEV-IgG positivity in injecting, inhalant and oral drug abusers was 22.8%, 9.1%, and 6.2%, respectively. There was a significant difference in the seropositive rates between injecting and non-injecting drug abusers (p<0.05). HEV-IgG were positive in heroin, crack and opiate users with a rate of 20.2%, 10.9%, and 11.6%, respectively. Other results about personal characteristics, epidemiological features, and co-infection with other viral infections, previous history of icter/hepatitis, addiction and type of substance which is used are shown in Tables 1, 2 and 3. As shown in Table 1, there is no significant difference in age, resident place, level of eduction, and drinking water between HEV-IgG-positive and -negative cases (p>0.05). Those with history of previous icter or hepatitis had a higher prevalence rate of HEV-IgG positivity than others (Table 2). Positive past history of viral infections in the family members in HEV-IgG-positive and -negative subjects was 5.7%, and 6.2%, respectively. Past history of hepatitis/icter was not found in family members. The mean±SD number of cigarettes smoked per day in HEV-positive and negative subjects was 6.2±2.6, and 5.4±3.1, respectively. The mean±SD amount of alcohol drunken a day in the two groups was 57.3±29.7, and 63.1± 31.3 mL, respectively.

Table 1. Epidemiological features of anti-HEV-IgG positive addicts.

Variables		HEV-IgG positive n (%)	HEV-IgG negative n (%)	P value
Age (yrs):	<25	9 (25.7)	37 (19.2)	
	25-50	20 (57.1)	129 (66.8)	0.33
	>50	6 (17.2)	27 (14)	
Gender:	Male	35 (100)	193 (100)	
Education level:	No education	19 (54.3)	113 (58.5)	0.71
	Primary	9 (25.7)	28 (14.5)	0.13
	Secondary	6 (17.1)	47 (24.4)	0.51
	High education	1 (2.9)	5 (2.6)	1.0
Resident place:	Rural	11 (31.4)	58 (30.1)	
	Urban	24 (68.6)	135 (69.9)	0.84
Imprisonment		29 (82.9)	154 (79.8)	0.81
Duration of prison:	<2 years	2 (5.7)	12 (6.2)	1.0
	2-5 years	10 (28.6)	62 (32.1)	0.84
	>5 years	17 (48.6)	80 (41.5)	0.46
Drinking water:	Pipe system	26 (74.3)	166 (86.1)	
	Non-pipe	9 (25.7)	27 (13.9)	0.12
Total		35 (100)	193 (100)	

HEV: hepatitis E virus; IgG: immunoglobulin

As shown in Table 3, there was no significant difference in the type of substances abused between HEV-positive and -negative individuals (p>0.05). The prevalence of HEV-IgG positive in prison and in addiction treatment centers was 15.8%, and 13.3%, respectively (p>0.05). Co infection with HIV, HCV, and HBV was not a risk factor or HEV seropositivity (P>0.05).

Table 2. Previous hepatitis, HBV vaccination and viral infection in the study population.

Variables	HEV-IgG positive n (%)	HEV-IgG negative n (%)	P value
Positive history of icter/hepatitis	24 (68.8)	18 (9.3)	<0.0001
HBV vaccination	4 (11.4)	21 (10.9)	1.0
Viral infection: HIV-positive	3 (8.6)	9 (4.7)	0.40
HBs-Ag positive	4 (11.4)	12 (6.2)	0.27
Anti-HCV positive	7 (20)	32 (16.6)	0.62
Total	35 (100)	193 (100)	

HEV: hepatitis E virus; IgG: immunoglobulin

Table 3. Addiction status, behaviors and used substances in the study population.

Variables	HEV-IgG positive n (%)	HEV-IgG negative n (%)	P value
Cigarette smoker	32 (91.4)	168 (87.1)	0.58
Alcoholic	11 (31.4)	43 (22.3)	0.28
Route of drug administration: IV	26 (74.3)	88 (45.6)	0.002
Inhalation	6 (17.1)	60 (31.1)	0.10
Oral	3 (8.6)	45 (23.3)	0.06
Kind of drugs: Heroin	6 (17.1)	47 (24.4)	0.51
Crack	1 (2.9)	5 (2.6)	1.0
Opiate	11 (31.4)	58 (30.1)	1.0
Total	35 (100)	193 (100)	

HEV: hepatitis E virus; IgG: immunoglobulin; IV: Intravenous injection

Discussion

The present study revealed that the prevalence of anti-HEV IgG was considerably high (15.4%) in addicts of Ahvaz. This finding is consistent with seroprevalence studies on HEV among Injection Drug Users (IDUs) in many parts of the world [11, 12, 15-20]. Christensen *et al.*, in their study on prisoners in Denmark showed a high prevalence of HEV-IgG in IDUs [11]. Trinata and colleagues [12] also reported a high prevalence of HEV-IgG among Brazilian IDUs. The seroprevalence of anti-HEV-IgG among IDUs was 11.8% whereas in blood donors, it was 4.3%. Bernal *et al.*, in a seroepidemiological study on HEV in different population groups found that the prevalence of HEV-IgG in IDUs was 5.6% which was higher than the general population (1.2%) [15]. Thomas *et al.*, reported a high prevalence HEV-IgG (23%) in non-endemic areas [21]. Other reports from Turkey, Italy and the former Soviet Union suggested a high prevalence of HEV-IgG in addicts [18-20]. Although seroprevalence of HEV in addicts are higher than normal population, the rate varies in different countries. This difference may be contributed to various factors such as socio-economic status, environmental sanitation, geographical variation, poor personal hygiene and differences in assays for anti-HEV antibodies. It is unknown for us why in endemic and non-endemic areas, those with risk of parenteral exposure have a high rate of HEV-IgG antibodies. We believe that the high risk behavior of IDU patients and possibly other routes of HEV transmission (non-fecal oral) may be contributed to this condition. We found no association between the presence of anti-HEV IgG and the age of drug abusers. Previous published studies suggested that an older age was significantly associated with anti-HEV IgG [18-20]. The correlation of HEV with age may reflect the fact that HEV infection was acquired some decades before. Anti-HEV IgG can persist for a long time. However, in our study because the study population suffer a similar poor health sanitation, they, regardless of age, are at similar risk for infection.

This study also showed that there was no association between the presence of HEV-IgG and variables such as resident place, level of educational, imprisonment, smoking, alcohol consumption, duration of staying in prison and the source of drinking water. Some of these findings are in keeping with and some are contradicting other reports [1, 2, 7, 11]. We believe that although some of these variables may be true risk factors of HEV infection, since our study population was at similar risk for these factors, we could not pick these variables up and show a statistically significant difference between HEV-positive and -negative cases.

Our study showed that although HEV seropositivity was not related to the type of substance abused (P>0.05), it was related to the route of administration (P<0.05). Injecting drug abusers had a higher prevalence rate of HEV-IgG than non-injecting drug abusers. Our finding is consistent with that of Christensen *et al.*, Trinta *et al.*, and Zanetti and colleagues [11, 12, 16]. This finding may reflect that oro-fecal transmission may not be the only route of transmission of HEV and drug addicts with a high risk for HBV and HCV infections could also be infected by HEV.

In this study, co-infection with HIV, HBV or HCV was not associated with a higher HEV infection. Balayan *et al.*, explained that in Russia, the rate of anti-HEV seropositivity in HIV-infected patients was 11.1% and increased with the progression of HIV infection but, in Belarus, anti-HEV seropositivity was not found among HIV-infected subjects nor among IDUs in the control

group [22]. The rate of positive past medical history in family members of the study population was similar (6.2% *vs* 5.7%) and had no confounding effect on our results.

However, in our study, the observed high prevalence of anti-HEV-IgG in that group of patients was shown to be due to the confounding effects of variables related to addiction or imprisonment.

In the present study, oral drug abusers (Table 3) were at lower risk of infection with HEV (8.6% vs 23.3%). Although this finding is statistically not significant (P=0.06), it may be contributed to local toxic effects of the abused substances on the viral particles in the bowel.

Conclusions

This study suggests that drug addiction is associated with an increased risk of exposure to HEV and resulted in a high prevalence of anti-HEV IgG in these people.

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