

# First report of simultaneous assessment of hepatitis A virus and hepatitis E virus seroprevalence among soldiers in Iran

Khodayar Ghorban<sup>1</sup>, Maryam Dadmanesh<sup>2</sup>, Hasan Mohammadnezhad<sup>3</sup>, Hamed Naziri<sup>4,\*</sup>

<sup>1</sup>Department of Immunology, School of Medicine, Aja University of Medical Sciences, Tehran, Iran

<sup>2</sup>Department of Infectious Diseases, School of Medicine, Aja University of Medical Sciences, Tehran, Iran

<sup>3</sup>Department of Microbiology, Shahr-e-Qods Branch, Islamic Azad University, Tehran, Iran

<sup>4</sup>Department of Microbiology, School of Medicine, Guilan University of Medical Sciences, Rasht, Iran

## Abstract

Hepatitis E virus (HEV) and Hepatitis A virus (HAV) have been considered as common causes of viral hepatitis to military service members since their discovery. Although Iran has been recognized as an endemic country for HAV and HEV there is no study about HAV and HEV simultaneous prevalence among Iranian soldiers. The purpose of this study was to assess anti-HAV and anti-HEV antibodies in Iranian soldiers concurrently. In this cross-sectional study, a total of 400 serum samples were collected by simple random sampling for detection of anti-HAV and anti-HEV IgG by commercial HEV enzyme-linked immunosorbent assay (ELISA) kit. Out of 400 individuals, all participants were male with ages ranging from 18 to 26 years. Totally, 12% and 0.5% of the tested specimens were positive for anti-HAV and anti-HEV respectively. There were no significant differences between the subjects grouped according to age groups. Our finding presented a dramatic decrease in seropositivity against HAV. Therefore, vaccination for HAV should be reevaluated for military services in Iran.

**Keywords:** HAV, HEV, Soldiers, Iran

## 1. Introduction

Despite significant decline in the prevalence of hepatitis A virus (HAV) and hepatitis E virus (HEV) infections in industrial countries recently, there remain a serious health problem in third world [1, 2]. All type of acute and chronic viral hepatitis are one of the most important public health concern worldwide [3, 4], and both HAV and HEV infections are the most important cause of oral-fecal hepatitis and are transmitted mainly through the fecal-oral route; either via person-to-person direct contact or consumption of contaminated food or water [5, 6]. While HEV infection frequently occur in young adults, HAV is more common in early childhood and immune

response against it usually leading to long-lasting protection [7].

Furthermore the prevalence of HAV in developing countries (27 % versus 81% in high class countries) is significantly higher than that of HEV in endemic areas (7.8% versus 45%) [8]. Access to safe water, basic sanitation and hygiene play an important role in disease transmission, especially in low-income regions [9]. Most sporadic cases and outbreaks of acute hepatitis are caused exclusively by HEV as an important public health concern in primarily developing countries in Asia and Africa, frequently related to contaminated water [7, 10]. The Iranian soldiers who developed hepatitis E was found to have anti-HEV antibodies were primarily estimated to be

### \*Corresponding author:

Hamed Naziri, Ph.D  
Department of Microbiology, School of Medicine,  
Guilan University of Medical Sciences, Rasht, Iran  
Tel/Fax: +98 13 33326061/+98 13 33326061  
Email: hamed.naziri65@gmail.com  
<http://orcid.org/0000-0001-6290-8944>

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2% and almost 98% of them were at risk for HEV infection [11].

In many parts of the world, the proportion of anti-HAV seroprevalence has been declining in recent years. Probably, it is related to the improvements in public health programs, availability of clean water and sanitary conditions [12, 13]. In addition, vaccinations against HAV have provided a safe and effective means of preventing of hepatitis A [14]. Like HAV, HEV is usually an acute self-limiting disease and with no progression to a chronic disease state. Since, there is no a suitable cell culture system for efficient HEV replication and susceptible small laboratory animal, Construction a live/attenuated vaccines is not possible [15]. The purpose of this study was to evaluate the seroprevalence characteristics of HAV and HEV and their co-infection among Iranian soldiers to determine whether vaccination should be administered routinely in Iranian army draftees.

## 2. Materials and Methods

### 2.1 Patients and methods

This cross-sectional study was approved by the Ethical Committee of Aja University of Medical Science. It was carried out among 400 Iranian soldiers in a military unit from May to December 2019 (Tehran, Iran). The average age of the study population was  $21.6 \pm 1.9$  years. All soldiers completed a questionnaire to assess other descriptive characteristics such as ethnicity, career before recruitment, education level, history of vaccination, and time of in-service. Five ml blood samples were collected from all soldiers after obtaining an informed consent. Serum stored in  $-20\text{ }^{\circ}\text{C}$  until anti-HAV IgG and anti-HEV IgG antibodies determination. Detection of anti-HAV IgG and anti-HEV IgG was performed by commercial HEV enzyme-linked immunosorbent assay (ELISA) kit (DIAPRO, Diagnostic Bioprobes, Milano, Italy) according to manufacturer's instruction. Samples with anti-HEV IgG or anti-HAV IgG ratio  $<0.90$  were recognised as negative, those with ratio  $\geq 0.90$  but  $<1.10$  were considered as borderline, and samples with ratio  $\geq 1.10$  were defined as positive.

### 2.2 Statistical analysis

Statistical analysis was done through SPSS (version 17) statistical software (Scientific Package for Social Sciences, Chicago, IL). Data were subjected to

the analysis of variance (ANOVA) to compare the proportions between groups. The level of P-value less than 0.05 were considered significant.

## 3. Results

Totally 400 soldiers were tested for detection of anti-HAV IgG and anti-HEV IgG antibodies. The mean age was  $21.63 \pm 1.92$  (range from 18 to 24). Out of 400 individuals, all of them were male. The duration of regular full-time service was  $11.13 \pm 5.49$  (range from 3 to 24 months). In 322 (80.5%) of them had high school diploma and higher degree and 78 (19.5%) had education less than a high school diploma. The majority of soldiers (96%,  $n=384$ ) were student before coming to compulsory military service. The overall anti-HAV IgG and anti-HEV IgG was found in 48 (12%) and only two (0.5%) of 400 participants respectively (Table 1). None of seropositive participants revealed any clinical symptoms similar to acute or chronic hepatitis at the time of sampling. Previous history of jaundice, receiving blood transfusion and history of hepatitis were negative in all soldiers. There were no statistically significant between the age, ethnicity, career, education level, and time of in-service with anti-HAV IgG and anti-HEV IgG antibodies. The seropositive of HAV is in rural and urban areas were 60.6 % and 39.4% respectively. There was no significant difference between these groups ( $P > 0.5$ ).

Table 1. Age-specific seroprevalence of anti-HAV antibody among soldiers

Age group (year)	Negative	Positive
18-21	188 (91.2%)	18 (8.8%)
21-26	164 (84.5%)	30 (15.5%)
Total	352 (88%)	48 (12%)

## 4. Discussion

This is the first cross-sectional study that compares prevalence of anti-HAV and anti-HEV antibodies among Iranian soldiers simultaneously. The results of this study suggest that prevalence of anti-HAV antibodies have declined dramatically during recent years. Both HAV and HEV infection can lead to severe and long-term disease including liver

damage which may last for six months or longer [16]. HAV and HEV infections are more common in overcrowding regions with inappropriate hygiene, lower income countries and directly related to sanitation.

Safety and clean water were available among Iranian forces. Health care such as the using of bottled water or healthy food is strongly recommended during missions in endemic areas. In one previous study, prevalence of HEV and HAV infection have been reported about 9.3% and 90% respectively [17, 18].

Our results did not confirm the hypothesis that vaccination for hepatitis A is not necessary for Iranian military conscripts and some previous reports about prevalence of HAV among them. Also the seroprevalence of HAV was less than estimated in other studies [19, 20]. The best protection way against HAV is vaccination among high risk groups.

One of the noticeable health problems in military service is HAV which deployed to countries with low socioeconomic status. An objective of this study was to assess the seroprevalence of anti-HAV among Iranian soldiers. Our results represented low anti-HAV seroprevalence which was unexpected. This proportion is completely different with previous reports of anti-HEV prevalence in the Iran, which were 80.3%–97% in Izadi et al. and Ghorbani et al. studies respectively, our proportion was significantly lower than those stated in more recent studies [11, 19]. One earlier study among Iranian blood donors represented seroprevalence rates of 70.3% [21]. Nevertheless, these results are also in discordance with seroprevalence was observed in previous studies, which may have been caused by hygiene promotion in Iran.

The current study exhibited that 0.5% of Tehran soldiers were positive for anti-HEV. Previous studies reported similar HEV seroprevalence among Iranian soldiers in non-endemic regions [11]. While hepatitis E is endemic in developing countries such as Iran [7], our data showed less prevalence of HEV compared to 30% in previous data. Also, our finding revealed an unprecedented reduction in seropositivity against HAV which shows individuals are at risk for HAV infection. Therefore, vaccination for HAV should be reconsidered for military services in Iran.

We identify the limitations of our study such as the overall sample size is small and lack of molecular tools. In addition to these limitations, clinical data collected

during the soldiering have not contained some risk factors, such as contact with animals, food regime, and travel to endemic regions.

In summary, there was a dramatic decline in seropositivity against HAV in our study. As a consequence, Iran should reevaluate the need for vaccination against HAV for its military services.

### Authors' contributions

HN: Designed and performed experiments, analyzed data and co-wrote the paper. KG: Designed and performed experiments, analyzed data. MD, HM: Analyzed data and co-wrote the paper. HN: Designed experiments, supervised the research. All authors read and approved the final version of paper

### Conflict of interests

None to declare.

### Ethical declarations

This study was approved by the Ethics Committee of AJA University of Medical Sciences (IR.AJAUMS.REC.1395.037) and is in compliance with the declaration of Helsinki.

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