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Detection of Hepatitis E Virus IgM Antibody among Patients with High Aminotransferase and Alanine transaminase Levels in Khartoum State (Sudan)

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Abstract

Background: The hepatitis E virus (HEV), which causes epidemic and sporadic forms of hepatitis is one of the major public health problems encountered in developing countries. Most outbreaks of HEV are associated with poor personal hygiene and waterborne infections. HEV infection is more common in patients with high aminotransferase (ALT) and alanine transaminase (AST) liver enzymes and is more often fatal in patients with liver disease.

Objective: To detect hepatitis E virus IgM antibody among patients with high aminotransferase and alanine transaminase levels in Khartoum State (Sudan).

Materials and methods: 61 serum samples were collected from patients with high ALT and AST liver enzymes attending the Military Teaching Hospital and Bashair Teaching Hospital in Khartoum State (Sudan). Samples were tested for HEV IgM antibody using the enzyme-linked immuno-sorbent assay (ELISA) technique. 51 patients were males and 10 patients were females.

Results: 3 (1.8%) out of 61 serum samples investigated were positive for HEV IgM antibody, using ELISA. One woman (0.6%) and 2 men (1.2%) were positive for HEV IgM antibody.

Conclusion: The frequency rate of HEV IgM antibody was significantly high in seropositive patients; however, gender wise the frequency rate of HEV IgM antibody was statistically insignificant.

Key words: HEV IgM antibody, ELISA, ALT, AST, Khartoum State (Sudan).

Introduction

Hepatitis E virus (HEV) is a spherical shaped virus, non-enveloped virus, with a single stranded RNA genome that belongs to the *Hepevirus* genus in the family *Hepeviridae*. The viral genome is a positive-sense RNA molecule organized into three open reading frames (ORF1, ORF2, and ORF3). HEV is divided into at least four genotypes, all belonging to a single serotype, which is

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Further divided into a total of 24 subtypes. Genotypes 1 and 2 are associated with human illness, while genotype 3 and 4 are animal strains which are occasionally transferred to humans. A large outbreak of hepatitis E virus infection was reported in June 2004 in the internally displaced population camps of Darfur in western Sudan. HEV primarily affects young adults and is generally mild¹.

Hepatitis E is also a zoonotic disease of some domestic animals such as cattle, sheep, goats, chicken, and pigs. Transmission of the virus to humans may occur via these animals. There is minimal person to person transmission, however, the virus may be transmitted by other routes, such as renal hemodialysis. Vertical transmission of HEV from infected mothers to their children has also been described. In addition, dental treatments and blood transfusions may be associated with HEV transmission. Hepatitis E is endemic in Iran and seroprevalence of this infection increases significantly with age².

HEV prevalence rate varies between countries and even within the same country. Its prevalence rate in Egypt and Taiwan is 26% and 11%, respectively. In different cities of Iran this variability is 3.8%, 11.5%, 7.8%, and 9.3% in Esfahan, Khozestan, Tabriz, and Nahavand, respectively. Hepatitis E virus is categorized as an acute and self-limiting infection. The course of infection has 2 phases: the prodromal phase and the icteric phase. Furthermore, in healthy individuals during the course of the infection (usually several weeks), hepatitis E occasionally develops into an acute, severe liver disease, which is fatal in about 2% of all cases. Mortality occurs in 20-25% of pregnant women with hepatitis E, and in patients with liver disorders this ratio may increase to 75%. In addition, liver failure and cirrhosis, can also occur, in solid organ transplant and immunocompromised patients. Auto-immune disease in liver, can also result from hepatitis E infections, but a fraction of patients progress to fulminant hepatitis which is the most severe form of acute hepatitis³.

Materials and methods

This was a cross-sectional study, carried out between May and June 2018. The study was conducted on patients with high AST and ALT liver enzymes attending the Military Teaching Hospital and Bashair Teaching Hospital in Khartoum State (Sudan). Demographic and clinical data were recorded for all study participants. SPSS software (v. 11.5) was used for statistical analysis of the data and descriptive statistics were reported. Quantitative variables were expressed as the mean \pm the standard deviation (SD), and comparisons performed using the two-sample t test. Statistical significance was set when $p < 0.05$. Ethical approval for this study was obtained from the Ministry of Health, Khartoum State, AL- Neelain University ethical committee board and from the federal Ministry of Health Sudan. Only patients who agreed to participate were enrolled in this study and informed consents were obtained regarding the data and collection of blood samples. Permission to collect the specimens was taken from authorities of Military Teaching Hospital and Bashair Teaching Hospital (Khartoum State, Sudan). 5 ml blood samples were collected from 61 patients with high AST and ALT levels. The samples were centrifuged at 5,000 rpm for 5 minutes. Separated sera were then stored at -20 until used. Serum samples were investigated using commercially ELISA Kits (EUROIMUN, Germany). ELISA procedure was conducted according to the manufacturer's instructions. The serum levels

of alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were measured by a spectrophotometer.

Results

A total 61 patients were investigated. They presented with symptoms of fever and jaundice. Their age range was 4-55 years, and mean age was 35.42 ± 9.38 . Patients were divided into 4 age groups: less than 25 years, 26-35 years, 36-45 years, and above 46 years. Three patients (5%) were found positive for HEV IgM antibody. As seen in Table (1), no significant difference was detected in age incidence ($p = 0.64$) or gender ($p = 0.57$).

Table (1): Sero-prevalence rate of high ALT and AST according to age incidence and gender

Parameters	Positive HEV IgM antibody	p = value
Less than 25 years	0	p = 0.64
26-35 years	1 (33.3%)	
36-45 years	2 (66.6%)	
Above 46 years	0	
Males	3 (100%)	p = 0.57
Females	1 (10%)	

Among 31 patients (50.8%) investigated in Khartoum City, 2 patients (66.6%) were found positive for HEV IgM antibody. Also, among 26 patients (42.6%) investigated in Omdurman City, 2 patients (66.6%) were found positive for HEV IgM antibody. Furthermore, among 4 patients (6.5%) investigated in Gazeera State, no patient was found positive for HEV IgM antibody. No significant residence correlation was detected ($p = 0.084$) in these areas.

On the other hand, among the total patients investigated, 13 cases (21.3%) were complaining of jaundice; and 48 patients (78.8%) were not complaining of jaundice. One patient (33.3%) from the jaundice group was found positive for HEV IgM antibody; and 2 patients (66.6%) from the non-jaundice group were found positive for HEV IgM antibody. No significant correlation was detected ($p = 0.51$) in the positivity of HEV IgM antibody in these two groups.

As shown in Table (2), the correlations of the liver enzymes AST and ALT with the seropositivity of HEV IgM antibody were not significant ($p = 0.6$ and $p = 0.27$ respectively).

Discussion

This study was conducted to detect HEV IgM antibody in patients with high liver enzymes. The study revealed a 5% (3/61) prevalence rate of HEV IgM antibody among the patients investigated. In Sudan (1992), cases of hepatitis E virus infection were reported as acute sporadic cases among children; and acute hepatitis E with positive anti-HEV IgM was found in 59% of the study population. In Darfur (Western Sudan), acute hepatitis E virus infection was diagnosed in 95% of the suspected cases in 2004. In this study 5% of the patients were HEV IgM antibody

positive. This result is similar to studies conducted in Brazil (27.5%) and Japan (7.1%)⁴.

Table (2): Correlations of AST and ALT with sero-positivity of HEV IgM antibody

Liver enzymes	Positive HEV IgM	Negative HEV IgM	p - value
AST (units/L)	183.3 ±104.8	140.4 ± 139.6	0.60
ALT (units/L)	131.6 ±103.9	98.43 ± 48.0	0.27

The frequency rate of HEV infection is relatively high in some developing countries. HEV seropositivity in India had been reported to be 18.6%; however the frequency rates in most developing countries had been reported to be 0.4-3.9%⁵.

Serosurveys in developed countries where HEV infection is not thought to be endemic, had consistently indicated seropositivity rates of 1-5%. Reports from Europe and the United States suggested that HEV infection may be endemic in some developed countries⁶.

Based on these reports, HEV infection is not unique to underdeveloped countries, although HEV infection is mainly transmitted via the fecal-oral route, transmission among humans, and transmission among domestic animals (pig, sheep, goats), and human-to-human transmission may occur via blood transfusion and in hemodialysis. Therefore, HEV infection is not area- or person-specific; and everyone worldwide is at risk for infection⁷.

In this study, the seroprevalence rates were higher in men than in women (66.6% and 33.3% respectively). ALT and AST levels were significantly higher in seropositive HEV patients. Similar results were reported in other studies. In Egypt (Nile Delta), a study conducted at least two times in 47 patients with high ALT level, 40 patients (89%) were found positive for anti HEV IgG⁸.

To date the degree and duration of HEV viremia has not been directly correlated with ALT or HEV antibodies. However, the results of the present context and previous studies indicate that elevated ALT may be due to sub-clinical HEV infections⁷.

Hence in patients with unexplained elevated ALT and AST, it is logical to consider HEV in the differential diagnosis.

Conclusion: The frequency rate of HEV IgM antibody was significantly high in seropositive patients; however, gender wise the frequency rate of HEV IgM antibody was statistically insignificant.

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