



## RESEARCH ARTICLE

## FREQUENCY OF HEPATITIS E VIRUS AMONG RENAL TRANSPLANT RECIPIENTS PATIENTS IN KHARTOUM - SUDAN

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## ABSTRACT

**Background:** Renal transplant recipients are known to be susceptible to viral infections, with more severe clinical presentations compared to healthy persons. Hepatitis E virus (HEV) is generally a self-limited disease, but it is a significant public health problem in organ transplant recipients, because it's responsible for chronic hepatitis in this group. **Objective:** This study aimed to detect the presence of anti-HEV IgG among organ transplantation recipient patient in Khartoum state during the period from July to September 2013. **Methods:** Enzyme-linked immunosorbent assay (ELISA) was used to detect anti-HEV IgG among 91-kidney transplant recipient patients. **Results:** 18 out of 91 patients (19.8%) were seropositive for anti-HEV IgG. There was no significant statistical correlation between HEV infection and duration of transplantation ( $P = 0.305$ ), and history of jaundice and HEV infection ( $P = 0.830$ ). **Conclusion:** This study found a high frequency of anti-HEV IgG antibody in Sudanese kidney transplant recipients.

**Key words:** Hepatitis E virus, ELISA, Anti-HEV IgG, Renal transplantation, Sudan

## INTRODUCTION:

Hepatitis E virus (HEV) infection is a significant public health problem in many parts of the world, causing large outbreaks of acute hepatitis <sup>(1)</sup>. Recent evidence suggests that in immune-compromised patients about 60% of acute hepatitis E evolve to chronic hepatitis with rapid progression to cirrhosis. Thus, HEV should be considered a cause of chronic hepatitis in immunocompromised patients, such as solid organ transplant recipients <sup>(2,3)</sup>. HEV is a single-stranded, non-enveloped RNA virus that is endemic in Southern Asia and Africa <sup>(4)</sup>. Hepatitis E virus has been reported to have four different genotypes, of which genotype 1 is the most prevalent type and is widespread in endemic regions, including most parts of Asia, and Northern Africa. The genotype of HEV causing HEV infections in developed countries is mostly different from that in endemic regions <sup>(5)</sup>. Viral particles are relatively stable in the environment and have been recovered from sewage samples <sup>(6)</sup>. The main route of HEV transmission is the fecal-oral route. However, several studies have also emphasized that transmission of HEV via non-fecal-oral routes appears to be possible <sup>(7)</sup>. There are reports of HEV infection in individuals who received blood transfusions in endemic areas <sup>(8,9)</sup>. The clinical features of hepatitis E are similar to those of acute viral hepatitis caused by other hepatotropic viruses. The incubation period has a range of 15 - 60 days, with a

mean of 40 days <sup>(10)</sup>. Hepatitis E clinically manifests with icterus, malaise, anorexia, fever, and hepatomegaly. HEV-infected persons exhibit a wide clinical spectrum, ranging from asymptomatic infection to fulminant hepatitis. <sup>(11)</sup>. There have been many large outbreaks reported in Asia and Africa. In contrast, while there have been sporadic cases of locally acquired hepatitis E in industrialized countries no epidemics have been reported <sup>(12,13)</sup>. Previous seroprevalence studies found that 6 - 16% of renal transplant recipients were positive for anti-HEV IgG antibodies <sup>(14,15)</sup>. Since the first retrospectively documented hepatitis E outbreak in India in 1955–1956 <sup>(16)</sup>, there have been many large outbreaks reported in Asia and Africa. In Sudan in 2004, there have more than 2600 cases affected by HEV infection is reported <sup>(13)</sup> and in Uganda in 2008, there have been many large outbreaks is reported <sup>(17,18)</sup>. The current study aimed to determine the seroprevalence of anti-HEV IgG among kidney transplant recipients in Khartoum state – Sudan.

## Patients and Methods:

The current descriptive, cross-sectional study carried out between July and September 2013. 91 patients were selected randomly from amongst patients who had undergone kidney transplantation in the Sudanese Kidney Transplanted Association Hospital Khartoum - Sudan. This study was approved by Al-Neelain University ethical

committee board and an informed consent was obtained from each patient or their relatives before collecting the demographic and clinical data. Five-mL blood samples were obtained by venipuncture for serological analyses. Samples were centrifuged and sera were separated immediately. Sera were stored at  $-20^{\circ}\text{C}$ , and tested for the presence of anti-HEV IgG antibody by enzyme-linked immunosorbent assay (ELISA) (DS-EIA-ANTI-HEV-G). The presence of anti-HEV IgG antibody was considered as the evidence for prior exposure to HEV. All collected data were analyzed using SPSS. Descriptive statistics were reported as the mean  $\pm$  SD for continuous variables and as the frequency (%) for dichotomous variables. To evaluate the relationship between different factors, we performed chi-square analysis. Quantitative variables were compared using independent t-test. *P. values* < 0.05 were considered statistically significant.

#### RESULTS:

Of the 91 kidney transplantation recipients attended Sudanese Kidney Transplanted Association Hospital

between July and September 2013, 62 (68.1%) were males and 29 (31.9%) were females. The age range was between 11 and 91 and the median age was 35.8 years. The duration of transplantation among the patients varies between a few months to several years, but about half of them (47.3%) were between 6 and 10 years. Regarding the signs and symptoms, 37 cases (40.7%) had a history of jaundice. According to patients medical records the major cause of renal failure was glomerulonephritis 31 cases (34.0%), followed by diabetes mellitus 23 cases (25.3%). All patients' blood samples were tested by ELISA for detection of anti-HEV IgG antibodies, 18 (19.8%) of those patients were positive. None of the participants, either in the anti-HEV positive group or in the seronegative group, were seropositive for other hepatitis viruses (hepatitis B virus [HBV], or hepatitis C virus [HCV]), except three cases (3.3%) were seropositive for hepatitis C virus [HCV] as demonstrated in the following table.

#### Demographic and clinical data

Characteristic	No.	%
Study group	<b>91</b>	100
Gender		
Male	<b>62</b>	68.1
Female	<b>29</b>	31.9
Age (Years)		
< 30	<b>31</b>	34.0
30 – 50	<b>34</b>	37.4
> 50	<b>26</b>	28.6
Duration of transplantation (Years)		
< 1	<b>25</b>	27.4
1 – 5	<b>43</b>	47.3
6 – 10	<b>10</b>	11.0
> 10	<b>13</b>	14.3
Signs and symptoms		
Previous history of jaundice	<b>37</b>	40.7
Cause of renal failure		
Glomerulonephritis	<b>31</b>	34.0
Hypertension	<b>22</b>	24.2
Diabetes mellitus	<b>23</b>	25.3
Urinary tract infection	<b>10</b>	11.0
Renal atrophy	<b>05</b>	05.5
Anti-HEV IgG antibodies		
Positive	<b>18</b>	19.8

Negative	<b>73</b>	80.2
Hepatitis B surface antigen (HBsAg)		
Positive	<b>0</b>	0.00
Negative	<b>91</b>	100
Hepatitis C virus antibodies (HCV Ab)		
Positive	<b>3</b>	03.3
Negative	<b>88</b>	96.7

#### DISCUSSION:

HEV virus is transmitted via the oral-fecal route; other possible routes of transmission include blood transfusions, drug vertical transmission, person-to-person contact, and zoonotic transmission. In endemic areas, exposure occurs in childhood<sup>(7)</sup>. In immunocompetent individuals, hepatitis E is a self-limited disease. However, HEV can cause chronic infection in solid organ transplants<sup>(2,3)</sup>, patients who receive chemotherapy<sup>(19)</sup>, so this study was carried out to estimate the frequency of the this virus in this group. HEV infection causes chronic hepatitis in more than 60% of recipients of solid organ transplants. Viral hepatitis E may progress rapidly to cirrhosis in renal transplant recipients<sup>(2,3)</sup>, so we recommend to screen for HEV at the time of transplantation is recommended in organ transplant donors and recipients. The diagnosis of viral hepatitis E in renal transplant HEV IgG is 6% to 16%<sup>(14,15)</sup>. In this study, about 20% were seropositive this variation may be due to differences in geographical variation and sample size. In outbreak among displaced population in western Sudan the prevalence rate of anti-HEV IgG was reported 65%<sup>(12)</sup>. The presentation of chronic hepatitis in renal transplant patients may be associated with normal liver enzymes and a negative serological assay<sup>(20)</sup>. This phenomenon underscores the need for molecular studies in suspected subjects. In the present study there is no significant statistical relationships between HEV infection and the patient's age ( $P = 0.845$ ), previous history of jaundice ( $P = 0.830$ ) and duration of transplantation ( $P = 0.305$ ).

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