Relative risk factors for seropositive hepatitis E virus among blood donors and haemodialysis patients: The pivotal role of primary health care education

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ABSTRACT

Background: Hepatitis E virus is a zoonotic virus with a worldwide epidemic outbreak. The aim of the study was to identify relative risk factors and co-infections concerning the seropositive HEV IgG among blood donors and haemodialysis (HD) patients in the central blood bank and renal dialysis centre in Wad Medani city, Gezira State, Sudan. Materials and Methods: This was a cross-sectional study that included 600 participants, among them 180 showed strong seropositive HEV IgG. The structured questionnaire was used to collect data of the participants’ demographics, disease risk factors and HEV IgG co-infections with HBV, HCV, HIV and syphilis. Results: Among the 180 strong seropositive HEV IgG respondents, 84 were blood donors and 96 were haemodialysis patients. The gender and age (18–30 years) had a significant association with the virus exposure (P = 0.000, P = 0.000). Importantly, a significant association of HEV prevalence due to the localities effect exhibited with the highest rate among South Gezira (OR = 38, CI = 14.1–107; P = 0.000). This also observed in Wad Medani, Umm Algura, East Gezira and Managil localities (P = 0.000). The effect of the animal contact on HEV distribution exerted the significant association among the respondents for blood donors and haemodialysis patients in univariate (OR = 4.09, 95% CI 1.5–10.9; P = 0.005) and multivariate (OR = 3.2, CI = 1.1–9.4; P = 0.027) analysis. Conclusion: The relative risk factors of the HEV seroprevalence were gender, age, locality and animal contact. Besides the need of a regular survey for the virus seroprevalence, primary health care physicians can play pivotal role in health education, especially in rural areas of Sudan. In addition, primary health care physicians in Sudan are expected to establish strategies and plans to eradicate and minimise the health impact of HEV.

Keywords: Blood donors, haemodialysis patients, HEV risk factors

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Introduction

The hepatitis E virus (HEV) classified as a single-stranded RNA virus of Hepevirus genus and Hepeviridae family is now one of the most causative agents of worldwide human hepatitis.[1] The viral isolation and phylogeny study of the entire viral genome revealed eight HEV genotypes (HEV 1–HEV 8).[2] Five genotypes (HEV1, HEV2, HEV3, HEV4 and HEV7) are known to cause human hepatitis.[3] HEV1 and HEV2 are a common cause of human hepatitis in developing countries due to contaminated water and poor sanitation measures, whereas HEV3 and HEV4 infect both human and various animals and in some cases, they can cause zoonotic infections.[1] The HEV1 and HEV2 Genotypes are endemic in most developing countries.[4] The virus have many routes of transmission: orally through contaminated food and water or through blood transfusion,[5] and it can also be transmitted through outbreak by faecal–oral routes, consumption of uncooked meat and zoonotic transmission,[6] or also through sewage contaminations of drinking water.[7] Possible transmission mainly through unprotected clean water and poor hygiene and contamination of water, especially in rural areas, can be attributed to animals.[8]

The seroprevalence of HEV in Sudan was identified among pregnant women during the outbreak with 14 intrauterine deaths and 9 premature deliveries[9] among the displaced camp population in Darfur Western Sudan.[10] Importantly, in Omdurman part of Khartoum state, the prevalence was found to be 26.7% among blood donors and risk increased with age.[11] Furthermore, in miscarriages, a significant association of HEV with diabetes mellitus, age and family history was found.[12] The HEV is widespread in African countries; for instance, in Egyptian population, HEV seroprevalence is significantly associated with older age over 30 years, people with the poor hand hygiene and contact with animals, especially cats.[13] Similar factors were also identified in Uganda.[14] Importantly, the use of wide opening tanks for water storage and the use of open bottles for washing hands in common places had a significant effect in virus transmission.[15] In Addis Ababa, Ethiopia, no association was concluded for the co-infection of HEV with the HIV prevalence,[16] whereas in Nigeria, risk factors identified were blood transfusion, animals contact, waste disposal, age, location, marital status, formal education and farming as an occupation.[17] It was also showed that alcohol consumption, rearing animals and locations were the risk factors that significantly correlated to the HEV distributions.[18]

Transmission can also occur with sharing a sanitation facility with other households as shown in a study from Chad.[19]

In the Afghan residence in Bushehr city, the HEV significant association resulted with variables concerned pregnant women aged over 34 years, ethnic groups, locations, pregnancy times and education level.[20] In a systemic review and meta-analysis for the HEV prevalence of 419 related studies that included 1519872 participants, the risk factors identified were contamination of meat, soil, blood, locations, contact with dogs and educational levels.[21] The other study conducted among Egyptian blood donors on screening of HEV, and co-infection with HBV and HCV, concluded a highly significant association with age, educational level, donor types and locations with an exception of an occupation.[22]

Furthermore, in a systematic search for several databases concerned the association of HEV among haemodialysis patients, 16 out of 31 studies identified that the patients on haemodialysis treatment were significantly associated with the HEV infection when compared with other groups.[23] However, in Sudan, there is lack of study in infections, co-infections and selected relative risk factors among seropositive HEV among blood donors and haemodialysis patients. Therefore, the aim of the study was to determine relative risk factors associated with seropositive HEV among blood donors and haemodialysis Sudanese patients.

Materials and Methods

A cross-sectional descriptive study with 600 participants in the period 2015–2016. Strong 180 seropositive HEV IgG out of 600 respondents were identified to study the relative risk factors and co-infections.

Data collection

The study took place at the Central blood bank and renal dialysis centre, Wad Medani, Teaching Hospital. The respondents were from the seven localities of Gezira state: Medani, El Managil, South Gezira, Eastern Gezira, Hasahisa, Umm Algura and El Gurashi.

The study recruited healthy people who attended the central blood bank for family blood donation and patients on renal dialysis treatment at renal dialysis centre. A structured questionnaire was used to collect data of the participants’ demographics, disease risk factors and HEV IgG co-infections with HBV, HCV, HIV and syphilis. Informed consents were obtained from all participants before enrolling in the study.

Statistical analysis

All the data of the enrolled participants concerned the results for HEV IgG seropositive and the risk factors associated with the disease were collected and analysed by SPSS version 24.

The analysed data were expressed in frequencies and percentages using cross tabulation that contained the HEV IgG seropositive results as dependent factors and the distribution of HEV IgG through healthy blood donors and haemodialysis patients concerning the relative risk factors for the HEV infection. Chi-square test, univariate analysis and multivariate analysis were used for analysis of the Odds ratio (OR) and the 95% confidence interval (CI), and the statistical significant was set as P < 0.05.
**Ethical approval**

The ethical approval for the study was obtained from the ethical and technical committee at Faculty of Medical Laboratory Sciences, University of Gezira, Sudan. Date of approval was 9/4/2017.

**Results**

**The sociodemographic effect on the HEV seroprevalence among the study groups**

The study revealed a distribution of the positive HEV IgG among 84/149 (56.4%) male blood donors versus 65/149 (43.6%) male haemodialysis patients, whereas, the seroprevalence among female blood donors resulted in 0.00% (no female blood donor) versus 31 (100%) haemodialysis patients (∼0). Furthermore, the study concluded that in a significant association by univariate and multivariate analysis for the virus seroprevalence concerned the age groups, the age group less than 30 years showed the highest risk to the virus exposures, 51/66 (77.3%) among the blood donors versus 15/66 (22.7%) among the haemodialysis patients (OR = 95.2, CI = 20.7–436.7; ∼0). However, the other age groups revealed the relatively lower risk to the virus exposures with a significant association with the viral seroprevalence (OR = 30.5, CI = 6.7–139.3; ∼0) [Table 1].

**Localities effect on the HEV seroprevalence among the study groups**

The current study concluded that HEV is an endemic virus in many localities in the Gezira State. Therefore, a significant association was found between the virus seroprevalence among the study groups and locality, with the highest association rate for the South Gezira locality (OR = 38.1, CI = 14.1–107; ∼0). In addition, a significant association also noted in localities of Umm Algura (OR = 35.2, CI = 9.1–135.1; ∼0), East Gezira (OR = 27.5, CI = 8.3–90.7; ∼0) and Medani (OR = 13.11, CI = 5.4–31.7; ∼0) [Table 2].

**Occupations effect on the HEV seroprevalence among the study groups**

The current study included respondents belonging to 10 different occupations that all revealed insignificant association to the HEV distribution in the blood donors and the patients of the haemodialysis. However, 60 out of 180 respondents had no work. Therefore, all of them were on haemodialysis, whereas 81 out of 180 had no definite occupation (workers) in which 70 (86.4%) were blood donors and 11 (13.6%) were haemodialysis patients (∼0) [Table 3].

**Water and food sources and animal contact effect on the HEV seroprevalence among the study groups**

The study included some relative risk factors regarding the virus seroprevalence among the study groups in which the factor of contact to animals or not revealed a significant association to the virus spread by univariate (OR = 4.09, 95% CI 1.5–10.9; ∼0.005) and multivariate (OR = 3.2, 95% CI 1.1–9.4; ∼0.007) analysis. The other relative factors (water and food sources) concluded insignificant association to the virus distribution among the study groups (∼0).

**HEV co-infections effect on the HEV seroprevalence among the study groups**

The study concluded that the infection with other viruses like HBV, HCV, HIV or infection with syphilis had no statistically significant association on the HEV seroprevalence among the study groups (∼0). However, the study concluded that the HCV was more likely associated with the haemodialysis patients (OR = 5.5, 95% CI = 0.65–46.9; ∼0.09). Furthermore,

### Table 1: Demographic effect on the positive HEV IgG seroprevalence

| Variables     | Positive HEV IgG | Total 100% | Univariate | Multivariate |
|---------------|-----------------|------------|------------|--------------|
|               | Blood donors    | Haemodialysis | OR (CI-95%) | P         | OR (CI-95%) | P         |
| Sex male      | 84-56.4%        | 65-43.6%    | 0.40       | 0.3-0.52    | 0.000      | 25.8      | 25.8      | 0.000    |
| Female        | 0-0.0%          | 1-100.0%   | 0.31       | 0.000       | 0.000      | 0.000     |
| Age-group 18-30 | 51-77.3%      | 15-22.7%   | 95.2       | 20.7-436.7 | 0.000      | 94.9      | 20.44-40.9 | 0.000    |
| 30-40 yrs.    | 31-55.4%        | 25-44.6%   | 56         | 7-156.5    | 0.000      | 30.5      | 6.7-139.3 | 0.000    |
| 40 and more   | 2-3.4%          | 56-96.6%   | 58         | 0.000      | 0.000      | 0.000     |

### Table 2: Localities effect on the HEV seroprevalence among the study group

| Localities | Positive HEV IgG | Total 100% | Univariate | Multivariate |
|------------|-----------------|------------|------------|--------------|
|            | Blood donors    | Haemodialysis | OR (CI-95%) | P         | OR (CI-95%) | P         |
| Medani     | 28-37.3%        | 47-62.7%    | 13.1       | 5.4-31.7    | 0.000      | 12.4      | 12.4      | 0.000    |
| Umm Al gura| 8-61.5%         | 5-38.5%     | 35.2       | 9.1-135.1   | 0.000      | 28.1      | 28.1      | 0.000    |
| South Al gezira | 23-63.9%   | 13-36.1%    | 38.1       | 14.1-107   | 0.000      | 32.8      | 32.8      | 0.000    |
| East Al gezira  | 10-55.6%       | 8-44.4%     | 27.5       | 8.3-90.7   | 0.000      | 20.8      | 20.8      | 0.000    |
| Managil      | 12-42.9%        | 16-57.1%    | 16.5       | 16.5-16.5  | 0.000      | 14.2      | 14.2      | 0.000    |
| Hasahisa     | 3-100.0%        | 0%          | 48.4       | 0.000-48.4 | 0.000      | 0.35      | 0.35-35.0 | 0.996    |
| Gurshy       | 0%              | 7-100.0%    | 48.4       | 0.000-48.4 | 0.000      | 0.35      | 0.35-35.0 | 0.996    |
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Discussion

This is a first study in Sudan about identifying relative risk factors associated with HEV in haemodialysis patients and blood donors. The previous studies in Sudan were about the seroprevalence of HEV during outbreaks, in pregnant women and in the blood donors. The current study demonstrated that HEV can be found in many localities in the Gezira State. The study found that there was a significant association between the HEV and a locality of the Gezira State. The study revealed that there is higher significant association of the virus with blood donors and haemodialysis patients. The risk factor of the age group concluded a significant association of the virus prevalence among the study groups with a higher HEV seroprevalence among the ages between 18 and 30 years and relative lower risk factor among the other age groups. The higher seroprevalence of the HEV among males is mainly between 18 and 30 years old. Therefore, males in this age are more likely to have the viral exposure. Our finding of the higher significant association of the virus among the younger age group is similar to that concluded by some authors in Sudan and Nigeria in contrast to a relatively lower among the elder in Sudan, Egypt, Ethiopia and Iran.

The current study demonstrated that HEV can be found in many localities in the Gezira State. The study found that there was a significant association between the HEV and a locality of

### Table 3: Occupation effect on the HEV seroprevalence among the study groups

| Occupation    | Positive HEV IgG | Total 100% | Univariate | Multivariate |
|---------------|------------------|------------|------------|--------------|
| Blood donors  |                  |            |            |              |
| Haemodialysis |                  |            |            |              |
| Not working   | 0%               | 60-100%    | 1.00       | 0.000        |
| Working       | 70-86.4%         | 11-13 0.6% | 14.0       | 0.000        |
| Driver        | 3-100.0%         | 0%         | 4.84       | 0.000        |
| Police officer| 3-100.0%         | 0%         | 4.84       | 0.000        |
| Engineer      | 1-50.0%          | 1-50.0%    | 22         | 0.000        |
| Teacher       | 1-50.0%          | 1-50.0%    | 22         | 0.000        |
| Health care   | 0-0.0%           | 1-100.0%   | 1.00       | 1.000        |
| Student       | 2-40.0%          | 3-60.0%    | 14.6       | 0.000        |
| Farmer        | 6-54.5%          | 5-45.5%    | 2.6        | 0.000        |
| House keeper  | 0-0.0%           | 14-100%    | 2.6        | 0.000        |

### Table 4: Water and food sources and animal contact effect on the HEV seroprevalence among the study groups

| Variables      | Positive HEV IgG | Total 100% | Univariate | Multivariate |
|----------------|------------------|------------|------------|--------------|
| Blood donors   |                  |            |            |              |
| Haemodialysis  |                  |            |            |              |
| Contact animal | 18-75.0%         | 6-25.0%    | 4.09       | 1.5-10.9     |
| No contact animal | 42.3-66%   | 90-57.8%   | 0.674      | 0.05-7.599   |
| Well           | 45.2-76%         | 54.8-92%   | 0.593      | 0.05-7.599   |
| Hafeer         | 4-66.7%          | 2-33.3%    | 0.463      | 0.62-13.5    |
| River          | 4-66.7%          | 2-33.3%    | 0.463      | 0.62-13.5    |
| Inside home    | 59-41.0%         | 59-0-85%   | 0.463      | 0.62-13.5    |
| Out side       | 13-81.3%         | 3-18.8%    | 0.463      | 0.62-13.5    |
| Inside and out side | 12-60.0% | 8-40.0%    | 2.889      | 0.18-1.2     |

### Table 5: HEV co-infections effect on the HEV seroprevalence among the study groups

| HEV co-infections | Positive HEV IgG | Total 100% | Univariate | Multivariate |
|-------------------|------------------|------------|------------|--------------|
| Blood donors      |                  |            |            |              |
| Haemodialysis     |                  |            |            |              |
| HBV Positive      | 4-33.3%          | 8-66.7%    | 1.82       | 0.52-6.2    |
| Negative          | 47.6-80%         | 88-52.4%   | 5.53       | 0.65-46.9   |
| HCV Positive      | 1-14.3%          | 6-85.7%    | 5.53       | 0.65-46.9   |
| Negative          | 83-48.4%         | 90-52.0%   | 5.53       | 0.65-46.9   |
| HIV Positive      | -1100%           | 0%         | 0.00       | 0.00        |
| Negative          | 83-46.4%         | 96-53.6%   | 0.048      | 0.38-5.2    |
| Syphilis Positive | 6-100.0%         | 0%         | 0.048      | 0.38-5.2    |
| Negative          | 78-44.8%         | 96-55.2%   | 0.048      | 0.38-5.2    |
| Co-infection      | 12-46.2%         | 14-53.8%   | 0.048      | 0.38-5.2    |
| Positive          | 72-46.8%         | 82-53.2%   | 0.048      | 0.38-5.2    |

the infection with the syphilis was more likely associated with the blood donors (P = 0.008) [Table 5].
the South Gezira. In addition to significant association in the localities of, Umm Alqura, East Gezira, and Medani. This higher prevalence of the virus might be due to more virus exposures via contaminated water or food and animal contact among the respondents in those localities. Several studies showed localities can be risk factors in Egypt, Nigeria and Iran.\cite{13,17,18,20,23}

We have shown that occupation had no direct effect to the HEV seroprevalence among the study group. Perhaps increasing the sample size may give better assessment for the impact of occupation on the risk of HEV. It was shown that farming as an occupation had a significant association with the HEV seroprevalence in Nigeria.\cite{17}

Our conclusion is that the animal contact had a significant association with the HEV seroprevalence among the study group. This finding is similar to that observed in the Egyptian population with frequent contact to cats,\cite{19} in Uganda among hunters (animal contact),\cite{14} in Nigerian among people whom rearing animals,\cite{19} in Chad among people sleeping inside an animal compound,\cite{19} and globally by a systemic review and meta-analysis among people having contact with dogs.\cite{21}

The study demonstrated insignificant association to the water and the food sources and places. However, many researchers indicated the responsibility of the water sources and the food places to the virus infections in Egypt, Napak District-Uganda, Northern-Uganda, and Plateau State, Nigeria.\cite{13,15,17}

The current study focused on the co-infection as one of the virus’ risk factors for the disease transmission observed no significant association with the HEV seroprevalence among the study group (\(P > 0.05\)). Therefore, it might be due to the difference in the transmission route between the HEV and of that of other blood-borne organisms. In contrast, study for blood transfusion in Egypt exhibited a significant association between HEV seroprevalence and the co-infection with HBV and HCV.\cite{22}

However, our conclusion is similar to that conducted in Addis Ababa, Ethiopia with no significant association with the reports for HIV status and the HEV infection.\cite{24}

Generally, the blood transfusion and the haemodialysis treatment are recognised risk factors for the HEV transmission.\cite{15,17,18,20,23}

Thus, effective control measures should be taken to minimise and control the HEV prevalence via these methods and establishing of a periodic survey, health education and provision of healthy water and food to populations.\cite{24}

The study is not without limitations. The samples were taken only from center in Sudan. Therefore, caution is need in the generalisation of the conclusion of this study to whole Sudan. Perhaps recruitment of patients from different places in Sudan will allow better characterisation of the risk factors. Despite these limitations, the study is novel and first in Sudan to characterise risk factors of HEV in haemodialysis patients and blood donors.

**Conclusion**

In conclusion, primary care physicians are expected to contribute in health education in rural and urban areas in Sudan for the risk factors associated with transmission of hepatitis E especially in relation to animal contact. For countries with low resource settings and system exhausted with COVID-19 pandemic, primary care physicians can educate and help extensively in the prevention of hepatitis E and surveillance of those at risk and also in introduction of control measures in the health system. Therefore, adopting all these strategies of prevention by primary health care physicians in Sudan may enhance the chance of eradication and minimisation of negative health impact of HEV in Sudan.

**Key points**

- The relative risk factors associated with seropositive HEV among blood donors and haemodialysis Sudanese patients were gender, age, locality and animal contact
- HEV can be found in many localities in the Gezira State (central Sudan); this can be related to richness of this area with water resource, agricultural schemes and animals.
- Primary care physicians have major role in regular survey for the virus seroprevalence, health education especially in rural areas of Sudan and establishment of strategies and plans to eradicate and minimise the health impact of HEV.

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**Conflicts of interest**

There are no conflicts of interest.

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