Original Article

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

Nassir A. Babiker[1], Adam D. Abakar[2], Nawal T. Mohamed[3], Nadir Abuzeid[4], GadAllah Modawe[5], Mohamed A. Iesa[6], Sami Assil[7], Hisham Osman[8], Mohamed Hamed[9], Mohamed H. Ahmed[10]

[1]Wad Medani Teaching Hospital for Obstetrics and Gynaecology, Gezira State, [2]Department of Medical Parasitology, Faculty of Medical Laboratory Science, Gezira University, Wad Madani, [3]Department of Parasitology NPHL Research Unit, Khartoum, [4]Department of Microbiology, Faculty of Medical Laboratory Sciences, [5]Department of Biochemistry, Faculty of Medicine and Health Sciences, Omdurman Islamic University, Khartoum, Sudan, [6]Department of Physiology, Al Qunfudah Medical College, Umm Al Qura University, Al Qunfudah, [7]Department of Community Medicine, Al Baha University, Al Bahah, Kingdom of Saudi Arabia, [8]Department of Gastroenterology, King's Mill Hospital, Sutton-In-Ashfield, Nottinghamshire, [9]Department of Gastroenterology, Inverclyde Royal Hospital, NHS Greater Glasgow and Clyde, Glasgow, [10]Department of Medicine and HIV Metabolic Clinic, Milton Keynes University Hospital NHS Foundation Trust, Milton Keynes, Buckinghamshire, United Kingdom

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

Access this article online

Quick Response Code:

Website:
www.jfmpc.com

DOI:
10.4103/jfmpc.jfmpc_2441_20

How to cite this article: Babiker NA, Abakar AD, Mohamed NT, Abuzeid N, Modawe G, Iesa MA, *et al*. Relative risk factors for seropositive hepatitis E virus among blood donors and haemodialysis patients: The pivotal role of primary health care education. J Family Med Prim Care 2021;10:2655-60.

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 shown 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-squire 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 (*P* = 0.000) [Table 1]. 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; *P* = 0.000). 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; *P* = 0.000) [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; *P* = 0.000). In addition, a significant association also noted in localities

of Umm Algura (OR = 35.2, CI = 9.1–135.1; *P* = 0.000), East Gezira (OR = 27.5, CI = 8.3–90.7; *P* = 0.000) and Medani (OR = 13.11, CI = 5.4–31.7; *P* = 0.000) [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 (*P* = 0.996) [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; *P* = 0.005) and multivariate (OR = 3.2, 95% CI 1.1– 9.4; *P* = 0.027) analysis. The other relative factors (water and food sources) concluded insignificant association to the virus distribution among the study groups (*P* > 0.05) [Table 4].

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 (*P* > 0.05) [Table 5]. However, the study concluded that the HCV was more likely associated with the haemodialysis patients (OR = 5.5, 95% CI = 0.65–46.9; *P* = 0.09). Furthermore,

Table 1: Demographic effect on the positive HEV IgG seroprevalence

V	Variables	Positive HEV IgG		Total 100%	Univariate			Multivariate		
		Blood donors	Haemodialysis		OR	CI-95%	P	OR	CI-95%	P
1111	Sex male	84-56.4%	65-43.6%	149	0.40	0.36-0.52	0.000	25.8	25.8	0.000
	Female	0-0.0%	31-100.0%	31						
2	Age-group 18-30	51-77.3%	15-22.7%	66	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	34.72	7.7-156.5	0.000	30.5	6.7-139.3	0.000
	40 and more	2-3.4%	56-96.6%	58						

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

V 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%	75	13.1	5.4-31.7	0.000	12.4	12.4	0.000
Umm Al gura	8-61.5%	5-38.5%	13	35.2	9.1-135.1	0.000	28.1	28.1	0.000
South Al gezira	23-63.9%	13-36.1%	36	38.1	14.1-107	0.000	32.8	32.8	0.000
East Al gezira	10-55.6%	8-44.4%	18	27.5	8.3-90.7	0.000	20.8	20.8	0.000
Managil	12-42.9%	16-57.1%	28	16.5	16.5-16.5	0.995	14.2	14.2	0.000
Hasahisa	3-100.0%	0%	3	48.4	0.000-48.4	0.995	0.35	0.35-.35	0.996
Gurshy	0%	7-100.0%	7	48.4	0.000-48.4	0.995	0.35	0.35-.35	0.996

Table 3: Occupation effect on the HEV seroprevalence among the study groups								
Occupation	Positive HEV IgG		Total 100%	Univariate			Multivariate		
	Blood donors	Haemodialysis		OR	CI-95%	P	OR	CI-95%	P
Not working	0%	60-100%	60	1.00	0.000	0.996	0.934	0.934-.93	1.000
Working	70-86.4%	11-13 0.6%	81	14.0	0.000	1.00	12.6	12.6-12.6	0.995
Driver	3-100.0%	0%	3	4.84	0.000	0.995	3	3	0.997
Police officer	3-100.0%	0%	3	4.84	48.4	0.997	4.4	4-4	0.994
Engineer	1-50.0%	1-50.0%	2	22	0.000	0. 996	2.3	2.3-2.3	0.996
Teacher	1-50.0%	1-50.0%	2	22	0.000	0.996	2.3	2.3-2.3	0.996
Health cares	0-0.0%	1-100.0%	1	1.00	1.000	0.996	1.0	1.0 -1.0	0.996
Student	2-40.0%	3-60.0%	5	14.6	0.000	0.996	14.2	14.2-14.2	0.996
Farmer	6-54.5%	5-45.5%	11	2.6	0.000	0.996	15.4	15.4-15.	0.996
House keeper	0-0.0%	14-100%	14	2.6	0.000	0.996	15.4	15.4-15.	1.000

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		OR	CI-95%	P	OR	CI-95%	P
Contact animal	18-75.0%	6-25.0%	24	4.09	1.5-10.9	0.005	3.2	1.1-9.4	0.027
No contact animal	42.3-66%	90-57.8%	156						
Well	45.2-76%	54.8-92%	168	0.413	0.74-2.317	0.315	0.674	0.05-7.599	0.688
Hafeer	4-66.7%	2-33.3%	6	0.413	0.74-2.317	0.315	0.593	0.05-7.599	0.688
River	4-66.7%	2-33.3%	6	1.000	0.911-1.02	1.00	0.593	0.05-7.599	0.688
Inside home	59-41.0%	59.0-85%	144	0.463	0.62-13.5	0.113	0.49	0.6-13.717	0.190
Out side	13-81.3%	3-18.8%	16	0.463	0.62-13.5	0.113	2.8	0.6-13.717	0.190
Inside and out side	12-60.0%	8-40.0%	20	2.889	0.18-1.2	0.18-1.2	2.8	0.6-13.717	0.190

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		OR	CI-95%	P	OR	CI-95%	P
HBV Positive	4-33.3%	8-66.7%	12	1.82	0.52-6.2	0.34	2	0.6-7.2	0.3
Negative	47.6-80%	88-52.4%	168						
HCV Positive	1-14.3%	6-85.7%	7	5.53	0.65-46.9	0.09	4.6	0.5-39.5	0.160
Negative	83-48%	90-52.0%	173						
HIV Positive	-1100%	0%	1	0.00	0.00	0.000	1.79	1.79-1.79	0.99
Negative	83-46.4%	96-53.6%	179						
Syphilis Positive	6-100.0%	0%	6	0.448	0.38-.52	0.008	2.79	2.79-2.79	0.996
Negative	78-44.8%	96-55.2%	174						
Co-infection Positive	12-46.2%	14-53.8%	26	0.648	0.26-1.5	0.336	0.595	0.24-1.5	0.268
Negative	72-46.8%	82-53.2%	154						

the infection with the syphilis was more likely associated with the blood donors (*P* = 0.008) [Table 5].

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.[10-12] This study concluded that, in 180 of strongly seropositive respondents, 149 were males and 31 were females and the study revealed that gender has a direct effect on the virus association 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[12,17] in contrast to a relatively lower among the elder in Sudan, Egypt, Ethiopia and Iran.[11,13,16,20]

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 South Gezira. In addition to significant association in the localities of, Umm Algura, East Cezira, and Medani. This higher prevalence of the virus might be due to more virus exposures via contaminated water or food and animal contact[5-8] among the respondents in those localities. Several studies showed localities can be risk factor in Egypt, Nigeria and Iran.[13,17,18,20,21]

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.[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,[13] in Uganda among hunters (animal contact),[14] in Nigerian among people whom rearing animals,[18] in Chad among people sleeping inside an animal compound,[19] and globally by a systemic review and meta-analysis among people having contact with dogs.[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.[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.[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.[16]

Generally, the blood transfusion and the haemodialysis treatment are recognised risk factors for the HEV transmission.[6,17,21,23] 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.[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.

Conflicts of interest

There are no conflicts of interest.

References

1. Larrue H, Abravanel F, Péron JM. Hepatitis E, what's the real issue? Liver Int 2020;40(Suppl 1):43-7.

2. Talapko J, Meštrović T, Pustijanac E, Škrlec I. Towards the improved accuracy of hepatitis e diagnosis in vulnerable and target groups: A global perspective on the current state of knowledge and the implications for practice. Healthcare (Basel) 2021;9:133.

3. Lee GH, Tan BH, Teo EC, Lim SG, Dan YY, Wee A, *et al.* Chronic infection with camelid hepatitis e virus in a liver transplant recipient who regularly consumes camel meat and milk. Gastroenterology 2016;150:355-7.e353.

4. Nelson KE, Labrique AB, Kmush BL. Epidemiology of Genotype 1 and 2 hepatitis e virus infections. Cold Spring Harb Perspect Med 2019;9:a031732.

5. Lin S, Zhang YJ. Advances in hepatitis E virus biology and pathogenesis. Viruses 2021;13:267.

6. Fu H, Wang L, Zhu Y, Geng J, Li L, Wang X, *et al.* Analysing complete genome sequence of swine hepatitis E virus (HEV),

strain CHN-XJ-SW13 isolated from Xinjiang, China: Putative host range, and disease severity determinants in HEV. Infect Genet Evol 2011;11:618-23.

7. Kluge M, Fleck JD, Soliman MC, Luz RB, Fabres RB, Comerlato J, *et al.* Human adenovirus (HAdV), human enterovirus (hEV), and genogroup A rotavirus (GARV) in tap water in southern Brazil. J Water Health 2014;12:526-32.

8. Shanan S, Abd H, Bayoumi M, Saeed A, Sandström G. Prevalence of protozoa species in drinking and environmental water sources in Sudan. Biomed Res Int 2015;2015:345619.

9. Rayis DA, Jumaa AM, Gasim GI, Karsany MS, Adam I. An outbreak of hepatitis E and high maternal mortality at Port Sudan, Eastern Sudan. Pathog Glob Health 2013;107:66-8.

10. Guthmann JP, Klovstad H, Boccia D, Hamid N, Pinoges L, Nizou JY, *et al.* A large outbreak of hepatitis E among a displaced population in Darfur, Sudan. The role of water treatment methods. Clin Infect Dis 2004;42:1685-91.

11. Ahmed AA, Hamedelnil YF. Seroprevalence of hepatitis E virus among blood donors in Omdurman locality, Sudan, Am J Res Commun 2015;3:252-8.

12. Ahmed NEIM, Abuzeid NMK, Mohammed A. Assessments of sero-detection of HEV antibodies IgG and IgM among spontaneous recurrent miscarriage women case control study in Gezira State 2018. Int J Sci Res 2020;9:1431-5.

13. Stoszek SK, Abdel-Hamid M, Saleh DA, El Kafrawy S, Narooz S, Hawash Y, *et al.* High prevalence of hepatitis E antibodies in pregnant Egyptian women. Trans R Soc Trop Med Hyg 2006;100:95-101.

14. Amanya G, Kizito S, Nabukenya I, Kalyango J, Atuheire C, Nansumba H, *et al.* Risk factors, person, place and time characteristics associated with Hepatitis E Virus outbreak in Napak District, Uganda. BMC Infect Dis 2017;17:451.

15. Howard CM, Handzel T, Hill VR, Grytdal SP, Blanton C, Kamili S, *et al.* Novel risk factors associated with hepatitis E virus infection in a large outbreak in northern Uganda: Results from a case-control study and environmental analysis. Am J Trop Med Hyg 2010;83:1170-3.

16. Abebe M, Ali I, Ayele S, Overbo J, Aseffa A, Mihret A. Seroprevalence and risk factors of Hepatitis E Virus infection among pregnant women in Addis Ababa, Ethiopia. PLoS One 2017;12:e0180078.

17. Junaid SA, Agina SE, Abubakar KA. Epidemiology and associated risk factors of hepatitis e virus infection in plateau state, Nigeria. Virology (Auckl) 2014;5:15-26.

18. Osundare FA, Klink P, Majer C, Akanbi OA, Wang B, Faber M, *et al.* Hepatitis E virus seroprevalence and associated risk factors in apparently healthy individuals from Osun State, Nigeria. Pathogens 2020;9:392.

19. Vernier L, Lenglet A, Hogema BM, Moussa AM, Ariti C, Vollmer S, *et al.* Seroprevalence and risk factors of recent infection with hepatitis E virus during an acute outbreak in an urban setting in Chad, 2017. BMC Infect Dis 2018;18:287.

20. Farshadpour F, Taherkhani R, Ravanbod MR, Eghbali SS, Taherkhani S, Mahdavi E. Prevalence, risk factors and molecular evaluation of hepatitis E virus infection among pregnant women resident in the northern shores of Persian Gulf, Iran. PLoS One 2018;13:e0191090.

21. Li P, Liu J, Li Y, Su J, Ma Z, Bramer WM, *et al.* The global epidemiology of hepatitis E virus infection: A systematic review and meta-analysis. Liver Int 2020;40:1516-28.

22. Ahmed AMA, Temerk HA, Galal HR, Bazeed SES, Sultan S. The seropervelance of infectious hepatitis viruses (HBV, HCV and HEV) among blood donors and their correlation to risk factors in Qena governorate, Upper Egypt. Virusdisease 2020;31:292-8.

23. Haffar S, Bazerbachi F, Leise MD, Dillon JJ, Albright RC, Murad MH, *et al.* Systematic review with meta-analysis: The association between hepatitis E seroprevalence and haemodialysis. Aliment Pharmacol Ther 2017;46:790-9.

24. Kirkwood CD, Dobscha KR, Steele AD. Hepatitis E should be a global public health priority: Recommendations for improving surveillance and prevention. Expert Rev Vaccines 2020;19:1129-40.