

Sero-Detection of HEV in Cancer Patients and Healthcare Workers, Sudan

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ABSTRACT

Background: Sudan, as a developing country, suffers from most of the risk factors related to the transmission of the hepatitis E virus (HEV).

Objective: This study aimed to determine the sero-frequency of HEV in cancer patients and healthcare workers and its associated risk factors.

Methods: A descriptive cross-sectional design was followed, recruited populations were 120 cancer patients and 120 healthcare workers. Socio-demographic data and risk factors of the study subject were collected using a questionnaire and patient records. HEV-specific anti-HEV IgM and IgG antibodies screened by a competitive ELISA technique. A Chi-square test was determined for the association between HEV IgG sero-positivity and subject information.

Results: The percentage of cancer patients positive for anti-HEV IgG and IgM antibodies was 50% (60/120) and 6.7% (8/120) while for the healthcare workers group was 25.8% (31/120) and 4.2% (5/120) respectively. The most documented risk factors for HEV among cancer patients were consumption of raw meat 94.2% (113/120), contact with animals 88.3% (106/120), and history of blood transfusion 81.7% (98/120) while raw meat consumption was commonly found in 94.2% (113/120) of healthcare workers group. A significant association was observed between IgG sero-positive healthcare workers and consumption of raw meat (p-value = 0.005).

Conclusion: The HEV sero-positivity was found at a high rate in both study groups, which requires further studies on its prevalence, epidemiology, and prevention.

Keywords: Cancer patients, Healthcare workers, HEV, Sudan.

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1. INTRODUCTION

Hepatitis E virus (HEV) is the most common hepatitis virus transmitted through the gastrointestinal tract and a major cause of water-related epidemics in Asia, Africa, India and Mexico [1], [2]. Recorded cases of HEV infection worldwide are on the rise, including deaths among high-risk groups and asymptomatic cases [3], [4]. Given the mode of transmission of the virus, developing countries are the most affected [5].

Cancer is one of the greatest threats to life in the world, with frightening mortality rates, especially in third-world countries, where the quality of life is poor [6]. Reducing the prevalence of cancer is a difficult task, so the incidence to the disease is increasing in most countries of the world. Cancer studies indicated that a large proportion of cancer cases are associated with microbial diseases, an example

of this is the relationship between hepatitis B virus protein and liver cancer development [7]. Like other hepatic viruses, HEV can destroy liver tissue, which can lead to pathological changes, such as regeneration of liver growth factors leading to neoplastic changes [8].

Hepatitis E virus can be diagnosed in its acute phase clinically, by detecting IgM and/or RNA. A recent surveillance recognized eight genotypes of HEV, of which HEV-1, 2, 3, 4, and 7 are related to humans only. Genotypes 1 and 2 have been encountered in outbreaks in lower-middle-income countries [9]. It is very clear that transmission of HEV is associated with occupation, such as exposure to pigs [10], [11] and sheep [12], so healthcare workers are at risk from contact with cases, including patients with hepatitis. In a separate study, we found high levels of HEV sero-frequency in pregnant Sudanese women, at a rate of 44% [13], although pregnancy weakens immunity, this

high percentage also indicates community spread of HEV. Eventually, we can summarize several reasons why there is a need to control HEV infection such as the development of appropriate vaccine: 1) HEV is re-emerging even in developed countries such as Europe [14], 2) HEV can cause epidemic cases [15], 3) Increase cases around the world [16] and 4) the licensing of a vaccine against HEV, as in China [17]. This study aimed to detect sero-positivity of HEV IgG and IgM among Sudanese cancer patients and healthcare workers from Gezira State and to identify associated risk factors.

2. METHODS

2.1. Design and Settings

This was a descriptive cross-sectional study aimed at investigating sero-positivity of HEV among cancer patients admitted to the National Cancer Institute, University of Gezira, and healthcare workers in Gezira State, Sudan from August 2016 to November 2018. Gezira State is well-populated and inhabited by a mixture of races and tribes from inside and outside Sudan. This study included the following localities: Greater Wad Medani, Elkamleen, El Managil, Southern of Gezira, Um-Alqura, Eastern Algezira, and Elhassaheasa.

2.2. Study Population

The study included two groups: cancer patients and healthcare workers; cancer patients are previously diagnosed cases and receive treatment at the National Cancer Institute at the University of Gezira while the other group includes workers in healthcare from various localities in the Gezira State and with different jobs and educational levels. Participants' data on socio-demographics and risk factors were obtained using a questionnaire and from patients' records.

2.3. Sampling and Sero-Detection of HEV

The study was based on a non-probability convenience sampling technique during the attendance of cancer patients and healthcare workers in Gezira State. In total, 240 venous blood specimens were obtained (120 cancer patients and 120 healthcare workers), and serum was collected and stored at 20 °C until used. Specific anti-HEV IgM and IgG were quantitatively measured using a competitive enzyme-linked immune-sorbent assay (ELISA) (MIKROGEN GmbH-Germany) according to the manufacturer's instructions.

2.4. Data Analysis

Descriptive analysis of frequencies and association of study variables was accomplished by SBSS computer program version 20. P-value of less than 0.05 is considered significant.

2.5. Ethical Approval

This study was approved by the Faculty of Medical Laboratory Sciences, University of Gezira, and Ministry of Health, Gezira State.

3. RESULTS

3.1. Socio-Demographics and Risk Factors

There were 120 cancer patients, their ages ranged from 3 to 90 years, with an average of 50.2 years. The frequency of female patients 68.3% (82/120) was higher than that of males 31.7% (38/120). The cases came from all localities in the State, Eastern Al-Jazeera 21.7% (26/120) and Greater Wad Medani 21.7% (26/120) localities were the most mentioned. Residence in rural areas among cancer patients included in the study accounted for 69.2% (83/120). The illiteracy rate and the level of primary education together reached 55.8% (67/120). Wells were the most commonly used source of water with a percentage of 66.7% (80/120). Personal hygiene observations of participating patients found that 64.2% (77/120) of them had a poor level of

TABLE I: SOCIO-DEMOGRAPHICS OF CANCER PATIENTS SUBJECT (No. 120) AND ITS ASSOCIATION WITH HEV IgG POSITIVITY

Socio-demographic		Frequency (%)	Frequency of positive IgG	p-value
Gender	Male	38 (31.7)	21	0.432
	Female	82 (68.3)	39	
	Total	120 (100)	60	
Locality	Elkamleen	2 (17)	2	0.481
	Elhassaheasa	11 (9.2)	3	
	Eastern Algezira	26 (21.7)	12	
	Um Elqura & South Algezira	19 (15.8)	9	
	Greater wad medani	26 (21.7)	13	
	Elmanagil	15 (12.5)	9	
	Other	21 (17.5)	12	
	Total	120 (100)	60	
Residence	Urban	37 (30.8)	17	0.553
	Rural	83 (69.2)	43	
	Total	120 (100)	60	
Occupation	House wife	53 (44.2)	25	0.486
	Worker	33 (27.5)	19	
	Employee	22 (18.3)	12	
	Other	12 (10)	4	
	Total	120 (100)	60	
Education level	Uneducated	40 (33.3)	18	0.110
	Primary	27 (22.5)	19	
	Secondary	28 (23.3)	13	
	University	25 (20.8)	10	
	Total	120 (100)	60	
Water source	Wells	80 (66.7)	40	0.951
	River	19 (15.8)	9	
	Canals	21 (17.5)	11	
	Total	120 (100)	60	
Hygiene	Bad	77 (64.2)	36	0.341
	Good	43 (35.8)	24	
	Total	120 (100)	60	
Dietary intake	Inside home	103 (85.8)	52	0.793
	Outside home	17 (14.2)	8	
	Total	120 (100)	60	

TABLE II: CLINICAL AND RISK FACTORS OF CANCER PATIENTS SUBJECT (No 120) AND ITS ASSOCIATION WITH HEV IgG POSITIVITY

Risk factor		Frequency (%)	Frequency of positive IgG	p-value
Jaundice	Yes	7 (5.8)	5	0.243
	No	113 (94.2)	55	
	Total	120 (100)	60	
History of viral hepatitis	Yes	13 (10.8)	4	0.142
	No	107 (89.2)	56	
	Total	120 (100)	60	
History of blood transfusion	Yes	98 (81.7)	46	0.157
	No	22 (18.3)	14	
	Total	120 (100)	60	
Consumption of raw meat	Yes	113 (94.2)	55	0.243
	No	7 (5.8)	5	
	Total	120 (100)	60	
Animal contact	Yes	106 (88.3)	54	0.570
	No	14 (11.7)	6	
	Total	120 (100)	60	
Type of cancer	CML	6 (5)	2	0.305
	Prostate	10 (8.3)	5	
	Breast	52 (43.3)	25	
	CLL	12 (10)	6	
	Ovary	9 (7.5)	4	
	Testis	4 (3.3)	4	
	Lymphomas	5 (4.2)	4	
	Esophagus	2 (1.7)	2	
	Other	20 (16.7)	8	
	Total	120 (100)	60	

Key: CML: Chronic myeloid leukemia, CLL: Chronic lymphoid leukemia.

hygiene (Table I). The most documented risk factors for HEV were consumption of raw meat 94.2% (113/120), contact with animals 88.3% (106/120), and history of blood transfusion 81.7% (98/120) while breast cancer was the predominated type with the percentage of 43.3% (52/120) (Table II).

For healthcare worker female participants, rural residence, employee occupation and university education represented 70% (84/120), 67.5% (81/120), 72.5% (87/120), and 83.3% (100/120) respectively (Table III). Raw meat consumption was commonly found in 94.2% (113/120) of participants (Table IV).

3.2. HEV Sero-Detection

In cancer participants, HEV IgG sero-positivity was 50% (60/120) while IgM equal 6.7% (8/120), no association was observed between IgG sero-positivity and socio-demographics or risk factors. Positivity to both HEV IgG and IgM antibodies was recorded in seven patients and only 1 patient showed positive IgM and negative IgG.

HEV IgG and IgM sero-positive results of healthcare workers were 25.8% (31/120) and 4.2% (5/120) respectively. The five cases that showed positive HEV IgM were also positive for IgG antibodies. A significant association was found between IgG sero-positive subjects and consumption of raw meat (p-value 0.005) (Table IV).

TABLE III: SOCIO-DEMOGRAPHICS OF HEALTHCARE WORKERS SUBJECT (No. 120) AND ITS ASSOCIATION WITH HEV IgG POSITIVITY

Socio-demographic		Frequency (%)	Frequency of positive IgG	p-value
Gender	Male	36 (30)	9	0.891
	Female	84 (70)	22	
	Total	120 (100)	31	
Locality	Elkamleen	2 (1.7)	1	0.839
	Elhassaheasa	10 (8.3)	3	
	Eastern Algezira	26 (21.7)	6	
	Um Elqura & South Algezira	19 (15.8)	4	
	Greater wad medani	26 (21.7)	9	
	Elmanagil	15 (12.5)	4	
	Other	22 (18.3)	4	
Residence	Urban	39 (32.5)	11	0.680
	Rural	81 (67.5)	20	
	Total	120 (100)	31	
Occupation	Worker	33 (27.5)	5	0.100
	Employee	87 (72.5)	26	
	Total	120 (100)	31	
Education level	Secondary	20 (16.7)	5	0.926
	University	100 (83.3)	26	
	Total	120 (100)		
Water source	Wells	80 (66.7)	21	0.883
	River	40 (33.3)	10	
	Total	120 (100)		
Hygiene	Bad	0 (0)		NA
	Good	120 (100)		
	Total	120 (100)		
Dietary intake	In side home	34 (28.3)	6	0.198
	Outside home	86 (71.7)	25	
	Total	120 (100)	31	

4. DISCUSSION

There is no doubt that the increase in cases of infection with HEV has made it a global health risk, especially in developing countries where there are many factors that contribute to the transmission of the disease [18]. The genetic variation of the HEV genotypes also helped in the transmission of the virus from animal sources such as pigs and sheep [19]. Very little has been studied about HEV in Sudan, and therefore there is no data available on the prevalence of the disease in the community and the existing genotypes, however, a large epidemic was documented in Sudan in the border region of Darfur in 2004 [20], [21].

This study examined the frequency of HEV antibodies in cancer patients and healthcare workers. Cancer and its treatment weaken the patients' immunity and predispose them to various diseases [22] while medical settings expose workers to viral pathogens, especially in the presence of limited resources, environmental pollution, and the absence of necessary infection control precautions [23].

TABLE IV: RISK FACTORS OF HEALTHCARE WORKERS SUBJECT (No 120) AND ITS ASSOCIATION WITH HEV IgG POSITIVITY

Risk factor		Frequency (%)	Frequency of positive IgG	p-value
Jaundice	Yes	0 (0)	–	NA
	No	120 (100)	31	
	Total	120 (100)	31	
History of viral hepatitis	Yes	0 (0)	–	NA
	No	120 (100)	31	
	Total	120 (100)	31	
History of blood transfusion	Yes	0 (0)	–	NA
	No	120 (100)	31	
	Total	120 (100)	31	
Consumption of raw meat	Yes	113 (94.2)	26	0.005
	No	7 (5.8)	5	
	Total	120 (100)	31	
Animal contact	Yes	0 (0)	–	NA
	No	120 (100)	31	
	Total	120 (100)	31	
Job type	Medical	14 (11.7)	5	0.222
	Worker	26 (21.7)	10	
	Nurse	48 (40)	9	
	Laboratory	32 (26.6)	7	
	Total	120 (100)	31	

The results showed that the sero-frequency of HEV IgG in cancer patients was 32.5%, which is higher compared to the estimated global rate of 12.47% [3] and indicative of a multiple transmission scenario. Cancer diseases usually weaken the body's immune lines, resulting in chemo or radiotherapy, in addition, a large number of cancer patients require blood transfusions, the latter represents one of the methods of transmission of HEV [24]–[26]. In the present study, we found that a large percentage (81.7%) of the cancer patients received blood. In this context, another study suggested the hypothesis that occult hepatitis B virus is mostly transmitted to patients with chronic kidney disease through blood transfusion [27].

According to the results of this study, HEV IgG positivity is not influenced by gender, age, place of residence, occupation, and educational levels. With some variation, other studies have published higher rates in men [28], [29] and rural individuals [30]. Differences in HEV IgG sero-positivity between urban and rural areas assume the presence of multiple risk factors in rural residence such as drinking river and canal water, and exposure to animals and soil [31], [32].

The current findings estimated the presence of anti-HEV IgM antibodies in 6.7% and 5% of cancer patients and healthcare workers, which is also more than the prevalence reported globally [3]. The reasons that explain the presence of anti-HEV IgG antibodies with a higher positivity than anti-HEV IgM are that HEV IgM is associated with acute illness and disappears in a short period, while HEV IgG remains for a longer period in the blood of the infected persons. IgG can also be detected in cases of exposure to the virus or previous infections [33].

Consumption of uncooked meat as one of the risk factors for transmission of HEV was recorded at high rates in both research groups, and more than that, it gave a significant association ($p\text{-value} = 0.005$) with the positivity of anti-HEV IgG antibodies in the healthcare workers, this because Sudanese people, like many others around the world, are accustomed to eating parts of sheep and cow meat without cooking. It is known that consumption of uncooked meat is a major cause of zoonosis [34] and some infectious diseases [35]. In general, the serological frequency of HEV among healthcare workers recorded in this study is an indicator of the extent of the spread of HEV in the community, so necessary precautions to limit the spread of the disease such as community surveys and vaccination studies should be activated.

5. CONCLUSION

In conclusion, the high sero-frequency of HEV among cancer patients and healthcare workers is a strong indicator of the endemicity of the virus in Sudan, which is a poor country with limited resources to confront infectious diseases. However, measures should be taken to prevent HEV transmission in community and healthcare settings, including the vaccination program.

5.1. Study Limitation

This study was limited by the lack of confirmatory identification of epidemic genotypes of HEV in antibody-positive cases and did not take into account other hepatitis indicators such as measurement of liver enzymes.

CONFLICT OF INTEREST

Authors declare that they do not have any conflict of interest.

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