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PREVALENCE AND RISK FACTORS OF HEPATITIS G VIRUS INFECTION AMONG YEMENI HEMODIALYSIS PATIENTS

KEY WORDS: Hepatitis G virus, Hemodialysis, Risk factor, Antibodies, ELISA, Yemen

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ABSTRACT

Background and Objective: Hepatitis G virus (HGV) is a recently described member of *Flaviviridae* viruses. Increasing the risk of blood-borne infections in hemodialysis patients is a main health care concern in different countries. The current study aimed to investigate the prevalence and risk factors of HGV among Yemeni hemodialysis patients.

Methods: Cross sectional study was conducted in hemodialysis patients who were selected randomly from haemodialysis units of different general hospitals at Sana'a city, from October 2013 to October 2014. Blood samples were collected and tested for human HGV IgG antibodies in patient's sera by commercially ELISA technique.

Results: Of the 360 hemodialysis patients, anti-HGV antibodies was determine in 24 (6.7%), female with highest rate 14(7.4%) and male 10 (5.8%). Furthermore, duration of dialysis ≤1 year 3.6 % to 2 years 12.8 %, was positively significant between HGV positive and HGV negative patients ($P < 0.001$), and sexual contact with HGV ($P < 0.006$).

Conclusions. Hepatitis G Virus was prevalent among hemodialysis patients in Sana'a Yemen, sexual transmission and duration of dialysis are very important to increase the risk of HGV transmission. Further epidemiologic monitoring of HGV may be helpful to control future potential variations of the virus.

INTRODUCTION

The prevalence of hepatitis infection among hemodialysis patients is high and varies between countries and between dialysis units within a single country. Hemodialysis patients are at a high risk of infectious complications. Hepatitis B virus (HBV) was the most common etiologic agent of hepatitis in chronic hemodialysis patients prior to developing screening system and vaccines. Afterwards, hepatitis C virus (HCV) was a main problem in chronic hemodialysis[1]. The new enveloped RNA virus similar to *flaviviruses* was isolated by two independent laboratories in the USA from 1995-1996. GB virus C/GBV-C as first laboratory names and the second as hepatitis G virus (HGV)[2]. HGV is a virus in the *flaviviridae* family and known to be infectious for human, but it has not been established to cause human disease with certainly[3]. However, there is a suspicious link between HGV infection and acute or fulminant hepatitis, chronic hepatitis and hepatic fibrosis[4,5]. HGV infection has a worldwide distribution. Until now, five major genotypes of HGV are known as genotype 1 is the most common in the West Africa, genotype 2 known in the US and Europe, genotype 3 in parts of Asia, genotype 4 is specific for Myanmar, Vietnam and Indonesia and finally genotype 5 is frequently observed in South Africa [6,7]. High prevalence is observed among subjects with risk of parenteral exposure including those with exposure to blood and blood products, such as Hemodialysis patients and intravenous drug users[8]. Hemodialysis patients and other kinds of chronic renal failure patients usually require blood transfusion. It is one of main risk factors of HGV transmission[9,10,11]. Some studies suggested links between HGV and transfusion requirement, dialysis duration, renal transplantation and other kinds of viral hepatitis in Hemodialysis patients[10,12]. Approximately 2% of healthy United States blood donors had viremia with HGV and up to 13% of blood donors had antibodies against E2 protein, indicating a possible prior infection[13]. Sexual contact and vertical transmission could be another route of HGV transmission.

Increased chronic disorders such as diabetes, renal failure and end stage renal disease have become important issues in health care policies. Therefore, hemodialysis and its complications are major hospital concerns. However, none of the studies indicated that HGV infection can cause any liver enzyme elevation or hepatic failure certainly, but co-infection with other hepatitis viremia can increase morbidity and mortality rates[14,15].

Therefore, estimating HGV infection in hemodialysis patient's units of different countries seems to be reasonable and applicable in health care system to design standard prevention and treatment plans. The aim of the present study was to determine the prevalence and risk factors of HGV among Yemeni hemodialysis patients.

MATERIAL AND METHODS

Study Population

Descriptive cross-sectional study was conducted in hemodialysis unit at Al-Thowra Hospital Hemodialysis Centre, University Science and Technology Hospital, Dr. Abdulkader Al-Motawkel Hospital, and Saudi Germany Hospital, Sana'a Yemen, from October 2013 to October, 2014. Survey covered 360 patients of 4 dialysis units, 172 males and 188 females, respectively. Epidemiological data were obtained from all patients; history of previous blood transfusion, length of time on dialysis, history of major surgery, blood group, household contact with hepatitis, family history of hepatitis, age and gender. Consent form was ensured before collection of data and drawing sample.

Enzyme Linked Immunosorbent Assay

ELISA Diagnostic Kit (Diagnostic Automation, INC, USA) was used for evaluates immunoglobulin G (IgG) developed against HGV protein. The two-step incubation process of ELISA was performed according to the manufacturer's where serums were diluted by sample buffer (1/10 ratio), the diluted samples were added to wells

and incubated at 37 °C for 30 minutes and then washed with antihuman antibody and conjugated with horse radish peroxidase (HRP) and then incubate at 37 °C. After well rewashing, substrate was added and the chromogenic reaction was blocked by stopping solution. Optical density of each sample was measured in 450 nm and 630 nm as reference filter. To evaluate HBV and HCV involvement in the patients, serological determination was done using hepatitis B surface antigen (HBs-Ag) and HCV-Ab ELISA kits (Diagnostic Automation, INC, USA) according to the kit manufacturers.

Statistical analysis.

Statistical analysis was conducted using Chi-square test, and the prevalence determination of each investigated variable; the confidence interval of 95% (CI = 0.95) was considered to estimate significant results. Data were recorded and analyzed using SPSS software ver. 19 (SPSS Inc., Chicago Ill., USA).

RESULTS

The study population consisted of 81 males (59%) and 57 females (41%), age and sex distribution of hemodialysis patients, 10.6% of the patients were under 20 years, 22.2% were from 20-29 years, 18.9% were from 30 – 39 years, 12.8% from 40-49 years, and 35.6% were equal or over 50 years (Table 1).

Table 1. Age and sex distribution of hemodialysis patients studying for HGV infection in 4 general hospitals in Sana'a Yemen.

Age groups	Male N = 172		Females N = 188		Total = 360	
	No	%	No	%	NO	%
> 20 years	18	10.5	20	10.6	38	10.6
20 – 29 years	44	25.6	36	19.1	80	22.2
30 – 39 years	20	11.6	48	25.5	68	18.9
40 – 49 years	18	10.5	28	14.9	46	12.8
≥ 50 years	72	41.9	56	29.8	128	35.6
Total	172	47.8	188	52.2	360	100

HGV infection was 6.7%, HBV infection was 20.7%, and HCV was 48.8% and female prevalence rate was 47.2% roughly similar to that the male as shown in Table 2.

Table 2. Prevalence rate of anti-HGV antibodies, anti-HBs antibodies and anti-HCV antibodies among hemodialysis patient in 4 general hospitals in Sana'a Yemen.

Variable	Male N = 172		Female N = 188		Total No = 360		*OR*	*CI*	X^2	*PV*
	No	%	No	%	No	%				
Anti-HGV antibodies	10	5.8	14	7.4	24	6.7	0.77	0.3-1.9	0.38	0.53
HBs antigens	44	25.6	30	16	74	20.7	1.8	1.1-3.15	5.1	0.02
Anti-HCV antibodies	84	48.8	86	45.7	170	47.2	1.13	0.7-1.7	0.34	0.55

OR Odds ratio > 1. (at risk) x^2 Chi-square ≥ 3.84 & $p < 0.05$ (significant).

Prevalence rates of hepatitis G virus infection with co infection hepatitis B hepatitis C viruses among hemodialysis patients. HGV infection was 6.7%, HBV infection was 20.7%, and HCV was 48.8% and female prevalence rate was 47.2% roughly similar to that the male as shown in Table 3.

Table 3. Co-infection of HGV with HBV and HCV and co-infection odds ratio among hemodialysis patient.

Co-infection	HGV positive N = 24		*OR*	*CI*	x^2	*PV*
	No	%				
Anti-HBs antibodies positive N = 74	6	8.1	1.3	0.45 – 3.7	0.31	0.57
Anti-HCV antibodies positive N = 170	14	8.2	1.6	0.65 – 4.04	1.27	0.25
Negative HCV& HBV N= 116	4	3.4	5.4	1.33 – 20.4	9.04	0.002

OR Odds ratio > 1. (at risk) x^2 Chi-square ≥ 3.84 & $p < 0.05$ (significant).

Additionally the marital status and occupation associated with HGV infection 108 (5.6%) among single HD patients with HGV positive in compare to 222 (8.1%) among married HD with OR 1.94 although it's non-significant. The prevalence rate HGV patients based on occupation working indoor equal to 9.2%, comparing with 5.2% outdoor working but the variation between the was not statistically significant as shown in Table 4.

Table 4. Occupation and marital status associated with HGV infection among hemodialysis patient.

Marital states	Positive HGV		*OR*	*CI*	x^2	*PV*
	No	%				
Single N = 108	6	5.6	0.76	0.26-2.12	0.31	0.58
Married N = 222	18	8.1	1.94	0.7 – 5.6	1.93	0.16
Divorced N = 30	0	0	0.0	0 – 2.2	2.3	0.12
Occupation						
Outdoors N = 230	12	5.2	0.54	0.22-1.34	2.15	0.14
Indoors N = 130	12	9.2	1.85	0.75-4.56	2.15	0.14

OR Odds ratio > 1. (at risk) x^2 Chi-square ≥ 3.84 & $p < 0.05$ (significant).

The occurrence of asymptomatic sigs of hepatitis among HD patients counted 258 patients, the prevalence rate of HGV among them was 5.4%, the first sign jaundice 96 (10.1%.) then 108 (9.3%) a history of hospitalization for hepatitis while OR 1.73 with non-significant Table 5.

Table 5. Clinical status associated with HGV infection among hemodialysis patients.

Clinical date	Positive HGV N = 24		*OR*	*CI*	x^2	*PV*
	NO	%				
Asymptomatic N = 258	14	5.4	0.53	0.2 - 1.33	2.25	0.13
Jaundice N = 96	10	10.4	2.1	0.8 – 5.2	2.96	0.08
Hospitalized for hepatitis N = 108	10	9.3	1.73	0.7 – 4.3	1.67	0.19

OR Odds ratio > 1. (at risk) $\mathbf{X^2}$ Chi-square ≥ 3.84 & $p < 0.05$ (significant).

There were association and highly significant association odds ratio for contracting HGV with sexual, with contact with HBV patients but not statistically significant contact with HCV but not statistically($P < 0.006$), indicating that the more sexual contact with patient could increase the risk of HGV infection in partner as shown in Table 6.

Table 6. Risk factor of HGV infection among hemodialysis patient.

Factors	Positive HGV N= 24		*OR*	*CI*	$\mathbf{X^2}$	*PV*
	No	%				
Contact with HBV N = 14	2	14.3	2.5	0 – 12.7	1.36	0.24
Contact with HCV N = 14	2	14.3	2.5	0 – 12.7	1.36	0.24
Sexual contact with HV N=18	4	22.2	4.6	1.2– 16.9	7.4	0.006
Dental visit N = 38	2	5.3	0.76	0.12- 3.5	0.13	0.71
Travel abroad N = 56	4	7.1	1.1	0.3 – 3.6	0.02	0.87
Repeated use of needles N = 62	4	6.5	0.96	0.3 – 3	0.01	0.94
Sharing blades needles N = 62	0	0	0	0 - 1.1	4.5	0.03
Tattoo N = 12	0	0	0	0 – 6.2	0.89	0.34
Blood transfusion N = 308	20	6.5	0.83	0.25-3.02	0.1	0,74
Cupping N = 46	2	4.3	0.6	0.1-2.8	0.46	0.49

OR Odds ratio > 1. (at risk) X^2 Chi-square ≥ 3.84 & $p < 0.05$ (significant).

Furthermore, duration dialysis ≤1 year 3.6 % to 2 years 12.8 %, had a substantial difference between HGV positive and HGV negative patients (P < 0.001), indicating that increasing dialysis duration could increase the risk of HGV infection in patients Table7.

Table 7. Association ratio of HGV infection with the duration of hemodialysis.

Duration month	HGV positive		*OR*	*CI*	X^2	*PV*
	No	%				
> 12 month N = 110	4	3.6	0.43	0,12 –1.4	2.3	0.03
12 – 24 month N=78	10	12.8	2.8	1.1 –7.11	6.1	0.02
25-48 month N = 78	2	2.6	0.31	0.05 –1.4	2.69	0.11
≥ 49 month N = 94	8	8.5	1.5	0.6 – 3.8	0.7	0.01

OR Odds ratio > 1. (at risk) X^2 Chi-square ≥ 3.84 & $p < 0.05$ (significant).

DISCUSSION

In Yemen, HGV prevalence rate and the role of this agent in acute and chronic liver disease in is not clear or at least poorly understood, and there has been no information on the prevalence of HGV among HD patients prior this study. Here, we investigated the prevalence and risk factors of HGV-antibodies in hemodialysis patient's units of different Yemeni hospitals in the Capitol.

The finding of this results indicated a high prevalence of 6.70% in those hemodialysis patients since, there are numerous reports about HGV prevalence worldwide. Polish survey reported the prevalence of HGV was 6.7% among 215 patients [16] which similar to our result.

Several studies revealed a variable prevalence rate of different countries, 3.89% in Iran[14] to 7% in Japan[14], Caucasians 4.5%, Asians 3.4% - 6% in healthy blood donors [18,] Turkey 14%[19, 20] among HD patients compared to 7.1% in blood donors[21].

The co-infection prevalence rate of this study with anti-HCV was detected in 170 (47.2%) out of 360 HD patients, in compare to high prevalence (54.1%) of HCV positive patients[12] while in Turkey dialysis patients rate was 10.5% and 8.6% versus HCV and HGV respectively[23], regardless the different finding of this co infection study in compare with Brazil previous studies among HGV positive patients 22.2%, 44% for HGV were co-infected with HCV indicating that HGV has been indecently wide spread in patients with chronic renal failure [18, 21,23].

Additionally the male gender rate was 5.8% slightly lower than 7.4% of female HD patients which is similar to former studied which found no association between HGV-RNA and sex among 98 HD patients[21,24]. However, Casteling *et al.* (1998) [25] found that males showed a significant higher level of HGV positivity, but differences between males and females were not statistically significant. Several investigators analyzed the potential risk factors of HGV infection insisting on significant correlation between the presence of HGV and the receipt of blood transfusion and duration of HD [21,26,27].

From one study reported that almost 90% of HGV positive patients had a history of blood transfusion, so there was no risk of contraction HGV with history of blood transfusion and the finding of this study shows that there was no association of HGV with other parenterally route of transmission in our study as repeated use of needle etc[21]. Transmission by blood transfusion was highly efficient route for HGV transmission and a significant risk factors for contracting HGV [28, 29] which different finding from our study. Our finding absolutely agreed previous reported with highly significant risk factor of contracting HGV infection among our HD patients with sexual contact with hepatitis patients (OR = 4.6 and *P* = 0.006), although Parenterally transmission is highly efficient for HGV, sexual transmission is the most common transmission routes of this virus [28,30] .The association of HGV infection with the duration of hemodialysis in our study, HGV positivity increased with the duration of dialysis, 3.6% with a duration ≤1 year to 12.8% with duration to 2 years (P < 0.001), indicating that increasing dialysis duration could increase the risk of HGV infection in patients.

Hinrichsen *et al* (2002) [24] who found that HGV positive (24.6%) could be seen in the first year of HD treatment indicating that pre-hemodialysis status is more important for acquisition of HGV. While HGV exposure can be correlated with the duration of HD therapy as 50% of their HD patients with HGV exposure had been infected before the start of chronic HD therapy. Nevertheless, they found that 22.5% of patients acquired new HGV infection after starting chronic HD therapy with an incidence rate of 2.6% per year[31].

CONCLUSION

In conclusion, patients on maintenance hemodialysis treatment are at high risk of acquiring parenterally transmitted viral infections. This study evaluated the prevalence of HGV among hemodialysis patient's units of Yemeni hospitals in Sana'a city. Sexual transmission and duration of dialysis are very important to increase the risk of HGV transmission. Further studies are needed to elucidate real prevalence, risk factors and characteristics of HGV infection in Iranian hemodialysis patients.

CONFLICT OF INTEREST.

The authors declare that there is no conflict of interests regarding the publication of this paper.

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