Prevalence of hepatitis G virus (HGV) among hepatitis-B patients and others suspected for PT-hepatitis in Baghdad

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Abstract
The aim of this research is to evaluate the prevalence of HGV among three different categories, group 1, composed of hepatitis –B patients (HB- patients), group 2, included people having hepatitis-like symptoms with sera negative for HBV and HCV markers, referred to as suspected for hepatitis (SUS-patients) while the third group is the control group. Serum samples were assayed for anti-HGV antibodies using ELISA technique-indirect method. Results revealed that HGV coinfection detected in only few number of HB-P 9.8%, 23.5% of HB-P having anti-HGV antibodies with titer lower than the cut-off value (COV) which are said to be in the shadow zone and the other 66.6% of the group are reported as negative cases, reporting a highly significant difference P˂0.001. Among the second group (SUS-patients), HGV was detected in only 4.8%, 58.5% detected as shadow cases while the other 36.5% were found to be negative for HGV. When both HB-P and SUS-P are gathered in one group a low percentage 7.6% of HGV infection was recorded, 39.1% of HB-/SUS-patients were in the shadow zone while the majority of this group 53.2% were detected as negative cases. In conclusion HGV play only a minor role as a confection agent with HBV and as a responsible agent among non-A-E hepatitis cases. Remarkable high percentages of shadow cases are reported in the three groups especially among non-A-E hepatitis patients.

Key wards: HGV Iraq, HGV coinfection
Introduction

Two novel Flavi viruses were identified in 1990s by two independent groups of researchers; GBV-C was first identified in the sera of West African population during an attempt to retrospective track down the causative agent of an incident acute hepatitis in a surgeon. The original virus characterized as GBV-A, GBV-B and GBV-C, only GBV-C was detected in human beings and especially in sera of several individuals with hepatitis [1], almost concurrently, hepatitis-G- virus (HGV) was independently cloned from a plasma of a patient with chronic hepatitis [2]. The similarity between the two viruses (HGV and GBV-C) regarding the nucleotide level is about 86% and reaches up to 96%-97% on the amino acid level therefore HGV and GBV-C could be two genotypes for same virus and so called HGV/GBV-C [3].

HGV is a transfusion –transmissible virus has a global distribution and has a high prevalence among the high risk-groups such as patients receiving hemodialysis, hemophiliacs and intravenous drug users (IVDU) [4]. In Taiwan which is endemic for HBV and HCV, a high prevalence of HGV infection has been reported, pointing to the parenteral route of transmission [3]. However, alternative routes such as sexual and vertical transmission have been proposed [5], HGV_RNA was found frequently in patients with homosexual life style [6]. Moreover, intrafamilial transmission between supposes and via the horizontal route was documented also [7].

Although the damage induced by HGV infection to the liver does not seem to be sever, but there are some cases with prolonged viremia [8], HGV-RNA could be found in sera 2-20 weeks after infection, HGV can cause persistent infection for 7-16 years [9].

HGV infection has a high rate of spontaneous remission which involves the disappearance of the viral RNA and the production of antibodies to the viral second envelop protein (anti-E2 Ab), most patients positive for anti-E2 Ab are found to be negative for HGV-RNA and vice versa, indicating an inverse correlation between these two viral markers [3].

Sever hepatitis caused by HGV is rare, most infections are mild or subclinical, no causative association with liver disease has been established [9] on the other hand HGV has been found in some patients with chronic and fulminant hepatitis without any evidence for a known hepatitis virus infection [3].

Materials and methods

A total of 108 blood samples were collected from three different categories, the first studied group was the hepatitis-B patients (HB-P), the second group included patients with a history of blood transfusion, having hepatitis symptoms like jaundice, light stool and dark urine color and their sera found to be negative for HBV and HCV, so they were designated as suspected for parenterally-hepatitis (PT-hepatitis)such patients referred to as(SUS-P) and the third studied group was the control group, consisted of healthy blood donors. Hepatitis B infection was defined by positivity hepatitis-B surface antigen (HBs Ag+), and hepatitis-C infection was defined by positive anti-HCV antibodies (anti-HCV+).

Blood samples were collected, centrifuged at 300rpm/15 min., liquated in eppendorf tubes and stored in freeze till testing time.
All sera samples were assayed for monoclonal anti-HGV Ab using ELISA technique-
indirect method for quantitative detection of antibodies, Diagnostic automation, INC, Calabasa, CA 91302.

Results

Three categories were included in this study, the first group is the HB-patients, the
total number 102, age ranging 20-53 years old, age mean 38.5±3.5 male: female ratio
(M:F) was 2.9:1. HGV confection was detected in 10 out of 102 (9.8%), 24 out of
102(23.5%) of HB-patients having anti-HGV Abs titer less than the cut off value
(COV) which is called the shadow region , while the other 68 out of 102 which
represented 66.6% were found to be negative for HGV infection.

Pearson Chi Square program (PCS) was used to investigate the significant difference
among each category, as far as it concerned with HB-P, most of them were negative
for HGV, a highly significant difference was detected, PCS DF-2=26.43, P <0.001.
The second studied category consisted from people having hepatitis-like symptoms
but their sera detected as negative for HBV and HCV markers(HBs- Ag and anti-HCV
Abs) with a history of maintenance blood transfer, their total number is 82, age
ranging 11-35, age mean 33±5.2, M:F ratio was 1:4.8. Results revealed that 4 out of
82(4.87%) of the whole number of this group found to be infected with HGV, 48 out
of 82 (58.5%) having anti-HGV antibodies but their titer did not reach up to the COV
so they still in the shadow region, while 30 out of 82 (36.5%) were negative for HGV
antibodies.

Among this category most of the patients were in the shadow region, a highly
significant difference was recorded PSC DF-2=38.8, P<0.001.
The third group is the control group which composed of 24 healthy blood donors their
age ranging 25-36 years old, age mean 28 ±3.3, the total M: F ratio was 3:1. Only 2
males out of 24 (8.33%) found to have anti HGV antibodies, about third of this group
8 out of 24 (33.33%) seem to be in the grey zoon and as in HB patients most of the
group 14 out of 24(58.33%) detected as negative for HGV. It is clear that more than
half of cases were negative for HGV antibodies but no significant difference was
found, PSC DF-2=4.190, P=0.123 Figure (1).

By comparing the three groups regarding positive and shadow cases, it was found
that most of positive cases detected among HB-P 9.8%, SUS-P 4.8%, and then
controls 2% but no significant difference was detected PCS DF-2=2.133, P=344.
Regarding shadow cases, most of them were in the SUS-P 58%, HB-P 23.5% and controls 33.33%, a highly significant difference was reported, PCS DF-2=19.9, P<0.001 table (1).

Table (1): Comparison between of HB-P/SUS-P and controls using PCS program DF-1

<table>
<thead>
<tr>
<th>Cases</th>
<th>HB-P/SUS-P</th>
<th>CONTROLS</th>
<th>PCS-DF-1</th>
<th>P -value</th>
<th>Decision</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M</td>
<td>F</td>
<td>M</td>
<td>F</td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>52</td>
<td>46</td>
<td>12</td>
<td>2</td>
<td>5.333</td>
</tr>
<tr>
<td>Shadow</td>
<td>28</td>
<td>44</td>
<td>4</td>
<td>4</td>
<td>0.370</td>
</tr>
<tr>
<td>positive</td>
<td>10</td>
<td>4</td>
<td>2</td>
<td>zero</td>
<td>0.762</td>
</tr>
</tbody>
</table>

S: significant difference  
NS: no significant difference

Both of HB-patients and those suspected for PT-hepatitis infection can be considered as susceptible for HGV since both of them are parenterally-transmitted (PT) so it is possible to gather them in one group (HBV/SUS-patients), the total number is 184 with 1:1 M:F ratio. It could be found that HGV antibodies was detected in only 14 out of 184 (7.6%), 72 out of 184 (39.1%) were in the shadow zone while the majority of them, 98 out of 184 (53.26%) were negative for HGV. And by comparing those results to that of the controls using the PCS DF-1, a significant difference was found between the two groups concerning the negative cases, PCS DF-2=5.33,p˂0.05. While no differences were recorded concerning both positive and those in the shadow region, PCS DF-2=0.762,P=0.383 and PCS DF-2 =0.370,P=0.543, respectively.

Discussion

Although sensitive tests for detection of knew hepatitis viruses are available, the etiology of 10-15% post transfusion and community acquired hepatitis cases has remained undefined suggesting the existence of unknown causative agents associated with this disease, HGV/GBV-C was newly discovered as putative non A-E hepatitis viruses [10].

A study conducted in Baghdad during the period 1999-2000 included jaundiced patients suspected for viral hepatitis, reported that 20% of the studied patients were found to be negative for the 5 hepatitis viruses HAV-HEV [11] and since HGV is well established as PT-hepatitis virus [12]. It was convenient to assess the impact factor of HGV in HB-P and patients suspected for PT-hepatitis with sera negative for HBs-Ag and anti-HCV Abs. It was found that HGV play a minor role as a coinfection agent with HBV that it was detected in only 9.8% comparing to 8.33% among controls, also HGV play a minor role in SUS-group that it was detected in only 4.8% of them, and when both HB- and SUS-patients were gathered in one group again the same results obtained when HGV was responsible for only few cases of hepatitis7.6%.

Similar studies were conducted in different countries revealed slightly higher HGV prevalence than that obtained in the submitted study. The frequency of HGV infection is 18% in anemic patients with multiple transfusion, 26% of hemophiliacs in Spain, 12.5% in USA, in Northeastern Thai 10% of blood donors are coinfected with HBV and HGV [9] in Khurassan /Iran HGV –RNA prevalence was 5% among hemophiliacs [12],while anti HGV antibodies prevalence was 12.9% in rural population in China[13].
In USA and Germany HGV viral genome is found in (1-2)% of healthy blood donors [7] Among healthy blood donors the prevalence of HGV is 0.9% in Japan, 3.2% in UK, 4.2% in France and 10% in Brazil [9]. In the submitted research it was notable that there is a considerable number of patients found to have a high titer of anti-HGV Abs, however it is lower than the COV, such cases are said to be in the grey or shadow zone and could not be considered as positive cases, such cases represented more than half 58.5% of the SUS-patients and third 33.33% of the controls and 23.5% among HB-P. It is thought that such patients may need a follow up for another test after several days, or since most of the shadow cases recorded among sus-group and controls that may refer to a subclinical signs and not intensive disease, especially that mild symptoms is one of the HGV infection properties[ 8]. Moreover, the COV was calculated by the kit equation (COV= NC+0.2), the absorbance of the negative control (NC) is provided by the kit, possibly that it should find our own NC since each community has its own properties, because of their different food and social habits and hygienic standards, may be that will be helpful to get a more precise decision for such critical cases. Otherwise a low Ab titer could represent one of the disease signs

References


