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Incidence of hepatitis Gvirus in patients with hematological malignancies withrepeated blood transfusion

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Background: *Hepatitis G virus and GB virus C (GBV-C) are RNA viruses that were independently identified in 1995, and were subsequently found to be two isolates of the same virus.Blood transfusion is the main risk factor for HGV transmission. Patients with hematological malignancies usually require frequent blood transfusions which make them more vulnerable to HGV infection. The aims of this study was to estimate the transmission rate of HGV in patients with hematological malignancies having multiple blood transfusion*
Methods: *This cross sectional study was carried out at the national center of hematology,Almustansiriya University and department of microbiology in Baghdad university college of medicine in Baghdad / Iraq from January till June 2012. The study involved 60 patients (39 males & 21 females) diagnosed with hematological malignancies.*
Results: *Of the sixty patients, seventeen patients (28.3 %) had IgM HGV positive, while 43 (71.7%) of patients had HGV IgM negative which was statistically significant when compared to control group*
Conclusion: *the incidence of HGV increase in patient with hematological malignancies receiving multiple blood transfusions*
Key words: *incidence, hepatitis G virus, hematological malignancies, blood transfusion*

I. Introduction

Two different laboratories in the USA isolated a new flavivirus- like RNA virus in the years 1995 and 1996. The first laboratory named it "G B virus-C (GBV-C)" and the other "hepatitis G virus (HGV)". Both viruses were subsequently considered different genotypes of the same virus because they were found to share most of the nucleotide and amino acid sequences [1]. Both viruses have a single stranded RNA genome of approximately 9.4 kb. It encodes a single poly protein of 2900 amino acids in which the nonstructural proteins are located at the C terminal end and the structural proteins at the N terminal end [2]. They are member of the Flaviviridae family and are phylogenetically related to hepatitis C virus, but appear to replicate primarily in lymphocytes, and poorly if at all in hepatocytes (3). GBV-A and GBV-B are probably Tamarin viruses, while GBV-C infects humans (4). Parenteral, sexual and vertical transmissions of GBV-C have all been documented, and because of shared modes of transmission, individuals infected with HIV are commonly co-infected with GBV-C. Among people with HIV infection, the prevalence of GBV-C viremia ranges from 14 to 43% (5)

Patients with hematological malignancies, such as acute or chronic leukemia require blood and blood products for sustaining life. Therefore, these patients are considered at a high risk for contracting transfusion transmissible infections [6]. Although the precise transmission rate is unknown, an elevated prevalence of HGV-RNA has been described in subjects at risk for parenteral infections, such as blood and blood products recipients, intravenous drug abusers, and patients on hemodialysis [6-8). The present data on the prevalence of HGV is conflicting with studies showing rates of 7% in Japan [9] up to 29% in Germany [10]. Somestudies reported that HGV prevalence in healthy blood donors ranged from 1.2 to 4.2 percent [4, 11].

II. Patient andMethods

This cross sectional study was carried out at the national center of hematology,AlmustansiriyaUniversity and department of microbiology in Baghdad medical college in Baghdad, Iraq from January till June 2012. The study involved 60 patients (39 males & 21 females) diagnosed with hematological malignancies with 30 healthy donor controls. Writteninformed consents wereobtained from all patients and controls. The study wasapproved by the ethical committee of the national center of hematology in Almustansiriya University. The age and gender ratioswere similar in the groups of patients and controls:median age 35.5 years (range 17-61) and 33.4years (22-55), M/F 1.8 and 1.7 respectively. Allpatients and controls were HIV negative and hadnot been transfused before starting the study; no other risk factors forblood-borne diseases

were present in patients orcontrols. All patients underwent blood tests, lymph node and bone marrow biopsy in orderto diagnose and characterize the hematological malignancy.

Five milliliters of blood samples were withdrawn from patientsand controls. They were centrifuged and serum was separated.Serum was stored in aliquots at -20°C. Repeatedfreezing and thawing was avoided. All the biochemicalparameters were done by routine laboratory methodsunless otherwise stated. HGV IgM and IgG were detectedwith commercially available enzyme linked immunosorbentassay (CUSABIO BIOTECH CO.LTD).

Statistical analysis

Statistical analysis was performed using Fisher'sexact test and the chi-square test, as suitable. $p < 0.05$ considered statistically significant.

III. Results:

There were no significant differences in age, gender between the two groups ($p > 0.05$) as intable 1. Of the sixty patients with hematologicalmalignancies, 17 patients (28.3%)had positive result for HGV IgM which was highly significant when compared to control healthy controls (6.6%) as shown in table 2, while the results for HGV IgG showed 23 patients(38.3%) and 5 healthy controls (16.7%) were positive which was statistically significant when compared to control group which shown in table 3

Regarding distribution of HGV IgM positive result according to hematological malignancies ,there were 3/14(21.4%) ,5/16(31.2%),2/13(15.3%) , and 7/17(41%) for AML,ALL,CML,and CLL respectively while for HGV IgG positive result there were 3/14,6/16,4/13,and 10/17 for AML,ALL,CML, and CLL respectively. The high incidence were found in CLL for both IgM and IgG with 41% and 58.8% respectively

Table 1. The demographic and clinical characteristics of all patients in study group

Characteristic	Patients	Controls	P value
Number of patients	60	30	
Age - Median (years) Range(year)	35.5 17-61	33.4 22-55	NS
Sex (male/Female)	37/23	19/11	NS
Primary Diseases	Patient Number (%)		
AML	14(23.3)		
ALL	16(26.6)		
CML	13(21.6)		
CLL	17(28.3)		

NS= not significant, AML; Acute myeloblastic leukemia, ALL; Acute lymphoblastic leukemia, CML; Chronic myelocytic leukemia, CLL; Chronic lymphocytic leukemia

Table 2: result of HGV IgM in patients and controls

IgM	Positive	Negative	P-Value
Patients	17(28.3%)	43(71.7%)	Chi-sq.(5.64)
control	2(6.6%)	28(93.4%)	P-value <0.017 Highly Significant

Table 3: Result of HGV IgG in patients and controls

IgG	Positive	Negative	P-Value
Patients	23(38.3%)	37(61.7%)	Chi-sq.(4.381)
control	5(16.7%)	25(83.3%)	P-value <0.036 Significant

IV. Discussion

HGV or the GB virus C (GBV-C) has recently beenisolated in patients with acute, chronic or post-transfusionhepatitis (12, 13). It is now absolutely clear thatHGV and its variant, GBV-C, are prevalent agents witha high carrier rate in the volunteer donor population (8, 13). Although there has been a rapid increase inthe epidemiologic and molecular knowledge of aboutthis virus, its clinical relevance remains largely unresolved (6). Our findings clearly showed that patients with hematological malignancies are frequently subjected to HGV due to multiple blood transfusions and that they suffer from severe immunosuppression, which has a significant influence on the clearance of HGV viremia and the production of anti-E2 immune response.

The prevalence of HGV-IgM in this study was 28.3%. This percentage is slightlylower than that reported in other studies for adult patients with acute leukemia with incidence of 30% to 48% (14, 15). This difference may be due to the age, therapeutic stage, or geographic area of the study populationsor may be due to the use of PCR base method for detection of HGV in previous studies while in this study ,ELISA was the main method for diagnosis.Patients with hematological malignancies are subjected to multiple units of blood and blood productswhich certainly represent a major route for transfusiontransmittedinfections such as hepatitis (HCV, HBV,HGV) and human immunodeficiency viruses[7,8,16,20].In the present study, the high incidence in hematological malignancies was found in CLL patients for both IgM and IgG with 41% and 43.4% respectively. This is differentfrom study done by De Ronzo et al in which she found that the prevalence of HGV in lymphoproliferative disorders (LPD) was 7.8% and non-Hodgkin lymphoma had the highest incidence among LPD (17), while our results were comparable to that found in Germanstudy (18). The possible pathogenic mechanisms for this strong association between LPD and HGV have been hypothesizedthat HGV has analogy with HCV, and it might be implicated in lymphomagenesis. (19)

In conclusion, this study showed that there is significant increase in incidence of HGV IgM and IgG in patient with hematological malignancies compared to healthy control donor, although multiple blood transfusionsare the most important risk factor for transfusionrelatedviral infections, still type of hematological malignancies play a role in this increment. Despite of strict screening programs for HBV and HCV in blood bank, HGV should be put into consideration in screening program to prevent and decrease this serious infection.

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