brief report

Prevalence of hepatitis C virus infection and human immunodeficiency virus in a cohort of Egyptian hemophiliac children

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BACKGROUND AND OBJECTIVE: The risk of blood-borne infections, especially hepatitis C virus (HCV) and human immunodeficiency virus (HIV) infection still remains in developing countries among children receiving blood products as hemophiliacs, but the risk is not known in Egypt. The objective of this study was to detect the prevalence of HCV and HIV infection among hemophiliac children to know the magnitude of the problem and determine potential risk factors.

PATIENTS AND METHODS: This was a cross-sectional study conducted on 100 hemophiliac children that assessed the liver clinically and by laboratory tests. All children were screened for HCV and HIV antibodies by enzyme-linked immunosorbent assay. Those with positive HCV antibody titre were tested by polymerase chain reaction (HCV-PCR).

RESULTS: Forty were positive for HCV antibodies with 19 children (47.5%) HCV-PCR positive as well. The mean age, average frequency of bleeds/year, dose of replacement therapy/year and alanine aminotransferase (ALT) levels were significantly high in HCV-antibody and PCR positive patients as compared to HCV antibody and PCR negative ones. None of our patients had clinical evidence of hepatic involvement or was co-infected with HIV.

CONCLUSION: HIV infection does not appear to be a current health problem in Egyptian hemophiliac children though the prevalence of HCV infection is still high.

Treatment of patients with bleeding disorders, especially those with hemophilia, with blood products, has been associated with infections with blood-borne viruses such as hepatitis B and C (HBV and HCV, respectively) and human immunodeficiency virus (HIV).[1] Though the development of virucidal methods and their application to clotting factor concentrates has eliminated the risk of transfusion of blood-borne infections by plasma products,[2] the risk still remains in developing countries where there is no ready access to these concentrates except in a few places. The prevalence of HCV varies in hemophiliacs among different countries from 15%[3] up to 71%.[4] However, HIV infection is considerably less, though it does exist and depends largely on the source of the plasma.[1]

In Egypt, the prevalence of HCV antibody in children varies from 3% to 9%[5,6] whereas HIV ranges from 2900 to 13 000 individuals.[7] There are some reports of HCV infecttion among multi-transfused patients in the Egyptian population,[8] yet the incidence of HCV infection in hemophiliac children is not known. We carried out this study to detect the prevalence of HCV and HIV infection among hemophiliac children and to determine the potential risk factors in this group of patients.

PATIENTS AND METHODS

This cross-sectional study included 100 patients, 88 with hemophilia A and 12 with hemophilia B followed in two large hematology referral centers: Paediatric Hematology Clinic, New Children's Hospital, Cairo University and the Hematology unit of the Egyptian Organization of Biological Products and Vaccinations (VACSERA). Patient ages ranged from 2 to 16 years. Consent was obtained from the patients and/or their parents before enrollment. The diagnosis of hemo-

philia was made clinically and confirmed by laboratory testing with severity scoring.[9] All patients underwent a detailed history taking focusing on the frequency of bleeds and details of replacement therapy, age of start of treatment, type, frequency as well as number of units received per year and any manifestations of hepatic involvement. All our hemophilia A patients received cryoprecipitate and a few received cryoprecipitate and factor VIII concentrate (locally manufactured or koate DVI, plasma-derived, double virally inactivated) according to availability, while hemophilia B patients received fresh frozen plasma (FFP) due to unavailability of factor IX (FIX) concentrate. All locally manufactured products are prepared from single donors. It is a routine practice in Egypt to screen all blood donors for HBV, HCV and HIV by enzyme-linked immunosorbent assay (ELISA) and in only in a few private centers by PCR. Hepatic assessment included clinical examination as well as liver biochemical profile: aspartate and alanine aminotransferases (AST and ALT), bilirubin (total and direct) and prothrombin time (PT). Liver biochemistry tests were done by routine methods. ALT (normal up to 40 U/L) and AST (normal up to 40 U/L) were considered elevated if any elevation above the upper limit of normal was detected.

All patients were screened for HCV and HIV by ELISA. Serum samples were withdrawn from all patients, stored at –20°C and thawed all at one time for analysis of HCV antibody (ELISA; Test kit 96 T manufactured by In Tec Products, San Diego, CA, USA, lot: 2006082402). Also, HIV1/2 antibodies were tested using a highly sensitive third-generation sandwich enzyme immunoassay (anti-HIV1/2 TETRA ELISA test).

Patient samples positive for anti-HCV antibodies were further analyzed for the presence of HCV- RNA by HCV RT-PCR kit (BioSewoom, Korea) according to the manufacturers' instructions. Patients were then divided into two groups: HCV-RNA positive and HCV-RNA negative. *P* values less than .05 were considered statistically significant.

RESULTS

Our study group included 100 patients from 92 families, all males except the daughter of a severely hemophiliac father. Their mean (SD) age was 8.6 (4.1) years. None of our patients had any clinical evidence of hepatic involvement. Forty children were positive for HCV-antibody titer with 19 (47.5%) HCV-PCR positive. The mean age, average frequency of bleeds/year, dose of replacement therapy/year, ALT and AST were significantly high in the HCV-RNA positive group as compared to HCV-RNA negative patients. All HCV-RNA positive children had hemophilia A and 14 cases (74%) were severe. None of our patients were HIV antibody positive. The clinical and laboratory data of hemophiliac patients according to the HCV-antibody and HCV-RNA status is shown in **Table 1**.

DISCUSSION

In the present study, the prevalence of HIV in children was 0% as compared to 0% to 3.8% in Egyptian thalassemic children.[10,11] Forty percent of our children were HCV antibody positive. However, in a recent study of children attending the general outpatient clinics of the same hospital of the present study, evidence of HCV infection was reported in 2.02% but children attending hematology and hepatology clinics were excluded.[12] Reviewing the literature of all Egyptian studies

Table 1. Clinical and laboratory data of hemophiliac children according to HCV-antibody and HCV-PCR status.

	HCV-antibody positive (n=40)	HCV-antibody negative (n=60)	*P*	HCV-PCR positive (n=19)	HCV-PCR negative (n=21)	*P*
Mean age in years (SD)	10.6 (3.5)	7.30 (3.9)	.001	10.8 (4.0)	8.1 (4.0)	.01
Frequency of bleeds/ year	23.0 (12.7)	9.8 (0.2)	.001	73.1 (33.8)	47.9 (32.5)	.014
Dose of replacement therapy/year	70.4 (39.3)	40.9 (24.0)	.001	29.6 (12.3)	11.7 (8.0)	.001
PTT (s)	84.8 (10.6)	83.4 (21.0)	.707	86.2 (10.6)	83.5 (19.0)	.564
PT (s)	13.7 (1.4)	13.7 (1.6)	.965	13.6 (0.6)	13.7 (1.7)	.763
AST (U/L)	33.0 (27.3)	25.6 (14.9)	.083	42.1 (36.1)	25.4 (14.0)	.001
ALT (U/L)	42.4 (34.2)	29.5 (2.4)	.025	53.9 (43.6)	30.1 (21.3)	.031

PT: prothrombin time, PTT: partial thromboplastin time, ALT: alanine transaminase, AST: aspartate transaminase.

of HCV infection in adults and/or children, there is no report of HCV prevalence in hemophiliac children to date though it was recently reported in thalassemics to be 64%.[8] The prevalence of HCV in different developing countries varies among hemophiliacs, ranging in the Brazilian population from 0% in those less than 5 years to 42.2% in those with a mean age of 19.5 years,[13] and up to 50% in Tunisia.[14]

None of our children showed clinical evidence of hepatic involvement, which is consistent with other studies,[15] but contrary to some other studies that did not include hemophiliacs and that reported symptoms to be significantly more common among Egyptian HCV-positive children versus controls.[12] In the present study, older age, the average frequency of bleeds/year, dose of replacement therapy/year were significantly high in HCV-antibody positive patients as compared to HCV-antibody negative ones. This is consistent with other studies,[15] but few studies reported no relationship between HCV infection and age.[16]

In our study group, mean ALT levels in seropositive patients and HCV-RNA positive patients were significantly higher than seronegative though all were asymptomatic, which is consistent with other studies.[17] However, some studies found no significant association between HCV viremia and abnormal liver enzymes.[15] The PCR results were negative in 52.5 % of our children who were HCV antibody positive, indicating either spontaneous clearance of the virus or very low viral load that could not be detected by PCR. In the study by El-Raziky et al, 2004,[17] 12.9% of their HCV RNA negative cases cleared the virus during follow-up. Jonas reported spontaneous viral clearance rate in 25% of children that may be as high as 50% in older children and adolescents.[18]

In conclusion, HIV infection does not present a current health problem in Egyptian hemophiliacs. The prevalence of HCV infection is still high among hemophiliac children in Egypt especially with increased age, frequency of transfusion and severity of the disease. Screening for evidence of HCV infection is important even in clinically asymptomatic patients. Adopting a national policy to screen blood and blood products by PCR will prevent HCV infection in those children. Further studies are necessary to elucidate the natural history of HCV infection in young hemophiliacs and to determine the rate of spontaneous clearance in this group of patients.

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