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

Magy S. Abdelwahab, Mona S. El-Raziky, Normine A. Kaddah, Heba H. Abou-Elew

From the Departments of Pediatrics and Clinical Pathology, Cairo University, Cairo, Egypt

Correspondence: Dr. Magy Abdelwahab · Department of Pediatric Hematology, 12. Marashli Street, Zamalek, Cairo, Egypt · magywahab@yahoo.com · Accepted: May 2011

Ann Saudi Med 2012; 32(2): 200-202
DOI: 10.5144/0256-4947.2012.200

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.
HCV HIV HEMOPHILIACS

philía was made clinically and confirmed by laboratory testing with severity scoring. 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 hemophilic 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-PCR 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. 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. 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)                 | .003  | 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 hemophilic children to date though it was recently reported in thalassemics to be 64%. 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, and up to 50% in Tunisia.

None of our children showed clinical evidence of hepatic involvement, which is consistent with other studies, 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. 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, but few studies reported no relationship between HCV infection and age.

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. However, some studies found no significant association between HCV viremia and abnormal liver enzymes. This is consistent with other studies, but few studies reported no relationship between HCV infection and age.

In conclusion, HIV infection does not present a current health problem in Egyptian hemophiliacs. The prevalence of HCV infection is still high among hemophilic 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.

Acknowledgment
We acknowledge Dr. Dina Ibrahim for her participation in recruiting patients from Department of Pediatric Hematology, Organization of Biological Products and Vaccinations (VACSERA).

REFERENCES

1. Yee TT, Lee CA. Transfusion-transmitted infection in haemophilia in developing countries. Semin Thromb Hemost 2005;31:527-37.
2. Mannucci PM. The choice of plasma-derived clotting factor concentrates. Bailleres Clin Hae matol 1996;9:273-90.
3. Seme K, Poljak M, Begovac J, Vence A, Tomazic J, Vidmar L, et al. Prevalence of hepatitis C virus among HIV type-1 infected individuals from Slovenia and Croatia. Acta Viral 2002;46:91-4.
4. Rezvan H, Abolghassemi H, Kafiabad SA. Tranfusion-transmitted infections among multitransfused patients in Iran: A review. Transfus Med 2007;17:425-33.
5. Medhat A, Shehata M, Magder LS, Mikhail N, Abdel-Baki L, Nafeh M, et al. Hepatitis C in a community in upper Egypt: Risk factors for infection. Am J Trop Med Hyg 2002;66:633-8.
6. Habib M, Mohamed MK, Abdel-Azz F, Magder LS, Abdel-Hamid M, Gamil F, et al. Hepatitis C infection in a community in the Nile Delta: Risk factors for seropositivity. Hepatology 2001;33:249-53.
7. Available from: http://www.unicef.org/egypt/hiv_aids.html. [Last accessed on 2010 May 25].
8. Rabab L, Helal S, Zaghloul N, El-Raziky M, Alfi R, Musallam KM, et al. Clinicoepidemiologic analysis of hepatitis C infection in transfusion-dependent thalassemia major children. Int J Lab Hematol 2010;32:184-90.
9. White GC 2nd, Rosendaal F, Aledort LM, Lusher JM, Rothschild C, Ingerslev J. Factor VIII and Factor IX Subcommittee. Definitions in haemophilia. Thromb Hemost 2001;85:560.
10. El-Beshlawy A, Kaddah N, El-Hassan AA, et al. The frequency of blood borne viruses (HBV, HIV and HCV) among Egyptian thalassemic children. Colloques de l’Institut National de la Santé de la Recherche Medicale 1996;234:314.
11. Abdel-Samei Sadeg R, Abdel-Hamid A, Al-Sharkawy HI. HCV and HIV transmitted by repeated blood transfusions among thalassemic children in Zagazig University Hospitals. Int Conf AIDS 1998;12:230-4 (abstract no. 23264).
12. El-Raziky MS, El-Hawary M, Esmat G, Abouzaid AM, El-Koofy N, Mohsen N, et al. Prevalence and risk factors of asymptomatic infection hepatitis C virus infection in Egyptian children. World J Gastroenterol 2007;13:1828-32.
13. Langar H, Triki H, Soudier E, Bahl O, Djebbi B, Sadraoui A, et al. Blood-transmitted viral infections among haemophiliacs in Tunisia. Transfus Clin Biol 2005;12:301-5.
14. Camarero C, Ramos N, Moreno A, Asensio A, Mateos ML, Roldan B. Hepatitis C virus infection acquired in childhood. Eur J Pediatr 2008;167:219-24.
15. Carro RA, Oliveira GC, Guimarães MD, Oliveira MS, Lima AA, Buzek SC, et al. Hepatitis C virus infection among Brazilian hemophiliacs: A virological, clinical and epidemiological study. Braz J Med Biol Res 2002;35:589-98.
16. Brettelet D, Alter H, Dienstag J, Forsberg A, Levine P. Prevalence of hepatitis C virus antibody in a cohort of hemophilia patients. Blood 1990;76:254-6.
17. El-Raziky MS, El-Hawary M, El-Koofy N, Oktash S, Kotb M, Salama K, et al. Hepatitis C virus infection in Egyptian children: Single centre experience. J Viral Hepat 2004;11:471-6.
18. Jonas MM. Treatment of chronic hepatitis C in paediatric patients. Clin Liver Dis 1999;4:855-67.