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

To the Editor: Abdelwahab et al[1] stated in their study that deranged liver function, particularly alanine aminotransferase (ALT) levels were significantly high in HCV-antibody and PCR positive patients as compared to HCV antibody and PCR negative ones. I presume that Abdelwahab et al solely attributed abnormal liver function to HCV as none of their patients was co-infected with HIV. I also presume that that finding needs to be considered with caution. Occult HBV infection is not uncommon in transfused immunocompromised children with HCV infection in Egypt. In a recent Egyptian study enrolling 49 children with hematological disorders and 51 with hematological malignancies,[2] anti-HCV was detected among 40/49 (81.6%) children with hematological disorders (24/49; 49% HCV-RNA positive) and 9/51 (17.6%) children with malignancies (12/51; 23.5% HCV-RNA positive). HBV-DNA was positive among 38%; positive C region in 33% (15/49 and 18/51 children with hematological disorders and malignancies respectively), S region in four leukemic patients and X region in one leukemic patient. Twenty-one patients had occult HBV infection; one (2.6%) was HBeAg positive, four (19%) total HBcAb positive, 20 (95.2%) C region HBV-DNA positive and one was S region positive (1/21; 4.8%). HCV-RNA was the significant predictor for occult HBV ($P<.05$), with an increased frequency of HBV-DNA in the HBsAg negative (HCV-RNA positive) (63.2%) compared with patients negative for HCV-RNA (25%) ($P=.009$). Abdelwahab et al did not consider the possibility of concomitant occult HBV in analyzing data in their studied hemophilic patients. This point, therefore, ought to be regarded as an important limitation in their study.

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Reply

Thank you for your interest in our article. In fact, according to the World Federation of Hemophilia Report last survey in 2010,[1] there are 5307 hemophiliacs in Egypt. It is true that 100 hemophilia patients is not enough to be generalizable to the Egyptian hemophilia population in general and the pediatric group in particular, but our study is a cross-sectional one with children collected from two of the biggest hematology referral centers for hemophiliacs in Egypt. This is referred to in the title by saying in a "cohort" of Egyptian children meaning "group."

Although the prevalence of HCV among patients with inherited coagulation disorders is 48.3% in Eastern Mediterranean region, it can exceed that percentage in Egypt. This can be attributed to the lack of accurate medical data as a lot of patients with inherited coagulation disorders, especially mild forms, receive replacement therapy irregularly and in different places and so are usually not screened for HCV. A screening program for HCV has started in Egypt in 1994 and is currently mandatory for all blood donors to be routinely screened. The study by Khalifa et al, among subjects with hematologic disorders before implementing the screening program, showed a HCV prevalence of 15%—higher than in our study group, pointing to the relative efficacy of the screening program.[2] This is further supported by another recent report that included only thalassemic patients showing a decrease in the prevalence of HCV antibody in our hospital hematology department pediatric patients from 71% in 1995 to 51.7% in 2011.[3]

In view of the significantly lower mean age of children with negative HCV antibody as opposed to those with positive HCV antibody, age can be considered another indicator of the relative efficacy of the screening program. However, it was better to compare the HCV infection rate of hemophilia patients before and after transfusion transmitted infections screening program for determination of the program efficacy. This was not possible in view of inavailability of accurate medical records are available to make this comparison as patients who were

children at the time the screening program started are either lost to follow up or are followed in adult medicine, usually in hospitals close to their residential areas.

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Ophthalmic complications of dengue: pathogenesis and prevention

To The Editor: The report of Tabbara[1] on dengue retinochroiditis is timely and makes practitioners and physicians to consider various ophthalmic manifestations and complications of dengue fever. Unfortunately these are discussed seldom during clinical rounds and teaching sessions. It is surprising that ophthalmic complications were not cited much in recent papers.[2,3] As genetic susceptibility[4] is known for dengue infections, genetic predisposition might explain the susceptibility of a subset of dengue affected individuals for ophthalmic complications which needs further study. Recently ophthalmic manifestations following West Nile virus infection, another flavivirus, have been reported,[5] so the author could have considered West Nile infection also.

Additional investigations such as functional status of platelets, platelet receptor polymorphism, defects in megakaryotes and platelet antibodies might have carried out in order to rule out platelet dysfunction as a contributory factor for hemaorrhagic episodes observed in the case reported. Dengue virus appears to infect the endothelial cells of blood vessels. As angiotension converting enzyme inhibitors (ACEIs) have a protective effect on blood vessels, the chemoprophylactic effects of ACEIs to prevent vasculogenic (vascular) complications of dengue fever are worth exploring. Also, it might be interesting to observe whether patients on ACEIs escape vasculogenic complications, if they are infected by dengue fever virus.

Investigators need to identify the various target proteins, amino acid residues and mimickers of amino acid residues, and their binding activity to dengue viral infection triggers or alters the immune mechanism resulting in post-dengue ophthalmic complications.[6] Overall, there is a need to identify the susceptible population for complications of dengue fever and to introduce prophylactic agents to prevent or minimize complications of dengue fever.

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Reply

I read with interest the comment of Uma and associates on the report of "Dengue retinochoroiditis."[1] I highly appreciate their comments in which they highlight four points: (1) the genetic predisposition to dengue virus infection, (2) the protective effects of ACE inhibitors, (3) additional investigations of platelet functions, and (4) molecular mimicry between vascular endothelial cells and dengue virus.

Dengue virus is composed of four distinct serotypes related to flaviviruses which represent the

most important emerging viral disease at the present time. First, in response to the genetic predisposition: genetic determinants of dengue virus susceptibility include human leukocyte antigens, blood type, and single nucleotide type polymorphisms in immune response genes.[2] At the same time, one has to consider other factors such as viral genetic determinants, age, ethnicity and the nutritional status of the individual related to dengue virus susceptibility. It is, therefore, conceded that functional genetic studies to complement available data would certainly help in defining the dengue virus susceptibility. Second, in reference to the ACE inhibitors protective effect in dengue, there are no clinical trials that have been reported on this subject and the hypothesis need to be verified by future studies. Third, our two patients had thrombocytopenia and we did not perform studies on antibodies against thrombocytes or platelet receptor polymorphism. Fourth, the concept of molecular mimicry that has been proposed by Liu and associates[3] is intriguing. They have found that dengue virus complex-specific mAb (DB16-1) targeted the same epitope in the dengue virus non-structural protein 1 (NS1) and lysine-rich CEACAM1 (LYRIC) protein in human endothelial cells suggesting that it may play a role in the pathogenesis of dengue hemorrhagic fever and dengue shock syndrome.[3] The role of this molecular mimicry in ocular and retinal vasculopathy remains to be determined. Furthermore, future studies on the role of anti-NS1 antibody as a cause of vascular permeability should be studied in individuals with endothelial cell dysfunction in dengue fever.

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erratum

In the folllowing article: Al-Alwani et al. Diagnosed congenital hypothyroidism with missing follow-up: Is it time for a national registry? Ann Saudi Med 2012;6:652, the first author's last (family) name was misspelled. It should have been Al Alwan.