

Letter to the Editor

Selection Bias in reporting the prevalence of Transfusion Transmitted Infection Diseases in Iranian Hemophiliacs

Peyman Eshghi^{1,2}, Hassan Abolghasemi^{1,3}

1. Iranian Blood Transfusion Organization Research Center, Tehran, Iran

2. Dept. of Pediatric Hematology and Oncology, Shahid Beheshti University of Medical Sciences, Tehran, Iran

3. Dept. Pediatric Hematology and Oncology, Baqiyatallah University of Medical Sciences, Tehran, Iran

In Issue 3 Summer 2008 of **Iranian Journal of Pathology**, a paper entitled “Seroprevalence of HIV and Hepatitis C infection in Hemophiliac Patients in Iran” with the authorship of Mohsen Nassiri Toosi *et al.* with affiliation of Hemophilia Center of Imam Khomeini Hospital in Tehran has appeared. It is initially noteworthy to inform you that the above hemophilia center is the most major and the most long standing hemophilia treatment center in Iran. In their article, Nasiri Toosi *et al.* after a short and suitable review of the consumption trend of plasma products in Iranian hemophiliacs and others across the world refer to the main objective of their study as being the determination of prevalence rate of viral infections and HCV genotypes in Iranian hemophiliacs (1,2). Out of 236 patients participating in this study, 171 were hemophilia A and 25 hemophilia B affected and 40 (16.9%) suffered from other bleeding disorders. Although the methodology of the study indicates that all patients under treatment in hemophilia center in 2003 have participated in the study, it is obvious that it has not been the case and probably a kind of selection has happened. The reason for our claim is the fact that there are about 550 severe A and B hemophiliacs living in Tehran (3); add to it the on-demand treatment protocol of Iranian patients and further the expected joint bleeding frequency of about 20-30 times a year (4). Thus, it can be easily estimated that the number of just these patients referring for examination, treatment, and drug prescription would go much higher than the number of participants mentioned in this article. Moreover, according to the published

reports, about 57% of all Tehran hemophiliacs are hemophilia A and B affected and the rest 43% suffer from other congenital bleeding disorders that all are different from the data presented in this article. It is also add why there has been no report on von Willebrand patients in this study while the severe type of this disease is the third most prevalent hemophilia in Iran and the affected are in regular need of blood components.

As far as the subject randomization is concerned, it again seems to be unlikely and there seems to be selection bias. The number of 0-9-year-old A and B hemophiliacs in this study is 4 (2% of the whole population under study), 10-19-year-olds 49 (25%), and the rest are above 20 (about 75%) while the population composition of these very patients in 2006 in Tehran shows a totally different image in which about 7% are under-five-year-olds, 15% are 5-14-year-olds, and about 50% above 25 (3). The initiation of country-wide vaccination in 1993 and blood donor screening for HCV in 1997 in Iran, increasing supply trend of virus inactivated coagulation components in recent decades (the consumption per capita of 1.3 units of Factor VIII and 0.2 units of Factor IX in 2006) (5), and treatment of HCV and HIV affected hemophiliacs (5) have led to the decrease of prevalence rate of transfusion transmitted viral infections in under-10-year-olds. However, the lack of proportionality in subject selection and biased randomization across different age ranges has made the generalization of the statistical findings to the whole Tehran hemophiliacs invalid. Even if we accept the results of this study,

Address communications to: Dr Peyman Eshghi, Department of Pediatric Hematology and Oncology, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

Email: peyman64@yahoo.com

they are not representative of the whole country as the title and the discussion section of the article aim to do because the access rate of different hemophiliacs to virus inactivated concentrates in the past decades considering the extensiveness of Iran and remoteness of some regions has not been consistent and compatible. This shortcoming (error in randomization) has been also observed in previous studies having led to very different reports as far as HCV, HBV, and HIV are concerned (6,7) and of course the main reason goes back to the fact that hemophiliacs are not always available to researchers. In this study and similar investigations, only patients being more accessible cause of their repeated complaints or concerns, or those suffering liver malfunction with higher likelihood for being infected with hepatitis, or those not facing phlebotomy problems due to poor vein access, and the hemophiliacs not having problems about parent permission have been usually enrolled as participants. Nonetheless, in 2006 annual report of Iran hemophiliacs prepared by an NGO affiliated to Iran Hemophilia Society, responsible to identify hemophiliacs and reflect their condition for their treatment facilities to be ensured, the prevalence rates of HIV and HCV in A and B hemophiliacs reported to be 4% and 47%, respectively but there has been no report on any cases of HCV and HIV in von Willebrand patients, though they receive cryoprecipitate and FFP more than A and B hemophiliacs (5).

Considering the above points, it seems that the statistical results of this study especially regarding HCV and HIV infection rates of 83% and 4.7% among Iranian hemophiliacs are only true in 10-15% of Tehran hemophiliacs and 3-4% of Iran hemophiliacs out of whom 98% are above 10 years of age and 70% above 20 and all of whom most probably have been involved in the study by nonrandom selection; actually they can not be representative of 6000-7000 hemophiliacs of Iran. Thus, extensive and country-wide studies for the determination of prevalence rates of HBV, HCV, and HIV in all hemophiliacs are strongly recommended.

References

1. Nassirtoosi M, Lak M, Karimi K, Managchi M, Samimi-Rad K, Abdollahi A, *et al.* Serum viral markers in Iranian patients with congenital bleeding disorder. *Ann Saudi Med* 2008;28(6):453-5.
2. Nassirtoosi M, Lak M, Karimi K, Managchi M, Samimi-Rad K, Abdollahi A, *et al.* Seroprevalence of Human Immunodeficiency Virus(HIV) and Hepatitis C infection in Hemophilic Patients in Iran. *Iranian J Pathol* 2008;3(3):119-124.
3. Mehdizadeh M, Kardoost M, Zamani G, Baghaeepour MR, Sadeghian K, Pourhoseinghol MA. Occurrence of haemophilia in Iran. *Haemophilia* 2008; 1-4.
4. Kashyap R, Choudhry VP. Management of Hemophilia in Developing Countries. *Indian J Pediatr* 2001;68(2):151-157.
5. World Federation of hemophilia Report on the Annual Global Survey 2006. Dec 2007.
6. Sharifi-Mood B, Eshghi P, Sanei-Moghaddam E, Hashem M. Hepatitis B and C virus infections in patients with hemophilia in Zahedan, Southeast Iran. *Saudi Med J* 2007;28 (10):1516-1519.
7. Rezvan, H. Abolghassemi, H. Amini Kafiabad, S. Transfusion-transmitted infections among multitransfused patients in Iran: a review. *Transfusion Medicine* 2007; 17: 425-43.

Authors reply

The distinguished professors are highly appreciated for the significant points they have mentioned.

In their view, it would have been much better to not generalize the study to the entire country, Iran, and specify it to a research center.

Under the aegis of the relentless efforts the Blood Transfusion Organization has undertaken in recent years, contaminations have dropped to near zero and viral infections stand much lower than the figures mentioned.

The study conducted at Imam Khomeini Teaching Hospital highlights higher levels of infection due to the fact that the survey is based on the samples taken before 1985. Or it may be related to the fact that the healthcare facility is a referral center and it receives cases from across the country.

Anyhow, the level of infection is definitely much lower than mentioned and as the esteemed professors have recommended, a wide-scale study should take place to examine the spread of viral infections in hemophiliac patients.

*Address communications to: Dr Alireza Abdollahi, Department of Pathology, Tehran University of Medical Sciences, Tehran, Iran.
Email: dr_p_abdollahi@yahoo.com*