Hepatitis B Virus Infection: Emerging Challenges for the Armed Forces

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Hepatitis B virus (HBV) infection is a health problem worldwide and the infected person remains at risk of developing chronic hepatitis, cirrhosis and hepatocellular carcinoma. Of the estimated 350 million HBV carriers worldwide, one fourth are likely to develop serious liver disease [1,2]. The prevalence rate of hepatitis B in India is around 4% [3]. However, when armed forces screened 22000 recruits over 25 regimental centres scattered throughout the country, the prevalence rate was 1% amongst healthy young males (Director General Hospital Services, personal communication, Aug 07). Even this level of seroprevalence among healthy recruits points towards the seriousness of this problem. A 'Hepatitis B & C Registry' was established at Army Hospital Research and Referral, New Delhi[4] where on date, 1193 patients have been registered which includes 786 patients with hepatitis B. Some interesting facts have emerged from this data. Nearly one fourth (200) of patients were detected during donor screening for blood transfusion. Despite conventional screening of donated blood for hepatitis B surface antigen (HBsAg), six patients developed HBV infection after blood transfusion.

Transfusion associated hepatitis B (TAH-B) continues to be a significant problem in our country. Its prevalence is estimated at approximately 1.5% in postsurgical blood transfusion recipients in India [5]. In two recent reports TAH was detected in 6.9-7.7% of blood transfusion recipients, of which TAH-B constituted about 20 % [6, 7]. Per unit risk for HBV infection was estimated at 0.37 %. This raises a question on how can we make transfused blood safer than what it is today?

Most doctors in India are conversant with the significance of HBsAg while significance of hepatitis B core antigen (HBcAg) or hepatitis Be antigen (HBeAg) are less clearly understood. HBcAg is expressed on the surface of infected hepatocyte and

cannot be detected in the blood. What can be detected in circulating blood are antibodies against HBcAg, which can be IgG or IgM type. In patients who are HBsAg negative, detection of IgG anti-HBc (also called anti-HBc) in blood may indicate resolved HBV infection in the remote past, low grade chronic infection or occult HBV infection with a mutant strain of HBV.

Should routine screening of donated units for anti-HBc be made mandatory for Indian blood banks? In a few countries, screening by anti-HBc and/or HBV nucleic acid amplification tests (NAT) have been introduced to reduce the risk of TAH-B. Anti-HBc screening could be employed as an additional safety feature in HBV low prevalence countries, but it would lead to rejection of a high percentage of otherwise acceptable donations in countries with moderate and high prevalence of HBV [8]. In the Armed Forces Transfusion Centre at New Delhi, data of anti-HBc testing of blood donors over four months showed that nearly 10% of donor units (522/5619 donations) were HBsAg negative, anti-HBc positive and were discarded. Unlike Japan, where a good correlation has been found between high anti-HBc titers and presence of HBV-DNA, no such correlation was found in India [5]. Simply discarding the blood positive for anti-HBc is likely to result in blood shortage as the anti-HBc can be false positive and there may be lack of concordance in serological assays [9,10].

In this setting, use of nucleic acid technology to check for HBV-DNA would be ideal, though expensive. A simpler algorithm would be to screen the anti-HBc positive blood for antibody to HBsAg (anti-HBs). Anti-HBs is a marker of recovery and protective immunity. Donor samples reactive for anti-HBc and anti-HBs are presumed noninfectious, safe and can be retained for transfusion. Use of this policy at All India Institute of Medical Sciences, New Delhi has led to only 4.32%

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samples being discarded [5]. However, the report that some anti-HBs positive donors can also be HBV-DNA-positive [9] implies that this approach is not foolproof. While the final answer to blood safety may lie in nucleic acid technology, the recommendations must be tempered by cost constraints for a universal application in the armed forces and the nation as a whole.

In an article in this issue of the journal, Kumar H et al [11], have proposed testing for IgM-anti-HBc amongst voluntary blood donors as a screening procedure for window period hepatitis B in donated blood. IgM-anti-HBc may be the only HBV marker present in acute HBV during the “window period” between the disappearance of HBsAg and the appearance of anti-HBs. Blood containing IgM-anti-HBc and absent HBsAg has been implicated in the development of transfusion associated hepatitis B. The authors have concluded that instead of screening for anti-HBc, we should test for IgM-anti-HBc to see “infectivity status of the blood donors in the window period and to discard blood only if positive for this marker.” Such an approach will pick up the small fraction of IgM-anti-HBc positive donors. While testing for IgM-anti-HBc may add marginally to blood safety, its yield is likely to be low as relatively larger fraction of anti-HBc positive replicating donors will be missed and use of only IgM-anti-HBc is not recommended as a blood screening procedure world over. This may be done in addition to IgG-anti-HBc screening modified with anti-HBsAg in our blood banks and consider discarding anti-HBc positive, anti-HBs negative blood. This will make transfused blood safer but will have the disadvantage of making HBV screening more tedious.

In another article published in this journal, Lahiri et al [12] have reported that HBeAg negative chronic hepatitis B is present in upto 8.3% of patients with chronic hepatitis B virus infection. HBeAg and HBV-DNA are markers of replication of HBV. Some patients who are HBeAg negative are actually replicating with HBV-DNA and have ongoing hepatitis. They represent a mutant strain of HBV. HBeAg negative chronic hepatitis B is a challenge in our country with multiple reports showing its high prevalence and poor outcome [13].

Guptan et al [14], have reported 15.5% prevalence of precore mutation (HBsAg positive, HBeAg negative/anti-HBe positive, and HBV DNA positive). Similarly, Chowdhury et al [15] in a community-based epidemiological study of HBV infection in West Bengal found G1896A precore stop codon mutants in 12% of people and base core promoter mutants in 18%. The significance of HBeAg negative and HBV-DNA positive chronic hepatitis B is that this variant is less responsive to available treatment and progresses rapidly

to cirrhosis and its complications [13]. American Association for Study of Liver Disease (AASLD) guidelines recommend one year interferon therapy for HBeAg negative group as compared to only 16 weeks for HBeAg positive group [16]. Study of HBeAg negative chronic hepatitis B have shown that while there may be an early virological response, majority of them will relapse on follow up [17]. Maintenance therapy with lamivudine following virological remission in this group after initial treatment may be an answer [18]. While significant prevalence of HBeAg negative chronic hepatitis B in India is an established fact, we eagerly await the results of therapy with newer drugs such as adefovir and entecavir which are now freely available to patients in armed forces.

References

1. Kane MA, Clements J, Hu D. Hepatitis B. In: Jamison DT, Mosley WH, Measham AR, Bobadilla J, eds. Disease control priorities in developing countries. New York: Oxford University Press, 1993; 321–30.
2. Kane MA. Global programme for control of hepatitis B infection. *Vaccine* 1995; 13 (Suppl 1): 47S–49S.
3. Thyagarajan SP, Jayaram S, Mohanavalli B. Prevalence of HBV in general population in India. In: Sarin SK, Singal AK, eds. Hepatitis B in India: problems and prevention. New Delhi: CBS, 1996; 5–16.
4. Anand AC, Seth AK, Chopra GS, Vijayalaxmi A. Armed Forces registry of chronic hepatitis B virus infection: A single hospital experience. *Ind J Gastroenterol* 2004; 23(Suppl1):1S.
5. Chaudhuri V, Nanu A, Panda SK, Chand P. Evaluation of serologic screening of blood donors in India reveals a lack of correlation between anti-HBc titer and PCR-amplified HBV DNA. *Transfusion* 2003; 43: 1142–8.
6. Dasarathy S, Misra SC, Acharya SK, et al. Prospective controlled study of post transfusion hepatitis after cardiac surgery in a large referral hospital in India. *Liver* 1992; 12: 116–20.
7. Saxena R, Thakur V, Sood B, et al. Transfusion-associated hepatitis in a tertiary referral hospital in India. A prospective study. *Vox Sang* 1999; 77: 6–10. Erratum *Vox Sang* 2000; 79:20.
8. Comanor L, Holland P. Hepatitis B virus blood screening: unfinished agendas. *Vox Sanguinis*. 2006; 91: 1–12.
9. Almeida NC, Strauss E, Sabino EC, Sucupira MC, Chamone DA. Significance of isolated hepatitis B core antibody in blood donors from São Paulo. *Rev Inst Med Trop Sao Paulo* 2001; 43:203–8.
10. Schmidt M, Nübling CM, Scheiblaue H, Chudy M, Walch LA, et al. Anti-HBc screening of blood donors: a comparison of nine anti-HBc tests. *Vox Sanguinis* 2006; 91:237–43.
11. Kumar H, Gupta PK, Jaiprakash M. Role of anti-HBc IgM in screening of blood donors. *MJAFI* 2007; 63 : 350–2.
12. Lahiri KK, Sahni AK, Gupta RM, Duhan SD, Kapila K, Jena J. Hepatitis B e Antigen negative chronic hepatitis in Indian Patients: A reality. *MJAFI* 2007; 63 : 318–21.
13. Saikia N, Talukdar R, Mazumder S, Khanna S, Tandon R. Management of patients with HBeAg-negative chronic hepatitis

- B. Postgrad Med J 2007; 83:32–9.
14. Guptan RC, Thakur V, Sarin SK, Banerjee K, Khandekar P. Frequency and clinical profile of precore and surface hepatitis B mutants in Asian-Indian patients with chronic liver disease. *Am J Gastroenterol*. 1996; 9:1297-8.
 15. Chowdhury A, Santra A, Chakravorty R, Banerji A, Pal S, Dhali GK, et al. Community-based epidemiology of hepatitis B virus infection in West Bengal, India: Prevalence of hepatitis B e antigen-negative infection and associated viral variants. *J Gastroenterol Hepatol* 2005; 20: 1712–20.
 16. Lok ASF, McMahon BJ. AASLD practice guidelines: Chronic Hepatitis B. *Hepatology* 2007; 45: 507-39.
 17. Seth AK, Nema SK, Kakkar S, Diwan RN. Efficacy of low dose and high dose of interferon in treatment of hepatitis B related chronic liver disease. *Ind J Gastroenterol* 2001; 20 (Suppl1): C5.
 18. Seth AK, Anand AC, Chopra GS. HBeAg negative chronic hepatitis B: Maintenance with lamivudine following virological remission with combination therapy of interferon and Lamivudine. *Ind J Gastroenterol* 2003;22:C3.

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