Implementing fourth generation human immunodeficiency virus enzyme-linked immunosorbent assay: One step forward in blood safety

Prasun Bhattacharya, Ravneet Kaur[1]

Department of Immunohaematology and Blood Transfusion Medicine, Kolkata Medical College, Kolkata, West Bengal, [1]Department of Transfusion Medicine, Government Medical College and Hospital, Chandigarh, India

Access this article online

Website: www.ajts.org

Quick Response Code:

Correspondence to:
Dr. Prasun Bhattacharya, Department of Immunohaematology and Blood Transfusion Medicine, Kolkata Medical College, 88 College Street, Kolkata - 700 073, West Bengal, India.
E-mail: pbhattach@gmail.com

Blood transfusion is a life-saving procedure and at the same time it always carries some inherent risks. In the context of the 20th century, with the rapid advancement in the diagnostics and laboratory medicine the early detection of markers for transfusion transmitted infections (TTIs) have been reduced from several weeks to few days. This has diminished the residual risks of TTIs to as low as 1 in 677,000 units for human immunodeficiency virus (HIV), 1 in 103,000 for hepatitis C virus (HCV) and 1 in 63,000 for hepatitis B virus (HBV).[1] At present, the greatest threat to the safety of blood supply is the donation of blood by seronegative donors during the infectious window period. Such people represent new or incident infections during pre sero-conversion period.

Blood transfusion in the 21st century is as safe as ever, with the implementation of nucleic acid testing (NAT) almost zero risk transfusion is possible if at all it is not challenged by the newer emerging pathogens. Although the NAT screening reduces the window period of viral infection, in India the conventional 3rd generation enzyme linked immunosorbent assay (ELISA) still remains the most common screening test for TTIs. The overall cost and infrastructure development are the major challenges for its universal implementation. So, an ideal screening test in the resource constrained set-up should be highly sensitive, easily operable and cost-effective as mentioned by Malhotra *et al.*[2] It also worth mentioning that an accurate estimates of the risks of transfusion-transmitted infectious diseases are essential for monitoring the safety of the blood supply and evaluating the potential effect of new screening tests.

The most direct way of estimating the risk associated with transfusion is to study the rate of infection prospectively in transfusion recipients. However, such studies are to be extensive, may be almost impossible considering the low prevalence of TTI markers[3] and in the absence of a well-organized hemovigilance network in India. There are only a few current estimates of the residual risks of TTIs by blood transfusion of HBV or HCV and HIV in India.[4] However, considering the significance of infective window period, introduction the 4th generation ELISA in HIV screening will definitely escalate the possibility of detecting HIV sero-conversion earlier in blood donors especially in countries where the prevalence of HIV is on the relatively higher side. This is due to the detection of HIV core protein (p24 antigen [Ag]) that appears transiently in blood donors prior to seroconversion. As per the World Health Organization recommendation for HIV testing, in addition to the detection of antibody, the screening assay should preferably also employ the detection of Ag. It further reduces the serologic window period by 3-7 days.[5]

In a very recent published comparative analysis on the performance of 3rd versus 4th generation HIV ELISA in North India showed, increased sero-reactivity is detectable by 4th generation ELISA. On analysis of 1075 donors' sample, an additional 4 samples were reactive by 4th generation ELISA with one of them was confirmed positive by Western Blot (WB) analysis.[6] The present status of WB as confirmatory test does have limitations and drawbacks due to non-specific band reactivity, contamination with human cellular Ag and positional presence of antigenic bands on WB strip. All these may relate to the indeterminate results, which may vary from none in high prevalence populations to 50% or more among blood donors in ELISA reactive samples.[7]

In the study by Malhotra *et al.*,[2] in the current issue of the journal showed 4th generation ELISA could detect higher number of seroreactive samples (37 vs. 14/ 10,200 donations), but the difference in seroprevalence expressed per 1,000 donations was not statistically significant. The difference in the seroprevalence of HIV among blood donors in various groups and subgroups using 3rd and 4th generation ELISA was also non-significant. One of the observation worth mentioning from this study was the

4th generation ELISA detected all the 11 samples, which were reactive to both WB and 3rd generation ELISA with an additional yield of 0.58 window period units per 1,000 donations (6 WB confirmed reactivity out of 10,200). However, a high rate of false reactivity was also observed (20 out of 37) in 4th generation ELISA against WB assay. This could be an explanation to the present status of WB as a confirmatory test for HIV as mentioned previously.

Since, NAT was not done to confirm the results of the 4th generation ELISA due to financial constraints, but there are few similar studies from the developing countries which had estimated the addition of p24 Ag, minipool NAT, and individual donation NAT assays would detect 3.9, 8.3 and 10.8 window period units per 10,00,000 in first-time donors respectively.[8]

Inclusion of the 4th generation HIV ELISA in the national blood screening mandate is likely to improve the safety of blood components without much financial burden. However, more multi-centric studies are required across the country to evaluate its effective potential. Implementing improved blood screening along with better donor education and identifying low-risk donor population are the major pillars of blood safety in the developing world, simply a highly sensitive blood donor screening strategy may not be adequate.

References

1. Schreiber GB, Busch MP, Kleinman SH, Korelitz JJ. The risk of transfusion-transmitted viral infections. The retrovirus epidemiology donor study. N Engl J Med 1996;334:1685-90.
2. Malhotra S, Marwaha N, Saluja K. Seroprevalence of HIV in North Indian blood donors using third and fourth generation ELISA. Asian J Transfus Sci 2013;125-9.
3. Sharma RR, Cheema R, Vajpayee M, Rao U, Kumar S, Marwaha N, *et al*. Prevalence of markers of transfusion transmissible diseases in voluntary and replacement blood donors. Natl Med J India 2004;17:19-21.
4. Makroo RN, Choudhury N, Jagannathan L, Parihar-Malhotra M, Raina V, Chaudhary RK, *et al*. Multicenter evaluation of individual donor nucleic acid testing (NAT) for simultaneous detection of human immunodeficiency virus-1 & hepatitis B & C viruses in Indian blood donors. Indian J Med Res 2008;127:140-7.
5. Kitchen A, Dax EM, Reddy R, Dhingra N, Fordham J, Lloyds S. Screening donated blood for transfusion transmissible infections: Recommendations, 2009. Available from: http://www.searo.who.int/linkfiles/BCT_WHO-recommendation-09.pdf. [Last accessed on 2013 April 20].
6. Kaur R, Basu S, Kaur G, Singh D. Fourth-generation enzyme immunoassays for screening of HIV in blood donors: Need of the hour. Indian J Pathol Microbiol 2011;54:433-4.
7. Icardi GC, Gabutti G. The Italian multi-centre study investigators. Multi-centre evaluation of RIBA™ HIV-1/HIV-2 SIA compared to HIV-1 Western blot. J Prev Med Hyg 1998;39:57-64.
8. Barreto CC, Sabino EC, Gonçalez TT, Laycock ME, Pappalardo BL, Salles NA, *et al*. Prevalence, incidence, and residual risk of human immunodeficiency virus among community and replacement first-time blood donors in São Paulo, Brazil. Transfusion 2005;45:1709-14.

Cite this article as: Bhattacharya P, Kaur R. Implementing fourth generation human immunodeficiency virus enzyme-linked immunosorbent assay: One step forward in blood safety. Asian J Transfus Sci 2013;7:107-8.

Source of Support: Nil, **Conflicting Interest:** None declared.