Transfusion Transmitted Diseases

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Abstract. Transfusion transmitted disease (TTD) is a major challenge to the transfusion services all over the world. The problem of TTD is directly proportionate to the prevalence of the infection in the blood donor community. In India, hepatitis B/C, HIV, malaria, syphilis, cytomegalo virus, parvo-virus B-19 and bacterial infections are important causes of concern. Hepatitis B and C infections are prevalent in India and carrier rate is about 1-5% and 1%, respectively. Post transfusion hepatitis B/C is a major problem in India (about 10%) because of low viraemia and mutant strain undetectable by routine ELISA. HIV prevalence among blood donors is different in various parts of the country. It may not be so alarming as projected by some agencies. In one study from north India, confirmed HIV positivity was found in 0.2/1000 blood donor. Post transfusion CMV is difficult to prevent but use of leukocyte filters may help to reduce it significantly. Parvo virus B-19 infection in blood donors is 39.9% which may increase morbidity in multitransfused or immunocompromised patients. Current syphilis tests may not be sensitive but it should be continued to exclude high-risk donors. Malaria is a real problem for India due to the lack of a simple and sensitive screening test. Incidence of bacterial contamination is greatly reduced due to improved collection/preservation techniques and use of antibiotics in patients. However, proper vigilance and quality control is needed to prevent this problem. Total dependence of altruistic repeat voluntary donors and use of sensitive laboratory tests may help Indian blood transfusion services to reduce incidences of TTDs. [Indian J Pediatr 2001; 68 (10) : 951-958]

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Blood transfusion is a life saving modality but it should be judiciously used. The transfusion of blood and blood products is much safer than ever before but far from attaining “zero risk” level at the present moment. There are various types of diseases, which can be transmitted to the recipient. Disease transmission is one of the most dreaded complications of blood transfusion.¹

The magnitude of the problem of transfusion-transmitted diseases varies from country to country depending on disease prevalence. Various measures are taken in a country to make therapy safe for the respective population. These strategies may be targeted to prevent transfusion-transmitted diseases in that country. There is a risk of 1 to 2 per 1000 recipients, to receive contaminated blood with viral, bacterial or parasitic agents. However, there is 50% risk of serious morbidity and mortality for the patients if blood transfusion is not done/undertaken.²

Viral infections assumes a great importance in transfusion associated mortality and morbidity in patients. Majority of the problems are due to prevalence of asymptomatic carriers in the society, as well as, blood donations during window period of infections. Concealing of medical history by captive, paid or professional blood donors, who widely exist in developing countries, also pose a great threat to safe blood supply. There is a long list of viruses, parasites and bacteria, which can be transmitted through blood transfusions. Among them, important transfusion-transmitted viruses are, human immunodeficiency virus (HIV-I/II), hepatitis B virus (HBV), hepatitis C virus (HCV), parvo virus B-19 and cytomegalo virus (CMV) etc.

Transfusion Transmitted Hepatitis B Virus

Transfusion associated hepatitis is a major problem in South-East Asian countries including India, due to endemic hepatitis infections in this region. The prevalence of HBV is low in USA and Western Europe (0.1% to 0.5%), while in South East Asia and China, which are endemic areas, it ranges from 5% to 15%.³ Prevalence of HBV and HCV in India is about 1-5% and 1% respectively.⁴⁵ According to the Drugs and Cosmetic Act (1992), every blood unit has to be tested for HBsAg, anti HIV I&II, VDRL and malaria.⁶ Since HCV testing is not mandatory in India, some blood banks are doing this test voluntarily. HBsAg testing is mandatory by the Act but it can either be carried out by enzyme linked immunosorbent assay (ELISA) or by reverse passive hemagglutination assay (RPHA).

Post Transfusion Hepatitis in India : Hepatitis B is a special problem in India since it is a medium endemic area. This problem is acutely reflected in blood transfusion services due to dependence on first time relative or paid blood donors and lack of non-remunerated repeat voluntary blood donors (VD). Many
commercial blood banks do not carry out tests with proper quality control and testing of blood units by RPHA or by rapid tests, which further reduces the safety due to their lower sensitivity and specificity. Anti HBC antibody (HBCAb) and serum ALT tests are not mandatory in blood banks and they are not carried out for logistic and cost factors. The prevalence of anti HBC positivity in India is 15% to 25% among apparently healthy general population. The prevalence of IgG/M HBcAb among HBsAg negative, healthy voluntary blood donors of our centre is 24.3%. Without any direct evidence of hepatitis and liver disease, it is difficult to defer blood donors only on the basis of positive HBCAb test. When 45 U/L of ALT was considered as a cut off level, about 15% of our HBsAg negative donor population showed raised ALT. No correlation was found between HBsAg, HBCAb and raised serum ALT level in voluntary donors. The usually accepted cut off value for serum ALT level (i.e., 45 U/L) is also not applicable for Indian blood donor screening. As mentioned above, we observed that 15% of HBsAg negative healthy VD showed raised serum ALT (45 U/L) level. When standard cut-off value (mean + 2SD) was calculated on 6,000 of our voluntary donors, it was found to be 57 U/L. About 5% VDs showed raised ALT when 57 U/L was taken as a cut off value, and there was a strong co-relation with HBsAg marker (unpublished data).

It is generally recommended that HBCAb test can prevent transfusion associated HBV. But it is well known that in most of the HBV endemic countries, HBCAb ELISA test cannot be implemented as such. If these two tests are implemented in India, the donor pool may be significantly reduced due to high prevalence of these disease markers without significantly decreasing the risk of transfusion transmitted hepatitis. One Japanese study suggests that blood banks in Asian HBV endemic countries should start doing anti HBC tests in a serum at fixed dilution. High titer HBCAb units exclusion from transfusion, in addition to the existing HBsAg screening test may help to prevent PTH in hepatitis endemic countries.

Cause of PTH in India: Routine HBsAg screening in blood units does not eliminate the risk of HBV transmission. HBsAg test may be negative in the window phase of HBV infection, in the convalescence phase (core window) and also, in HBV chronic infection, with very low level of viraemia. Also, mutant forms of HBV with mutation in single or multiple sites of the HBsAg "a" determinants are not detected by the kits used for HBsAg testing. Study report reveals that about 9.91% of HBsAg (3rd generation ELISA) negative VD was HBV DNA positive by dot blots technique. Bodhiphala et al (1999) observed similar results where 7(3.5%) out of 200 HBsAg negative Thai blood donors, were positive for HBV DNA. The risk of this type of blood transfusion is always obvious in prospective sero-conversion studies. In one of our prospective studies, it was observed that the PTH (HBV and HCV) among open-heart surgery patients was 14.6%. Out of them, two-third patients developed icteric PTH-B and one-third patients developed anicteric PTH-C. All these patients received 3rd generation ELISA negative blood units. And when, frozen samples were retested, after patients developed PTH by ELISA tests, samples were also negative. But 11 samples out of 30 ELISA negative samples were positive for HBV DNA. Another study from India showed that 16% patients developed PTH and two thirds of them were due to HBV infection. Prevention of PTH: Prevention of PTH starts with selection of blood donors. The safety of blood transfusion is compromised in India due to absence of non-renumerated repeat blood donors and dependence on first time relative blood donors (RD). It forces blood centres to rely totally on serological tests. Use of tests with low sensitivity like RPHA is also allowed by the existing law to test HBV infection in blood donors. In majority of blood banks, rapid HBsAg tests like flocculation test, chromatographic strip tests are carried out. For the prevention of PTH, sensitive tests like ELISA are also not sufficient as discussed earlier. It has been even observed that polyclonal antibody based ELISA gives better sensitivity and provides better detection of mutants. The routine serological tests to identify viral hepatitis in blood donors generally take some time to become reactive after viremia. HBsAg test requires high level of HBV for detection of antigen. In case of HCV infection, it needs weeks to months to diagnose infection in blood donors. Moreover, some of the routine tests like ELISA fail to detect in case of low viremia and presence of mutants. In many western countries, nucleic-acid amplification (NAT) tests have been made mandatory in blood donors from the year 2000. This test is quite specific and very sensitive but extremely expensive. The transfusion services have attempted to make these tests more automated, simple and fool proof and to perform on pooled serum to reduce cost. Risk of PTH in Subcontinent: The situation in the Indian sub-continent is complex due to medium endemicity of hepatitis B infection and high cost of screening. Besides, these issues have not received attention of the health planners in India. About 7 million units of blood are transfused in India every year and according to Sarin et al there should be 1,19,700 new PTH every year in India. This is a preventable health problem and overall morbidity and mortality can be significantly reduced with the help of proper screening of blood units. It is clearly evident from our experience and, as well as, from literature that the present methods for screening of blood units cannot prevent PTH in recipients. There is a desperate need to offer reasonable safety net for transfusion recipients in terms of surrogate testing and other direct testing like nucleic acid testing. It is also not clear why the routine 3rd generation ELISA in Indian set-up do not detect about 10% HBV infection in blood donors and how it can be reduced in a cost effective