Original Article:

Clinical profile of transfusion-related human immunodeficiency virus (HIV) infection in a tertiary care hospital in South India

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ABSTRACT

Background: Transfusion-related infection is an important mode of human immunodeficiency virus (HIV) transmission. There are very few reports in the literature on transfusion-related HIV from India.

Methods: Retrospective study of clinical profile of patients with transfusion related HIV infection presenting to a tertiary care hospital in South India between May 1999 to December 2011.

Results: Among the 1332 records of HIV positive patients reviewed, 80 (6 %) had transfusion-related HIV infection; their mean age was 32.2 ± 12.2 years; there were 47 (58.8%) women. Sixty nine patients (86.3%) were infected with HIV-1, while 11 patients (13.8%) were infected with HIV-2 The average number of units of blood transfused was 2.8. The indications for transfusion were perioperative (n=37, 46.3%); haematologic disorders (n=15, 18.8%); trauma (n=9, 11.3%); upper gastrointestinal bleed (n=3, 3.8%); miscellaneous (n=3, 3.8%) and diagnosis not clear at the time of transfusion (n=13, 16.3%). Twenty six of the 64 patients (40.6%) had CD4+ count less than 200 cells/mm^3; 32 patients (40%) were receiving highly active antiretroviral therapy. Tuberculosis was the most common opportunistic infection.

Conclusions: Transfusion-related HIV infection, especially due to HIV-2 remains a significant problem in India even till recently; females seem to be more often affected probably due to the more frequent need for blood transfusion in them due to gynaecologic and obstetric reasons.

Key words: *Transfusion related infection, HIV, India*

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INTRODUCTION

Blood transfusion has the potential to save millions of lives each year. The risks of transfusion include the transmission of viral infections, bacterial contamination of blood components, haemolytic reactions, transfusion-related acute lung injury, and transfusion-associated graft-versus host disease. The first descriptions of human immunodeficiency (HIV) infection following blood transfusion occurred in late 1982. HIV-antibody testing began in 1985. In resource rich nations, the risk of contracting HIV infection from a unit of blood is now approximately one case per million units.[1] However, the scenario in India is unclear owing to poor documentation. There are very few reports in the literature on transfusion related HIV from India from a clinical point of view. This study highlights the details of our experience on the clinical profile of patients with transfusion-related HIV infection presenting to a tertiary care hospital in South India.

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MATERIALS AND METHODS

Data were obtained retrospectively from the medical records of the department of Medicine from May 1999 to December 2011. The case records of all HIV positive patients were studied and records of patients with transfusion-related HIV were identified. The records with other associated risk factors for HIV infections including high-risk behaviour were excluded. Demographic profile, clinical features, routine laboratory investigations, Western Blot test, CD4+ count, HIV viral load, mode of presentation and opportunistic infections were studied. HIV testing was done by HIV Vironostika [4th Generation enzyme linked immunosorbent assay (ELISA), BioMerieux, France]. All reactive specimens were then tested by HIV Tridot (J Mitra, India), a rapid assay that allows differentiation between HIV-1 and HIV-2. The reactive samples were further confirmed by a Western Blot assay (HIV Blot 2.2, Gene labs Diagnostics, USA). CD4+ counts were

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determined by using the FACS Count machine (Becton Dickinson, USA). HIV viral load was estimated by the Amplicor assay (Roche, USA).

RESULTS

Out of the 1332 case records of HIV positive patients screened, 80 (6%) patients were found to have transfusion-related HIV infection. Records of these 80 patients were analyzed. Maximum number of cases were observed in the years 2001 and 2002 with 13 cases in each year. The majority of these patients were referred from Rangareddy and Guntur districts.

Their mean age was 32.2 ± 12.2 years; there were 47 (58.8%) women. Sixty nine patients (86.3%) were infected with HIV-1, while 11 patients (13.8%) were infected with HIV-2. There were no cases of dual infection. Among 63 married patients, spouse was non-reactive in 30 (47.6%), reactive in 8 (12.7%) and status of the spouse was not known in 25 (39.7%) patients. There were 17 (21.3%) unmarried patients.

Prior to reporting to our institute, all patients had received transfusion at various other hospitals or clinics. Three of the patients came to know about the HIV status of the donors long after the transfusion. One of the donors of the patient was her brother who transmitted the infection. The donor also transmitted the infection to his wife subsequently which was detected during her pregnancy. The other two received blood from their relatives who subsequently came to know about their HIV status. The average period before transfusion to the presentation in this series is 7.3 years. The mean number of units of blood transfused prior to diagnosis was 2.8 (range 1-25 units). Ten patients had received a single unit of packed red cells. Obstetric and gynaecological surgery was the major indication for transfusions in our series followed by haematologic disorders. The indications for transfusion are listed in Table 1. Fifteen (18.8%) patients were asymptomatic. Salient clinical manifestations at presentation included fever (n=22, 27.5%); chronic diarrhoea (n=4, 5%); cough with fever (n=8, 10%); weight loss and generalized weakness (n=31, 38.8%). One patient had lymphoma and was successful treated with chemotherapy at our institute.

The CD4+ count reports were available in 64 patients; 26 (40.6%) had a CD4+ count less than 200 cells/mm^3, 15 (23.4%) had a CD4+ count between 200 and 350/ mm^3; and 23 (35.9%) had a CD4+ count above 350 cells/mm^3. The mean CD4+ count in those with HIV-1 infection was 319.9 cells/mm^3 and in those with HIV-2 infection was 436 cells/mm^3. Viral load was available at the time of presentation in 38 (55.1%) of the 69 HIV-1 positive patients. The viral loads ranged from less than 20-750,000 copies/mL. Viral load was not tested in patients with HIV-2 infection. Thirty-eight patients (48.1%) were receiving antiretroviral therapy. Of these, 31 patients were on first-line highly active antiretroviral therapy (HAART) and seven were started on second-line HAART. In this series, 11 (13.8%) patients were diagnosed to have tuberculosis (TB). Pulmonary TB was diagnosed in five, lymph node TB was seen in four, multicentric vertebral TB and disseminated tuberculosis were seen in one patient each. Other opportunistic infections observed included oral candidiasis in seven and oesophageal candidiasis in two. Severe chicken pox and cutaneous herpes zoster infection were observed in two patients each. Genital herpes and *Pneumocystis jiroveci* pneumonia and Cytomegalovirus retinitis were diagnosed in one patient each. HIV and hepatitis B virus (HBV) co-infection; and HIV and hepatitis C virus (HCV) co-infection were seen in three patients each. None of the patients were co-infected with HIV, HBV and HCV.

DISCUSSION

Blood transfusion remains a significant mode of transmission of HIV in India with a reported incidence of 2% to 15% from different parts of the country.[2,3] The reasons for such high prevalence of transfusion associated HIV in our country are due to lack of proper screening of blood products and the lack of strict adherence to the indications for transfusion of blood products, lack of supervision on places of blood transfusion, scarcity of non-remunerated voluntary donors and high prevalence of HIV in our country. There were 17

(21.5%) unmarried patients in this cohort. Among the 62 married patients, spouse was non-reactive in 29 (46.8%) patients, spouse was reactive in eight (12.9%) patients and status of the spouse was not known in 25 (40.3%) patients. With the circumstantial evidence of transfusion, absence of high-risk behaviour and other known risk factors for HIV, it was concluded that HIV was acquired due to transfusion of blood products.

Currently under the Drugs and Cosmetics Act, it is mandatory to test blood to be transfused for anti-HIV 1 and 2 antibodies, hepatitis B surface antigen, HCV antibody, malarial parasite and rapid plasma regain (RPR) test for syphilis in India.[4]

Table 1: Indications for blood transfusion

Indication		No. (%)
Perioperative		37 (46.3)
	Obstetric and gynaecologic indication	30
	Surgery (other than gynaecologic and obstetric indications)	7
Defined haematologic disorders		15 (18.8)
	SLE with haemolytic anaemia	2
	Haemophilia	3
	PNH	2
	ITP	4
	MDS	2
	Thalassemia	1
	Sickle cell anaemia	1
Trauma (road traffic accidents and stab injury)		9 (11.3)
Miscellaneous causes		3 (3.8)
Hanging followed by prolonged hospital stay		1
Snake bite		1
Corrosive injury		1
Upper gastrointestinal bleeds		3 (3.8)
Anaemia (aetiology not defined)		13 (16.3)

SLE = systemic lupus erythematosus ; PNH = paroxysmal nocturnal haemoglobinuria; ITP = idiopathic thrombocytopenic purpura; MDS = myelodysplastic syndrome

Infectivity estimates for infected blood transfusion are much higher than for other modes of HIV transmission as viral dose per exposure is far larger than for other routes to the tune of 90%.[5] Transfusions of whole blood, packed red cells, platelets, leucocytes, and plasma are all capable of transmitting HIV infection. The status of blood donors, who are in the early stages of HIV infection i.e., during window period, may not be detected by current screening methods. The first part of window period is called *eclipse window period* which lasts for three to seven days.[6] During this period circulating virus cannot be demonstrated since all markers of infection, including the viral ribonucleic acid (RNA) and proviral deoxy ribonucleic acid (DNA) are negative, and the individuals are regarded as (false) negative for HIV infection when the person is truly infected and also infectious.The second part of the window period is called *viraemic window* period, which lasts for 8 to 22 days. In the viraemic phase of the window period, since HIV is present in the circulation, early markers (RNA, DNA and p24 antigen) are detectable but HIV antibody is not detectable.[7] Testing for p24 antigen reduces the diagnostic window period to 9 to 14 days and nucleic acid detection assays reduce it to one week.[8] However, the majority of blood banks in India do not have the fourth generation assays (which test for p24 antigen and antibody) due to high costs involved.

The natural history and the prognosis of these patients with transfusion associated HIV differs from other modes of transmission of HIV; 50% of patients with transfusion associated HIV, progress to AIDS in less than seven years.[8] We observed female preponderance in our cohort and the possible reason for this is the large number of patients undergoing gynaecologic and obstetric procedures and requiring transfusions. Brushundi et al[9] observed similar findings in their study and opined that strategies to intensify rational use of blood and reduce the proportion of blood units in 'window period' such as donor deferral, HIV counselling, and promotion of voluntary blood donation are critical in achieving 'zero risk' transfusions. Thirteen patients (16.3%) were transfused for anaemia but the aetiology was presumed to be nutritional as the records did not mention the etiology of anaemia.

Ten patients in this cohort received single unit of packed red cells. Single unit transfusions raise the haemoglobin by 1 g/dL only, which is therapeutically insignificant. Therefore, according to World Health Organization's strategy for promoting and practicing rational use of blood and blood products the use of a single unit of blood therefore is strongly discouraged. The transfusion associated HIV infection in these patients could have been prevented if only the principles of safe blood transfusion are understood and adhered to. At least some of these elective patients could have received treatment with haematinics few weeks prior to surgery thereby avoiding the transfusion associated HIV.

In 1984, the Centers for Disease Control (CDC), Atlanta announced that, between the years 1979 and 1984, 90% of patients with haemophilia who were treated with clotting-factor concentrates had been infected with the HIV. The risks of transmission of viruses by plasma-derived products in haemophiliacs were reduced by the manufacture of recombinant factor VIII and factor IX.[10] Haematological conditions including haemophilia also accounted for a large number of patients in this cohort as our unit also renders the haematology referral services. In India due to limited availability of anti-haemophilic factors, patients continue to receive plasma or whole blood for bleeding episodes.

The earliest patient in our series of transfusion-related HIV dated back to 1987 when the awareness and screening techniques were just beginning to develop in India and the last transfusion which caused HIV infection was in 2008 and this brings to light the grave dangers, which we face till recently from this mode of transmission. Active look back and trace back programs were proved effective in identifying the donors and recipients of infected blood in countries like Canada[11] but stigma associated with HIV is a strong hurdle to implement such programs in countries like India.

HIV-2 is not common in India. However we observed 11 (13.8%) cases with HIV-2 infection in this cohort. In south India, where the estimate based on molecular studies, HIV-2 is 3% of all HIV infections.[12] The high incidence of HIV-2 in our cohort could be due to transfusion as the mode of transmission of HIV in this cohort. The mean CD4+ count in those with HIV-2 infection was higher compared to HIV1 and this is consistent with the natural history of slow progression of disease with HIV-2.

Like most patients in India, the most common opportunistic infection we found in this cohort of patients was TB. Forty eight (66.7%) patients in this group are receiving HAART in our study. Clinicians managing TB in HIV need to understand drug interactions and overlapping toxicities of antiretroviral drugs and anti-TB drugs. Rifampicin induces the activity of cytochrome P-450 CYP3A, which lowers the concentrations of HIV-protease inhibitors and non-nucleoside reverse-transcriptase inhibitors to sub therapeutic levels.

Practising strict adherence to indications for blood transfusions and planning an auto-transfusion when possible in elective surgeries would lessen the chances of this devastating complication of transfusion associated HIV. Implementation of nucleic acid amplification tests (NAT) and p24 antigen testing will improve the safety of blood supply in India. However, the cost-benefit ratio of

introduction of such expensive tests has to be carefully considered in a country with limited health budget.

Despite the best efforts of science, one cannot completely eliminate the risk of transfusion related transmission of HIV since current technology cannot detect HIV RNA in the immediate period following infection. The possibility of transfusing inadequately tested blood cannot be ruled out in our country, as not all blood banks and blood transfusing hospitals and clinics are completely under strict quality control. Link between the people, doctors, hospitals, government, non-governmental agencies, blood banks, celebrities and media may help bring the awareness in the lay public on this subject of safe transfusion practices in India too.

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