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TRANSFUSION TRANSMISSIBLE INFECTIONS AMONG BLOOD DONORS AT A TERTIARY CARE HOSPITAL, UDAIPUR

Pathology

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ABSTRACT

INTRODUCTION: Blood transfusion is an essential part of modern day healthcare; it can be a life-saving intervention. However, like all treatments, it may result in acute or delayed complications and carries the risk of transfusion transmissible infections.

AIMS & OBJECTIVES: To study the nature and frequency of transfusion transmissible infections (viz. HIV, HBsAg, HCV, syphilis, Malaria) in blood donors.

MATERIAL & METHODS: All blood donations received in Blood Bank, GMCH Udaipur were included in the study. All donors were selected by standard donor selection criteria by taking the relevant history and physical examination. Once the donors were found suitable for blood donation, complete details of their previous donations (any reaction, number of donations, donor status, occupation, etc.) were noted.

RESULT: Seroprevalence for Hepatitis B, Syphilis, HIV and Hepatitis C was observed to be 1.17%, 0.86%, 0.10% and 0.07% respectively. Prevalence among VD (2.65%) was higher than RD (1.97%). It was highest among MVBD (2.57%) followed by MRBD (1.92%), FVBD (1.23%) and FRBD (1.14%).

CONCLUSION: High prevalence rate of TTIs is a significant public health issue. The modes of transmission of TTIs are only few & validated; diagnostic tests having high sensitivity and specificity are available which can be utilized to control such infections. Intervention at primordial prevention level is still the best choice for all; specially limited resource settings. Federal effort continues in pursuance of further reducing it at least until it ceases to be a public health problem.

KEYWORDS

TTI, TTD, Blood Donor, ELISA, HBV, HIV

INTRODUCTION

Blood transfusion is an essential part of modern day healthcare; it can be a life-saving intervention. However, like all treatments, it may result in acute or delayed complications and carries the risk of transfusion transmissible infections. Safety and effectiveness of transfusion depends on two key factors:

1. A supply of blood and blood products those are safe, accessible at reasonable cost and adequate to meet the demand.
2. The appropriate clinical use of blood and blood products.

Blood is fluid containing cells that circulate through the heart, arteries, veins and capillaries and carries nutrients, electrolytes, hormones, vitamins, antibodies, heat and oxygen to the tissues and removes waste matter and carbon dioxide. Approximately 5-6 litres of blood circulate in the body in an adult weighing 70 kgs. Blood consists of liquid part called plasma which is a clear straw coloured liquid representing 55% of total blood volume and the cellular components which represent 45% of total blood volume; these are Red blood cells (RBC), leucocytes (WBC) and platelets. Plasma contains 91% water and 9% solids which comprise of 1% inorganic molecules like Na^{+}, Ca^{++}, HCO_3^{-}, K^{+}, Mg^{++}, Fe^{++} etc., 8% organic molecules like plasma proteins, non-protein nitrogen (NPN) substances, sugar, fats, enzymes and hormones. Plasma proteins consist of 55% albumin, 38% globulin, 7% fibrinogen and small amount of prothrombin.

Transfusion of blood and its components is life-saving as well as it has life threatening hazards. With every unit of blood there is a 1% chance of transfusion associated problems including transfusion transmitted diseases.[1] Majority of the cases of post transfusion diseases have been caused by hepatitis B virus (HBV), human immunodeficiency virus (HIV), hepatitis C virus (HCV), *Treponema pallidum* and malaria parasites.

Tranfusion Transmissible Infections

Transmission of syphilis (*Treponema pallidum*) was recognised in the early days of transfusion when blood was transferred directly from donor to recipient. Testing donations for Treponemal antibodies and storage of blood between collection and transfusion has overcome this problem. Since then, three viral infections - HBV, HCV, and HIV - have been the predominant transfusion transmitted agents to cause disease and to prompt changes in transfusion practice.

There are three basic conditions that will determine whether an infectious agent is likely to be transmitted by transfusion[2]:

1. The agent must be capable of using the blood stream as a route of entry in host.
2. The infected donor must be essentially free of any noticeable signs and symptoms of disease, otherwise, they would have been identified during donor screening and the donor would have been excluded or deferred.
3. The agent must exist naturally for a period of time, either free in the plasma or present in a cellular component in the blood stream of an infected donor.

However, whether transmission actually occurs or not depends on a number of other factors, particularly on the immune status of the patient and the amount of infectious agent transfused[3].

The length of time between infection and the development of detectable serological markers (the window period) also varies between agents (for example, 22 days for anti-HIV and 66 days for anti-HCV using current assays). During the very start of this period - often referred to as the "eclipse" infectious agent (nucleic acid) is either absent from the blood or found in very small numbers and blood is unlikely to be infectious if transfused.

The infectious window period is therefore shorter than the total window period. The shorter the infectious window period, relative to the total asymptomatic seropositive infective period, the better is the detection of infectious donations by serological testing.

VIRAL INFECTIONS

Donor selection and donation testing prevent HBV, HCV and HIV infectious donations from entering the blood supply. However, these interventions are not 100% effective and transmissions of HBV, HCV and HIV by blood that tested negative for markers of infection have been documented. These factors, probably along with some transmissions resulting in mild or non-specific symptomatology that is not precisely diagnosed, account for the rarity of clinically apparent HAV, parvovirus B19, CMV or EBV infection associated with transfusion[2]. Donor screening for HTLV-1 should be considered in those countries where HTLV-1 is endemic. Preliminary epidemiological studies are therefore necessary[3].

Examples of viral infectious agents that have the potential for transmission by blood transfusion.[4]
Hepatitis viruses
• Hepatitis A (HAV) - no carrier state (rarely transmitted)
• Hepatitis B (HBV) - carrier state

• Hepatitis D (HDV, or delta virus) - requires HBV
• Hepatitis C (HCV) - carrier state
• Hepatitis G Virus (HGV)
Human retroviruses
• Human immunodeficiency viruses, HIV-1 &2- latent state
• Human T-cell leukaemia, HTLV-I & II - latent state
• Simian foamy virus[5]
Herpes viruses
• Cytomegalovirus (CMV) - latent state
• Epstein-Barr virus (EBV) - latent state
Others
• West Nile virus
• TT virus
• SEN virus
• GB virus
• Parvovirus B19

NON-VIRAL INFECTIONS

Potentially, a large number and variety of non-viral agents may be transmitted by transfusion, both endogenous agents present in the donor at the time of donation and exogenous contamination occurring during collection and processing. The transmission of syphilis was a serious problem with early transfusions given directly from donor to patient. Although rare, serious sequelae such as septicaemia and septic shock do occur and approaches to identify and reduce the risks are under consideration.

Examples Of Non-viral Infectious Agents That Have The Potential For Transmission By Blood Transfusion.[6]
BACTERIA
A. Endogenous bacteria
• Syphilis (*Treponema pallidum*)
• Lyme disease (*Borrelia burgdorferi*)
• Brucellosis (*Brucella melitensis*)
• *Yersinia entercolitica* (and others)
B. Exogenous bacteria
• Environmental species, for example *Staphylococcus epidermidis,*
• Pseudomonas spp. and *Serratia marcescens*
RICKETTSIAE
• Rocky mountain spotted fever (*Rickettsia rickettsii*)
• Q fever (*Coxiella burnettii*)
PARASITES
• Malaria (Plasmodium spp.)
• Toxoplasmosis (*Toxoplasma gondii*)
• Trypanosomiasis (Chaga's disease and sleeping sickness)

Even though present worldwide, it is predominantly noted in tropical and subtropical countries particularly Asia and Africa. Malaria is a major health problem in India, being one of the biggest burdens in terms of morbidity and mortality among all infectious diseases. Despite the early success of the malaria eradication programme in the 50's & 60's there was an upsurge of cases to 6.74 million in 1976 which dropped to 2.1 million in 1984. Since then it has reached a plateau.

Malaria causing plasmodia are parasites of blood and hence induce haematological alterations. The haematological changes that have been reported to accompany malaria include anaemia, throm bocytopenia & mild to moderate atypical lymphocytosis, monocytosis, eosinophilia and neutrophilia.

STRATEGIES TO REDUCE THE RISK OF TRANSFUSION-TRANSMITTED INFECTIONS[6]

- The careful selection of donors to ensure that, as far as possible, blood is not collected from people who are likely to be carriers of infectious agents. Safe blood donation depends on, building a panel of regular, voluntary, non - remunerated donors as the first step in ensuring a safe and adequate supply of blood. In our country where most of the blood is collected from family/replacement donors, the risk of transfusion transmissible infection is higher.
- The direct screening of the blood for evidence of the presence of infectious agents or markers produced by them.
- The removal of specific components of blood thought to harbor infectious agents, for example, by the filtration of blood to remove white blood cells.
- The physical/ chemical inactivation of any contaminating agent that may be present: for example, heat treatment of 5% albumin during production.

AIMS & OBJECTIVES

1. To study the nature and frequency of transfusion transmissible infections (viz. HIV, HBsAg, HCV, syphilis, Malaria) in blood donors.
2. To study the relationship between transfusion transmissible infections with socio-demographic variables.

MATERIAL & METHODS

All blood donations received in Blood Bank, GMCH, Udaipur were included in the study. All donors were selected by standard donor selection criteria by taking the relevant history and physical examination. Once the donors were found suitable for blood donation, complete details of their previous donations (any reaction, number of donations, donor status, occupation, etc.) were noted.

CRITERIA FOR INCLUSION

Venous blood was collected from donors in 350 ml disposable blood bags as per standard operative procedure. Blood from the tube of the bag was collected in a separate test tube and the serum was separated. Serological tests for HBsAg, HCV Ab and HIV Ab were performed in the serum by the methods mentioned below. In addition, other mandatory tests such as VDRL and MP testing were done but not included in the present study.

All cases found positive using different serological tests employed for each of the transfusion transmitted diseases during the one year duration were included in the study.

CRITERIA FOR EXCLUSION

Donors previously diagnosed positive but still presenting for repeat donations were included in the study only once.

TESTING METHODOLOGY

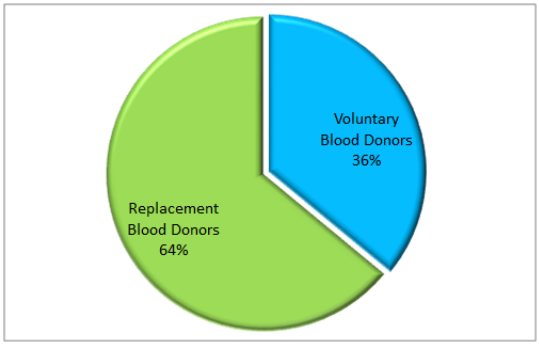
3rd generation ELISA kits for all the mandatory serological tests done on blood donation bags. The kits were supplied by NACO, manufactured by different companies.

Specimen Collection And Storage

1.03 ml blood in plain vial and 02 ml blood in EDTA (ethylene diamine tetra acetic acid) vial was taken from the satellite bag for testing.
2.The whole was centrifuged at 1000-2000 rpm for 10 min to get plasma or serum specimen.
3.Specimens which could not be immediately tested were refrigerated at 2-8 ºC and brought to room temperature prior to use.

The seropositivity of HBsAg, HCVAb and HIVAb were correlated with the age, sex, caste, education status, occupation and rural/ urban backgrounds. The datas were statistically evaluated wherever found necessary.

OBSERVATIONS & RESULTS



Number of blood units collected during study

Sex wise distribution of blood units collected during the year

Maximum numbers of blood donors were males (2291, 34.75%) for both voluntary as well as replacement blood donors groups. While female donors were less in number (231, 3.38%) to total donations, most of them were voluntary donors (163, 70.56%). Similarly for males, replacement donors (4302, 65.25%) were ahead of voluntary donors (2291, 34.75%). However increasing male donors per year had no significant correlation with the trend of TTIs.

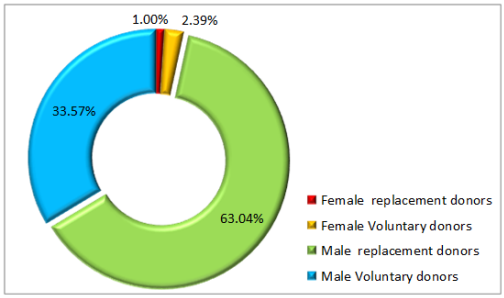


Table 1: Monthly Incidence Of TTIs

Months	Units collected	HBsAg	VDRL	HIV	HCV
Jan	773	1.68%	0.65%	0.00%	0.00%
Feb	360	1.94%	0.00%	0.00%	0.00%
Mar	538	0.93%	0.93%	0.00%	0.00%
April	544	1.29%	1.10%	0.00%	0.00%
May	534	0.94%	0.94%	0.19%	0.19%
June	591	0.51%	1.18%	0.17%	0.51%
July	567	0.71%	1.41%	0.00%	0.00%
Aug	804	1.37%	0.75%	0.37%	0.00%
Sept	550	0.91%	0.55%	0.00%	0.00%
Oct	509	1.18%	0.98%	0.00%	0.00%
Nov	531	1.69%	0.56%	0.00%	0.00%
Dec	523	0.96%	1.15%	0.38%	0.19%
Total	6824	1.17%	0.86%	0.10%	0.07%

Out of 6824 units tested, maximum prevalence was observed for Hepatitis B (1.17%) followed by VDRL (0.86%), HIV (0.10%) and Hepatitis C (0.07%). During the study period.

Table 2: Age-wise Distribution Of Seropositive Cases

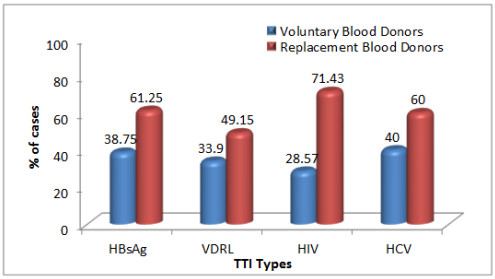
Age (in years)	HBsAg	VDRL	HIV	HCV	Total
18-20	3	3	-	-	6 (3.97%)
21-30	34	22	2	3	61 (40.40%)
31-40	24	21	4	2	51 (33.77%)
41-50	14	6	1	-	21 (13.91%)
51-60	5	7	-	-	12 (7.95%)
Total	80	59	7	5	151 (100%)

Maximum numbers of TTIs were in the age group 21-30 (61; 40.40%) and along with donors of 31-40 years age group contributed (112; 74.17%) of the total cases. Least were in the beginners age <20 years (6, 3.97%). Mean age for seropositive cases was 31.01 years with highest mean age for VDRL (34.61 years) and least mean age for HCV (30years) ($\chi^2 = 7.62, p > 0.05$).

Table 3: Sex Wise Prevalence Of TTIs

TTI	Male		Female	
	VD	RD	VD	RD
HBsAg	1.31%	1.12%	0.61%	1.47%
VDRL	1.18%	0.66%	0.61%	1.47%
HIV	0.09%	0.11%	0	0
HCV	0.09%	0.07%	0	0
Total	2.57%	1.92%	1.23%	2.94%

TTIs were more prevalent among males (2.24%) than females (2.08%). All diseases individually were also more common in males. Though male voluntary donors comprised the largest seropositive group, highest prevalence was observed in male donors (2.57%). On the other hand, females of both RD and VD groups had significantly lower prevalence of 2.94% & 1.23% respectively.



TTIs In Voluntary And Replacement Blood Donors

Table 4: Prevalence Of TTIs In Voluntary And Replacement Blood Donors

TTI	Voluntary Blood Donors	Replacement Blood Donors
HBsAg	1.26%	1.12%
HIV	1.22%	0.66%
HCV	0.08%	0.11%
Syphilis	0.08%	0.07%
TOTAL	2.65%	1.97%

Overall seroprevalence was higher in voluntary blood donors (2.65%) as compared to replacement blood donors (1.97%). (Total voluntary blood donors 2454 and Total replacement blood donors 4370).

DISCUSSION

Since the blood donation and transfusions are also on the rise in this part of Rajasthan State, this study was aimed at finding out the prevalence of the TTD Viz. Hepatitis B, C & HIV by using highly specific and sensitive ELISA techniques and to correlate the seropositivity of these diseases with various factors like age, sex, domicile, occupation, type donors, frequency of donations, educational and socio-economic status of the donors.

Seroprevalence of TTIs among blood donors is an indicator of prevalence and changing trends of these diseases in the population. A higher prevalence in healthy group like blood donors is a public health concern and introduction of grave iatrogenic infections like HIV in no amount is acceptable. Therefore, the present study was conducted to find out the prevalence of TTIs in blood donors in Udaipur, Rajasthan.

In our study number of male donors (98.65%) was much higher than females (3.38%), which was in accordance with other studies conducted in the country by Sharma DC et al[9], Sunderam S et al[10] and Pachori G et al[11] as well as in Palestine by Shiha AM et al[20].

Increase in voluntary donors may be attributed to the increasing public awareness, various national blood donation programs and involvement of Government bodies like NACO in response to WHO initiative, that actively propagate voluntary blood donation in our country[9].

In our experience, overall seroprevalence of TTIs was 2.21%. This was in concordance to studies done at Ranchi and Nagpur by Sunderam S et al[10] and Bobde V et al[12] respectively. Higher prevalence of TTIs was reported at other places e.g. Gwalior, Ludhiana and Wardha.

Our results were in concordance with studies done in other developed countries including China, Tunisia (Song Y et al[15], Zeng et al[14], Jemia et al[8]), where seroprevalence was around 2%, achieved a low seroprevalence of TTIs in the late 20th century, as evidenced by Soldan K[2] on a large population in UK (England & Wales) in 1997(0.02%). While in developing countries like Pakistan, Nigeria and Western China had higher rate of TTI attributable to overall higher prevalence in general population and old, less educated, married, first-time donors.

On further categorization of donors according to voluntary and replacement donations, RMD (1.92%) had a lower preponderance of TTIs than VMD (2.57%). On the contrary, RFD (2.94%) had higher rates of prevalence than VFD (1.23%). However, HBsAg was more prevalent in voluntary female donors than replacement female donors (1.47% vs. 1.12% respectively).

Hepatitis B

Among all the TTIs, Hepatitis B (1.17%) was observed to be the most common infection throughout the study period. This coincides with several studies conducted in other parts of the country by Bobde V et al[12], Chandra T et al[21] and Karmakar PR et al[13] as well as outside the country by Ataullah S et al[18], Jemia RB et al[8] and Fessehaye N et al[16]. In other study done in Rajasthan in 2001 at Jodhpur by Garg S et al[7] and at Udaipur by Pachori G[11] in 1999, a higher prevalence of 3.44% & 3.1% was reported respectively. Suggesting that prevalence of Hepatitis B in Rajasthan was higher during 90's and early 21st century but has been declining over last few years.

HIV

HIV infection with a prevalence of 0.10%. Variation in prevalence was seen in other studies conducted within and outside India. Studies

conducted in Western and Southern India reported higher prevalence whereas those conducted in North India reported lesser rates[21]. A parallel trend also observed by Sharma DC et al[9] and Sheikh M et al while Sunderam S et al[10] reported a continuous increase in incidence from 2008 to 2012. These differences suggest that the dynamics of HIV may be specific to geographical location and the social, cultural, religious and sexual practices of the population. The decrease in HIV prevalence seen in our study might be because of increase in the awareness of HIV and other STDs.

Hepatitis C

HCV prevalence was very low (0.07%) in our study, significantly lower than other parts of the country and abroad except in developed countries like UK as observed by Soldan K^2. The geographical variation in prevalence, local trend of disease, testing methodology employed may be the reason for this difference as highlighted by Kumar A et al[17]. Our findings were in agreement with those of Sharma DC et al[9], Karmakar PR et al[13] and Kumar R et al[17].

Syphilis

VDRL positivity was found to be the second most common (0.86%) among all TTIs. Our finding was in concordance with studies done by Sunderam S et al[10] and Chandra T et al[21] in India and Soldan K^2 from UK. This was in discordance with studies done by other authors from India and abroad who reported higher prevalence rates of VDRL

CONCLUSION

TTIs are useful surrogate marker of these diseases among population in general and correlate with their epidemiology. High prevalence rate of TTIs is a significant public health issue. The modes of transmission of TTIs are only few & validated; diagnostic tests having high sensitivity and specificity are available which can be utilized to control such infections. Intervention at primordial prevention level is still the best choice for all; specially limited resource settings. Federal effort continues in pursuance of further reducing it at least until it ceases to be a public health problem. For developing countries like ours with large population, there is much scope of improvement.

Over the years, efforts of both Govt. & Non Govt Organizations towards educating the people about transmission of HIV and other TTIs led to change in high risk behavior and abstinence of high risk donors from voluntary donation. Better training & awareness of health workers at blood banks is also effective in screening out those with high risk of TTIs by simple questionnaires administered to prospective blood donors.

Mandatory testing of blood donors for various common transfusion transmitted diseases is of prime importance and by discarding the seropositive blood unit, TTD can be prevented to a great extent. We feel that more tests for other transfusion transmitted diseases should be preformed to safeguard the transfused patients against transfusion transmitted diseases. Further, we advocate the following points to improve blood bank services considering the risk of transfusion to the patients:

1. More sensitive and more specific Nucleic Acid Testing (NAT) based screening systems for TTDs should be introduced in blood bank to screen donors.
2. Effort should be made to achieve 100% voluntary blood donation as they have very low prevalence of TTDs and for this donor motivation and education is advised.
3. Donors blood products should be irradiated particularly in patients requiring frequent multiple transfusions.
4. Education of public at large is necessary to increase the general awareness towards TTD's.

It is recommended that further research should be done to assess the cost effectiveness of currently available confirmatory and supportive tests e.g. NAT, Anti- HBc in screening for TTIs. New, cheaper and safer technologies are still welcome to help in resolving these issues.

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