Clean Blood: Transfusion Transmitted Infection days are not over

Mahwish Majid Bhatti[1,2], Ayesha Junaid[1,2] and Fouzia Sadiq[3*]

[1]Department of Pathology, Shifa College of Medicine, Shifa Tameer-e-Millat University, [2]Shifa International Hospital, [3]Directorate of Research, Shifa Tameer-e-Millat University, Islamabad, Pakistan.

Received: 18 August 2021

Accepted: 13 December 2021

***Corresponding Author:** Director.research@stmu.edu.pk

DOI 10.5001/omj.2022.65

Abstract

Objective: Blood transfusion saves millions of lives but there is always a potential risk of transmission of blood borne infections from the donor to the recipient if the blood is not thoroughly screened. A high seroprevalence of transfusion transmitted infections (TTI) in donated blood remains the blood safety issue in Pakistan. This study was aimed to determine the frequency of TTIs (Human Immunodeficiency virus (HIV), Hepatitis B Virus (HBV), and Hepatitis C Virus (HCV), syphilis and malaria) among blood donors.

Methods: Data records of all registered blood donors (n=120,968) during 2008-2019, at blood transfusion center in the tertiary care hospital were assessed. Frequency of the seropositive donors for HIV, HCV, HBV, syphilis and malaria was analyzed.

Results: Donors were predominately males (99%) with age groups ranging from 25-65 years. HCV, syphilis and malaria positive cases were mostly in the age range of 26-35 years. Most of the donors (81.1%) were residents of Islamabad. The most prevalent infection among the

screened blood donors was HCV (1.52% with 95% CI 0.423-0.661) followed by syphilis (0.85% with 95% CI1.149-1.432). HCV and syphilis were most frequently observed in blood group B positive patients while HIV was common in O positive patients. The frequency of co-infection of syphilis with HCV and HIV was 0.02% and 0.01% respectively.

Conclusion: Among males, the most prevalent TTI infection was HCV followed by HIV; the latter is on the rise. However, HCV and syphilis are the most frequent co-infections. So, TTIs days are not over.

Keywords: Blood transfusion; Infections; Hepatitis; Malaria; HIV.

Introduction

Blood transfusion is an imperative therapeutic act that saves millions of lives. However, these therapies are associated with a high potential risk of transmitting blood borne infections from the blood donor to the recipient. Parenteral administration of blood or its product is a potential "legal" route for the transmission of various blood borne infectious agents of public health importance. A high seroprevalence of transfusion transmitted infections (TTI) in donated blood is alarming and remains the main blood safety issue of major concern.[1] The magnitude of TTI varies among different countries depending upon the TTI load in that particular population. It has been estimated that there is 1% likelihood of transfusion related risk in some industrialized countries [2] but the risk of blood safety is higher in middle and low income countries of the world due to high prevalence of TTIs.[3] Among these Human Immunodeficiency virus (HIV), Hepatitis B Virus (HBV), Hepatitis C Virus (HCV),

Treponema pallidum (pathogen causing syphilis) and malaria are the major contributors of TTIs.

In 2016 the Global Health Sector Strategy (GHSS) on viral hepatitis, called for the elimination of viral hepatitis i.e. 90% reduction in incidence and 65% in mortality by 2030. The core components of the strategy include blood and injection safety, HBV vaccination, prevention of vertical transmission of HBV from mothers to children and horizontal transmission of HBV and HCV among people through injections and testing and treatment of viral hepatitis. The transmission of viral hepatitis can be dramatically reduced by the implementation of evidence-based prevention and interventions.[4, 5] The effective primary prevention include ensuring blood safety through screening of blood supplies.[6]

Pakistan and Egypt bear 80% of the disease burden due to viral hepatitis in Eastern Mediterranean Region. Pakistan has the second highest global burden of HCV infection, with 5% prevalence which accounts for 8 million of people [7] whereas prevalence of HBV is 2-8% with approximately 9 million population infected with this deadly virus.[8] Each year there are 150,000 and 250,000 new cases for HBV and HCV respectively in Pakistan.[9, 10] HCV is a leading TTI in a multi transfused thalassemia major patients and the recent detection of HIV is also an alarming situation in Pakistan.[11] High frequency of HCV infection (3.52%) has been reported in blood donors in Hyderabad.[12]

In Pakistan there is a strong reliance on replacement and paid donors and due to the lack of screening strategy, the recipients are posed to high risk of TTI as compared to the voluntary donors. More than 1.5 million units of blood is donated annually in Pakistan.[13] There is increased demand of blood in Pakistan due to burden of Thalassemia, Hemophilia,

Hemodialysis, pregnancy and other related issues like road side accidents. Many viral infections like HCV and HBV are transmitted through blood transfusion which then leads to chronic disorders like liver Cirrhosis and Hepatocellular carcinoma.

Pakistan is a Malaria endemic country and by WHO standards every blood should be screened for anti-Plasmodium parasite. Sexually Transmissible Diseases (STDs) such as syphilis can lead to permanent disability, including sexual dysfunction, pregnancy, childbirth complications, neurological and cardiovascular problems. Syphilis positive patients are more prone to HIV infection.[14] It is therefore imperative that transfused blood is free of bacteria Treponema pallidum that causes syphilis. We aimed to determine the frequency of TTIs among blood donors at a tertiary care hospital in Islamabad.

Methods

It was a retrospective study conducted from year 2008 -2019; in which data records of all the blood donors registered at blood transfusion center in a tertiary care hospital at Islamabad were assessed. The study was approved by Institutional Review Board and Ethical Committee. Until year 2014, blood donors were only screened for HIV and HCV at this facility but from year 2015 onwards, HBV, syphilis and malaria were also included among the screening tests. All adult blood donors having body weight of 50kg and above were included in the study. Anemia (defined as hemoglobin <12.5g/dl for females and <13.5g/dl for males) was ruled out in the donors. All donors who were infected with Malaria were eligible to donate blood three months after completion of their anti-malarial treatment. Exclusion criteria of American Association for Blood banking was followed. Incomplete files or missing data were also excluded from the study.

All the blood donors were counseled by the staff nurse before donations. Each potential donor was required to fill a detailed health history questionnaire. This includes data regarding their demographic information, i.e., name, age, sex, marital status, profession, address and contact numbers. It also included donor status, current or previous medical illness, immunization, dental extraction, surgical history, blood transfusion and donation history along with the travel history. TTIs risk factors, transfusion transmitted infection results and their notification and a basic medical assessment was also included in it.

The blood donors at the tertiary care hospital in Islamabad are routinely screened using gold standard methods i.e., HBcAg, HCV, HIV, by Nucleic Acid Amplification Technique (NAT) on cobas Tigman, syphilis by Enhanced Chemiluminiscence Immunoassay (ECLIA) on cobas e 602 and anti-palsmodium parasite by Immunochromatographic Test (ICT). Data were analyzed using SPSS version 21. Descriptive and analytical statistics were applied for qualitative variables like gender, blood group, infection type etc. The frequency and percentages were calculated for each variable.

Results

Between years 2008-2019, 120,968 potential donors were registered and screened in the blood transfusion center at the tertiary care hospital. Donors were predominately males 119,808 (99%) while the females were 1160 (1%) with age groups ranging from 18 to 65 years. Among the donors age, 47% were of less than 25 years while only 0.3% were of more than 56 years of age. A significant majority of the donors (81.1%) were the residents of Islamabad while Punjab, KPK, Azad Kashmir and Gilgit Baltistan accounts for 13.8%, 3.5%, 1.05% and 0.1% respectively.

The overall reactive and non-reactive donors with HIV and HCV from year 2008 - 2019 are shown in Table I. The frequency of reactive cases of HIV was highest 24 (0.19%) in year 2017 however the frequency of HCV was found to be highest 234 (1.59%) in year 2015. Overall, the frequency of HCV was relatively higher among the blood donors, compared to HIV. Table II shows the year wise frequency of HBcAg, syphilis and malaria infections. Table III shows that out of 120,968 total tested donors, most prevalent infection was HCV (1.52% with 95% CI 0.423-0.661) followed by syphilis (0.85% with 95% CI1.149-1.432). Compared to HBcAg and Malaria, a considerable proportion of donors tested positive for syphilis during 2016-2019. However, the frequency of these infections was decreasing over time.

Table I. Year-wise frequency of HIV & HCV (n=120968)

Year	HIV		HCV		Total
	Negative n	Positive n (%)	Negative n	Positive n (%)	
2008	135	0 (0)	135	0 (0)	135
2009	5471	5 (0.09)	5370	106 (1.94)	5476
2010	7771	5 (0.06)	7613	163 (2.10)	7776
2011	8642	2 (0.02)	8511	133 (1.54)	8644
2012	9493	5 (0.05)	9332	166 (1.75)	9498
2013	11523	5 (0.04)	11337	191 (1.66)	11528
2014	12947	5 (0.04)	12753	199 (1.54)	12952
2015	14696	11 (0.07)	14473	234 (1.59)	14707
2016	13886	21 (0.15)	13725	182 (1.31)	13907
2017	12778	24 (0.19)	12658	144 (1.12)	12802
2018	11540	19 (0.16)	11414	145 (1.25)	11559
2019	11961	23 (0.19)	11821	163 (1.36)	11984

Table II. Year-wise frequency of HBcAg, syphilis & malaria

Year	HBcAg		Syphilis		Malaria		Total
	Negative n	Positive n (%)	Negative n	Positive n (%)	Negative n	Positive n (%)	
2015	1508	0 (0.00)	1508	0 (0.00)	1508	0 (0.00)	1508
2016	13845	1 (0.007)	13711	135 (0.98)	13845	1(0.007)	13846
2017	12797	2 (0.02)	12691	108 (0.84)	12798	1(0.008)	12799
2018	11559	0 (0.00)	11453	106 (0.92)	11559	0 (0.00)	11559
2019	11983	0 (0.00)	11901	82 (0.68)	11983	0 (0.00)	11983

Table III. Frequency of HIV, HCV, HBcAg, syphilis & malaria among blood donors

Variable	Donors screened n	Time Span	Sero-positive n (%)	95 % CI
HIV	120,968	2008-2019	125 (0.10)	(0.191-0.283)
HCV	120,968	2008-2019	1837 (1.52)	(0.423-0.661)
HBcAg	51,695	2015-2019	3 (0.01)	(0.951-1.002)
Malaria	51,695	2015-2019	2 (0.004)	----
Syphilis	51,695	2015-2019	437 (0.85	(1.149-1.432)

The predominant blood groups of the donors were B positive (31.2%), O positive (28.8%) and A positive (22.5%). In females HCV infection was most prevalent in the blood group O positive; 8 cases were of O positive out of the total 22 HCV positive cases (Table IV). In males HCV was the most prevalent TTI infection too followed by syphilis and HIV respectively. HCV and syphilis was most frequently seen in blood group B positive patients while HIV was mostly detected in O positive male patients. There was no significant association between blood groups and TTIs. However, significant association of age with HCV and syphilis was observed.

Table IV. Gender wise Blood group vs TTI

Gender	Blood Grou	HIV (n= 120,968)			HCV (n= 120,968)			HBcAg (n= 51,695)			Malaria (n= 51,695)			Syphilis (n= 51,695)		
		Neg	**Po**	**Total**	**Neg**	**Pos**	**Total**	**Neg**	**Po**	**Total**	**Neg**	**Po**	**Total**	**Neg**	**Po**	**Total**
F	A-	35	0	35	34	1	35	10	0	10	10	0	10	10	0	10
	A+	237	0	237	232	5	237	80	0	80	80	0	80	80	0	80
	AB-	9	0	9	9	0	9	2	0	2	2	0	2	2	0	2
	AB+	81	0	81	80	1	81	27	0	27	27	0	27	27	0	27
	B-	40	0	40	39	1	40	10	0	10	10	0	10	9	1	10
	B+	366	0	366	360	6	366	114	0	114	114	0	114	114	0	114
	O-	45	0	45	45	0	45	23	0	23	23	0	23	23	0	23
	O+	387	0	387	379	8	387	121	0	121	121	0	121	120	1	121
	Total	**1200**	**0**	**1200**	**1178**	**22**	**1200**	**387**	**0**	**387**	**387**	**0**	**387**	**385**	**2**	**387**
M	A-	2485	1	2486	2451	35	2486	1071	0	1071	1071	0	1071	1059	12	1071
	A+	27008	27	27035	26627	408	27035	11650	1	11651	11651	0	11651	11549	10	11651
	AB-	939	1	940	922	18	940	391	0	391	391	0	391	389	2	391
	AB+	10367	12	10379	10224	155	10379	4459	0	4459	4459	0	4459	4414	45	4459
	B-	3468	9	3477	3422	55	3477	1408	1	1409	1409	0	1409	1397	12	1409
	B+	37353	30	37383	36822	561	37383	15973	1	15974	15974	0	15974	15841	13	15974
	O-	3653	3	3656	3591	65	3656	1548	0	1548	1548	0	1548	1531	17	1548
	O+	34371	41	34412	33895	517	34412	14805	0	14805	14803	2	14805	14693	11	14805
	Total	**119,64**	**12**	**119,76**	**117,95**	**181**	**119,76**	**51,30**	**3**	**51,30**	**51,30**	**2**	**51,30**	**50,87**	**43**	**51,30**

Table V shows gender distribution in different TTIs infections. HIV was positive in 125 male patients and was not detected in females. Similarly, HBcAg and malaria was positive in only male patients while HCV and syphilis positivity was seen in both sexes. Table VI revealed age wise positive cases of HIV, HCV, HBcAg, syphilis & Malaria among blood donors. The highest number of HIV positive cases were observed in males less than 25 years of age. HCV, syphilis and malaria positive cases were mostly in the range of 26-35 years. We also analyzed the trend of co-infection (risk to be infected by more than one pathogens) among the blood donors. The frequency of co-infection of syphilis with HCV and HIV was 0.02% and 0.01% respectively while co-infection of HIV with HCV was 0.001%.

Table V. Gender vs TTI

Gender	HIV (n=120968)			HCV (n=120968)			HBcAg (n=51695)			Malaria (n=51695)			Syphilis (n=51695)		
	Neg	Pos	Total	Neg	Pos	Total	Neg	Pos	Total	Neg	Pos	Total	Neg	Pos	Total
F	1160	0	1160	1138	22	1160	377	0	377	377	0	377	375	2	377
M	119683	125	119808	117993	1815	119808	51315	3	51318	51316	2	51318	50883	435	51318
Total	120843	125	120968	119131	1837	120968	51692	3	51695	51693	2	51695	51258	437	51695

Table VI. Age-wise positive case frequency of HIV, HCV, HBc, syphilis &malaria among blood donors

Age group (Years)	HIV (n=120,968) Seropositive n (%)	HCV (n=120,968) Seropositive n (%)	HBcAg (n=51,695) Seropositive n (%)	Syphilis (n=51,695) Seropositive n (%)	Malaria (n=51,695) Seropositive n (%)
<25	59 (0.05)	625 (0.52)	1 (0.002)	94 (0.182)	0 (0.000)
26-35	43 (0.04)	819 (0.68)	1 (0.002)	210 (0.406)	2 (0.004)
36-45	19 (0.02)	330 (0.27)	1 (0.002)	108 (0.209)	0 (0.000)
46-55	4 (0.003)	55 (0.045)	0 (0.000)	24 (0.046)	0 (0.000)
>55	0 (0.00)	8 (0.007)	0 (0.000)	1 (0.002)	0 (0.000)

Discussion

Almost 120 million units of blood is donated each year globally.[15] Although blood transfusion is a therapeutic medical procedure worldwide, it is also a source of spread of infections if transfused without standard screening protocols.[16] This study was conducted at a tertiary care Joint Commission International (JCI) accredited hospital in Islamabad. Blood transfusion services (BTS) at the hospital collect more than 15,000 blood units every year

and screened for HCV, HBV, Malaria, syphilis and HIV. In the present study, we aimed to analyze frequency of TTIs among donors to contribute towards formulation of evidence-based policies for better patient care at National level.

We analysed the data of 120,968 donors, from year 2008 to 2019, who were tested for viral and parasitic pathogens and showed 1.99% positivity for at least one pathogen. Other studies have reported prevalence of TTI up to 5.44% which was much higher than that observed in our study.[4 , 17]

Almost half of the donors over the last ten years belonged to the age group less than 25 years, followed by age groups 26 – 35 years (39%). This is consistent with the studies conducted within and outside Pakistan.[13 , 16 , 18 , 19]

In this study 99% of the blood donors were males. This result was comparable with several studies worldwide where the proportion of the male donors was significantly higher than that of females.[13 , 16 , 17 , 18 , 20 , 21] The comparatively lower percentage of female blood donors can be attributed to several physiological factors in females like menstruation, lactation and pregnancy.[16] The most common cause of deferral for blood donation in females was reported to be low hemoglobin concentration.[22]

The major influx (81.1%) of donors reported were from Islamabad which was the local population around the tertiary care facility from where our data were collected. The proportion of donors from Punjab and KPK was13.8% and 3.5% respectively. Islamabad is an Urban area and the low percentage of TTIs observed in our study can be attributed to the fact that the literacy rate and awareness about clean blood is higher among the residents of

Islamabad compared to other regions of the country. A prospective cohort study over a course of two years from 2013 to 2015 revealed that 64.02% of study population belonged to urban areas while 35.98% belonged to rural areas.[13]

Considering the year wise frequency of TTIs in our study population, we did not find any consistently falling or rising trends in the number of positive cases over the years. This may be due to the higher awareness about clean blood among the residents of Islamabad. The highest percentage of HIV positive case reported was in year 2017 while in year 2015 the highest percentage of HCV positive cases (2.1%) were reported. The percentage of HCV cases is higher than that reported (1.6%) in a retrospective study conducted at Rehman Medical Institute, Peshawar.[17]

HCV was found to be the most common transfusion transmitted infection (1.52%) in our data followed by syphilis (0.85%). Similar results were reported by Memon *et al* where HCV was the most frequent TTI among blood donors (3.52%) followed by syphilis (3.01%) where data was collected over the period of January, 2014 to June, 2015.[12]

The frequency of HIV in our data was reported to be 0.10% which is comparable with 0.24% reported by Siddiqui *et al* [18] and 0.26% by Chandekar *et al.* [20] Nevertheless there is a trend towards an increase in the frequency of HIV cases over the last ten years.

We found that only 0.01% of the donors tested positive for hepatitis B which can be attributed to the availability of vaccine against hepatitis B that has significantly decreased its incidence.[23 , 24 , 25] This very low percentage of hepatitis B is in contrast with those reported by Batool *et al* [17] and Chandekar *et al* [20] which was 2.3% and 1.30% respectively.

Malaria was the least commonly transfusion transmitted disease reported in this study (0.004%). This was consistent with the previous studies conducted in Pakistan and in India.[18, 21] Although Pakistan is considered to be malaria endemic with significant rise in cases in summer and post-monsoon in Punjab [26], the low incidence of malaria in our data can be attributed to the fact that blood donors were not tested for malaria until the year 2015 at the transfusion centre of the hospital. Furthermore, malaria has been reported to be more prevalent in rural and low socio-economic setting while significant majority of donors in our study were from Islamabad which is an urban city. [26]

In terms of TTIs with respect to blood groups, the overall seroreactivity in our data was seen to be high in blood group B positive (0.6%), similar to that reported by Arif *et al*, while seroreactivity for the O positive and A positive was reported to be (0.56%) and (0.45%) among the blood donors.[21] HCV and syphilis were found to be most prevalent in blood group B positive, followed by O positive in which malaria was also positive which was consistent with previously published study.[27] We found that HIV was also most prevalent in blood group O positive but this was in contrast with the results reported by Memon *et al* according to which HIV was more prevalent in individuals with blood group A positive.[12] There was no significant association of HbcAg with any blood group in our study as opposed to the study by Memon *et al* ; which reported O negative blood group as the most prevalent for HbcAg.[12]

In contrast, a study in China has previously shown that co-infection of HIV/syphilis and HIV/HCV was highly prevalent in West China with percentage of 18.9% and 5.7% respectively.[28] Only 1 case of HIV & HCV co-infection was observed in our study (0.001%). A study carried out in Iran has also reported close to zero co-infection among the general

population (0.01%).[29] The number of cases with co-infection of HIV & syphilis and HCV & syphilis were 4 and 10 respectively in our study. Others have reported HIV and hepatitis B as the most common co-infection followed by HIV and syphilis.[20]

Limitations of the study: One of the limitations was that only 1% of the whole sample size was females. So, our data does not reflect the prevalence of TTIs among female population. Secondly, we have only acquired the data from one tertiary care hospital in Islamabad. The awareness about clean blood is much higher among the residents of Islamabad compared to other regions of the country. In order to map prevalence of TTIs at National level, we need to reach out to other regions of the country.

Conclusion

Prevalence of TTIs among blood donors in the current study suggests that TTIs days are not over. The most common blood group with prevalence of TTIs is B positive; HCV is the most prevalent TTI infection followed by HIV in males. HCV and syphilis are the most frequent co- infections reported in our study. A significant number of donors were below the age of 35y suggesting seropositive donors must be followed up to prevent further transmission of infectious agents to family and others in contact with them. Referral of blood donors who are seropositive for one or more infectious agent to specialist care is important to prevent vertical or horizontal transmission of TTIs.

Prevalence of TTIs in other parts of the country has been reported to be higher than that observed in the current study. Hence, a lot needs doing in terms of proactive advocacy for clean blood and standardized blood screening practices prior to blood transfusion across Pakistan.

Competing Interests: None declared

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