An assessment of the potential risks of Transfusion Transmitted Infections in patients transfused in Zimbabwean Hospitals

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Abstract

Blood safety remains the main objective for pretransfusion testing procedures. For the safety of patients, blood is routinely tested for infectious agents in donated blood such as HIV, HBV, HCV and Syphilis. A retrospective study to determine the seroprevalence and trends of HIV, HBV, HCV and Syphilis in donated blood was carried out by reviewing records of the Zimbabwean donors from January 2013 to December 2016.

The prevalence of TTIs declined during this study period. HIV and HBV showed a significant decrease due to improved donor selection criteria. There was no HCV detection from 2013. Other studies also showed declining HCV concentrations. Syphilis increased during the same period.

Despite the noted decline, the risk of TTIs remains high. There is need to reduce this risk in transfused patients by the introduction of the highly sensitive nucleic acid testing (NAT) test in Zimbabwe to improve on the detection TTIs in donated blood.

Keywords: *Blood donors, HBV, HCV, HIV, seroprevalence, syphilis, TTIs.*

1. Introduction

Blood transfusion is an integral part of the health care system in the world (*Ijeoma et al., 2014*). However, it is well known that transfusion is also associated with many adverse effects such as transfusion transmitted infections (TTIs), haemolysis, graft-versus-host disease, transfusion related acute lung injury (TRALI), iron overload and congestive heart failure (*Alter and Klein, 2008; Pallavi et al., 2011*). The major TTIs are human immunodeficiency virus (HIV), hepatitis B virus (HBV), hepatitis C virus (HCV) and Syphilis (*Tessema et al., 2010*). Although malaria infection is often not given the attention it deserves, transfusion transmitted malaria is a serious threat in blood transfusion in malaria endemic countries because the parasites

have been detected in blood donors using rapid detection tests (*Samakande et al., 2017*). TTIs pose a great threat in transfusion practice, with a 1% chance of each unit of blood causing infections if donor blood is not effectively screened. WHO has estimated that 160000 new cases of HIV infections every year are caused by lack of proper screening before blood is transfused in developing countries. HBV and HCV infections were estimated to be 16 million and 5 million respectively (*Ahmed et al., 2016*).

HIV is transmitted mainly through unprotected sex, blood transfusion, intravenous drug use, sharing injecting equipment and pregnancy. It is, by far, the major cause of high morbidity and mortality related to viral infections compared to HBV and HCV in the world, especially in developing countries. It is responsible for causing acquired immune deficiency syndromes (AIDS) such as opportunistic infections and various malignancies. Before the early 1980s, Sub Saharan Africa was disproportionally the most affected region by transfusion transmitted HIV. This was due to its high prevalence in the general population and lack of resources to implement effective control measures. During this period, blood transfusion services were poorly developed. Despite the above obstacles, Zimbabwe was among the first few countries in the world to test for HIV in prospective voluntary blood donors in 1985 after the first AIDS case was diagnosed in the same year using the antibody detection technique. As result of this intervention, there has been a noticeable decline in HIV prevalence in voluntary blood donors from 8.8% in 1995 to 0.77% in 2009 (*McFarland et al., 1998; Fleming, 1997; Duri et al., 2013*). The introduction of the nucleic acid test (NAT) in 1999 has significantly reduced the window phase from 22 days to 11 days, thereby increasing the sensitivity for HIV testing (*Bihl et al., 2007*). However, the cost of implementing this technique in resource limited settings has made its application in Zimbabwe difficult.

HBV is transmitted in the same way as HIV. It is the most common viral infection affecting more than 350 million people globally. There are two types; acute HBV, which takes about 1 week to six months of illness and chronic HBV, which takes more than six months and is characterized by severe hepatic inflammation, liver necrosis and cirrhosis (*Paar, 2001*). Diagnosis of HBV came much earlier than HIV by detection of HBsAg antigen in patient serum or plasma in 1971. The Hepatitis B Core Antibody test was first used in 1986. The NAT test was first used for the specific detection of the HBV virus in 2009 (*American Red Cross Team, 2007*). As a result of these developments, it became easier to screen blood donors for HBV before transfusion using more sensitive tests.

HCV is transmitted by sharing drug injection equipment, reuse or inadequate sterilization of medical equipment and transfusion of unscreened donor blood. It is responsible for causing Hepatitis C which is a liver disease associated with acute and chronic hepatitis. The disease can be mild to severe life-long illness. About 70 million people are infected with chronic HCV and it has been estimated that a large number of these will develop cirrhosis or liver cancer (*WHO Team, 2017*). Diagnosis of HCV started in 1990 with the detection of anti-HCV 3.0 antibodies in patient serum or plasma. NAT testing for the virus was introduced in 1999. Due to its high specificity, the NAT test has greatly reduced the window phase/period (*period between onset of infection and detection of virus*) for HCV by about 50 to 60 days . Again, this test is not applicable in resource limited settings due to cost. There has been a significant decline in global HCV epidemic (*American Red Cross Team, 2007*).

Syphilis is an infection transmitted by a bacterial spirochete called *Treponema pallidum* through unprotected sex, pregnancy and blood transfusion. Although the risk of transmission by blood transfusion is now low, testing for syphilis is still an important part of pretransfusion

testing protocol. The disease has been afflicting humans globally for centuries (*Singh, 1999*). It is characterized by vascular endarteritis and periarteritis and granulomatous inflammation with ulcer surface covered with an exudates. Congenital syphilis is characterized by stillbirth and miscarriages. In Zimbabwe, congenital syphilis accounts for 21% of perinatal deaths (*WHO Team, 2005*). Testing for syphilis started in the 1950s using qualitative screening test for antibodies to *Treponema pallidum* antigen (*American Red Cross Team, 2007*). Blood transfusion transmitted syphilis has not been reported in developed countries for the past 50 years (*American Red Cross Team, 2007*). In Zimbabwe Syphilis is tested using the Abbott Architect System which measures total antibody detection method.

As part of a process of continuous provision of safe blood and blood products, NBSZ has maintained the practice of testing for the above TTIs in voluntary blood donors for the past 32 years (*Duri et al., 2013)*. Monitoring the trends of seroprevalence of HIV, HBV, HCV and syphilis in blood donors provides mechanism to assess the risks of transfusion transmitted infections in people undergoing transfusion in Zimbabwe. Socio-economic environment and behavioral changes in the past 20 years have imposed challenges in the health of blood donors. This study focuses on the determination of the latest seroprevalence and trends in the above mentioned TTIs in order to assess the risks of transfusion transmitted infections to patients who require blood in the country.

2.0 Materials and Methods

2.1 Study design

A four year retrospective study was carried out on data from voluntary non-remunerated blood donors who came to donate at various NBSZ blood collection sites (Harare, Bulawayo, Mutare, Gweru and Masvingo) in Zimbabwe from January 2013 to December 2016.

2.2 Ethical Approval

Permission to carry out the study and access to data was granted by the Joint Research Ethics Committee for the University of Zimbabwe College of Health Sciences and Parirenyatwa Group of Hospitals (JREC/399/16) and the Medical Director of the National Blood Service of Zimbabwe respectively. Strict confidentiality was maintained by use of codes for identification of collected data.

2.3 Data collection

Data on TTI testing results from all new and repeat donors who were eligible to donate blood after meeting the donor selection criteria was retrieved from NBSZ-Laboratory Information System (LIS) and exported to the Microsoft Excel for cleaning. New donor was defined as a first time donor who donated blood after meeting the NBSZ prescribed donor selection criteria whereas a repeat donor was defined as a one who donated more than once after repeatedly meeting the NBSZ prescribed donor selection criteria. Information on the age and gender of the blood donors was made available from the NBSZ database.

2.4 Testing Technologies

The NBSZ uses the following technologies for testing TTIs:

1. *ARCHITECT HIV Ag/Ab Combo test:* A two-step immunoassay for the detection of HIV_1 and HIV_2 p24 antigen in human serum or plasma with a window period of 20.3 days.

2. *ARCHITECT HBsAg Qualitative II test*: A one-step immunoassay for qualitative detection of hepatitis B virus in human serum or plasma with a window period of 53.3 days.
3. *ARCHITECT Anti-HCV test*: A chemiluminescence immunoassay for the detection of antibodies to hepatitis C virus in human serum or plasma with a window period of 58.3days.
4. *ARCHITECT Syphilis TP test*: A two-step chemiluminescence immunoassay for the qualitative detection of antibodies to TP in human serum or plasma with a window period of 30 to 48 days.

The above tests employ the as 4th generation enzyme linked chemiluminescence assay (ELIZA) technologies that are considered to be very specific.

2.5 Statistical Analysis

Statistical analysis was done using the ***Stata version 13.0*** statistical tools for median and interquartile ranges to summarize continuous data and frequencies and percentages for categorical data. Bar and linear graphs were used to show trends of the transfusion transmissible infections in voluntary blood donors.

3.0 Results

There were a total of 250747 blood donations from the five NBSZ collection sites countrywide from January 2013 to December 2016. A total of 2555 (1%) of the blood donors were positive for TTIs. Males who tested positive for TTIs were 1484 (58.1%) and females were 1071 (41.9%). The prevalence of TTIs among blood donors decreased with age group, being highest in the 18-20 years age group with 1671 (65%) infections and lowest in the 51-70 age groups with 14 (0.05%) infections (*Table I*).

One thousand seven hundred and seventy-four (69.4%) of the infected blood donors were new donors and 781 (30.6%) were repeat donors.

There was a decline and a high prevalence of TTIs in regular donors and first time blood donors respectively during the four year period (*Table II*). There was an overall decline in TTIs during the four years. HCV was only detected in 2013, while HIV and HBV prevalence showed a significant gradual decline. Although Syphilis prevalence was low, it showed marginal increases from 2013 (*Table III & Figure 1*).

HBV declined until 2015 when it started to increase in male blood donors. HIV increased and subsequently declined in the same year. HCV and Syphilis disappeared and increased respectively in same population in that year (*Figure 2*).

There was a gradual increase and decline in HIV and HBV respectively in female blood donors. There was a complete disappearance and gradual increase of HCV and Syphilis respectively in the same population in 2015 (*Figure 3*).

Coinfections of HIV, HBV, HCV and Syphilis in blood donors during the four year period of study were very low; HIV/HBV 19 (0.74%), HIV/Syphilis 12 (0.47%) and HBV/Syphilis 3 (0.12%).

Table I: Age Distribution of TTIs among Voluntary Blood Donors (2013-2016).

Age group (Years)	No. of samples with positive reactions				
	Total sample	HIV **n (%)**	Syphilis **n (%)**	HBV **n (%)**	HCV **n (%)**
≤20 years	1671	755(45.2)	61(3.7)	862(51.6)	5(0.3)
21-30	542	264(48.7)	65(12.0)	223(41.1)	2(0.4)
31-40	258	142(55.0)	15(5.8)	110(42.6)	0
41-50	70	28(40.0)	2(2.9)	40(57.1)	1(1.4)
51-60	12	8(66.7)	1(8.3)	3(25.0)	0
61-70	2	2(100)	0	0	0
Total	2555	1199(46.9)	144(5.64)	1238(48.5)	8(0.3)

Table II: Prevalence Transfusion Transmitted Infections By Donor Type (2013-2016)

Year	**Donor Type**		**Total**
	New **n (%)**	Regular **n (%)**	
2013	585(66.1%)	300(33.9%)	885
2014	451(68.8%)	205(31.2%)	656
2015	360(70.7%)	149(29.3%)	509
2016	378(74.8%)	127(25.2%)	505
Total	**1774(69.4%)**	**781(30.6%)**	**2555**

Table III: Blood Donations and Trends in TTI prevalence 2013-2016)

Year	Donations (n)	Positives	HIV	Syphilis	HBV	HCV
2013	67419	885(1.31%)	379(0.56%)	32(0.05%)	478(0.71%)	8(0.01%)
2014	58602	656(1.12%)	301(0.51%)	34(0.06%)	328(0.56%)	0(0.00%)
2015	59836	509(0.85%)	268(0.45%)	36(0.06%)	213(0.36%)	0(0.00%)
2016	64890	505(0.78%)	251(0.39%)	42(0.06%)	219(0.34%)	0(0.00%)

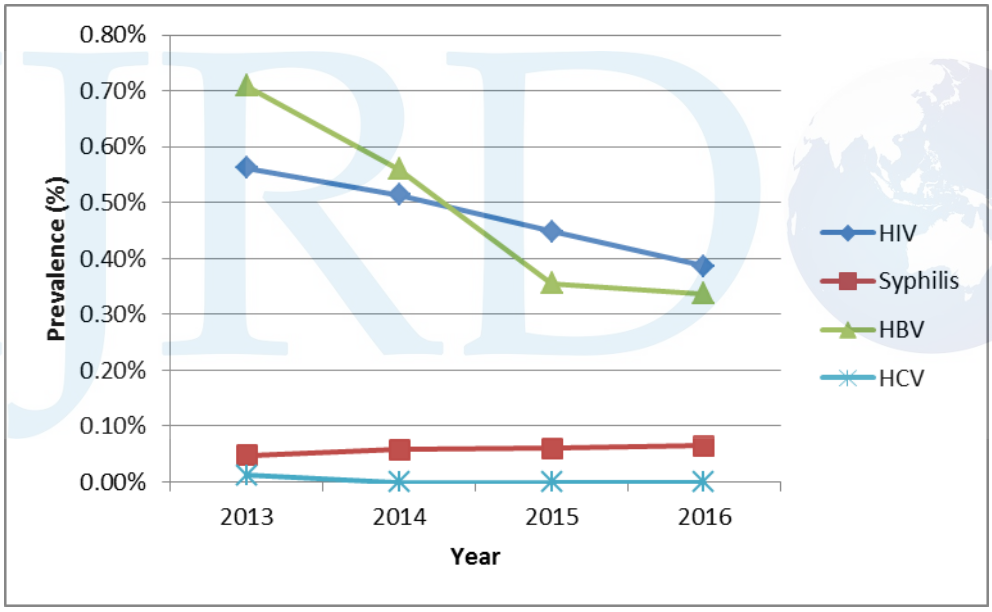

Figure 1: Trends in TTI prevalence (2013 -2016)

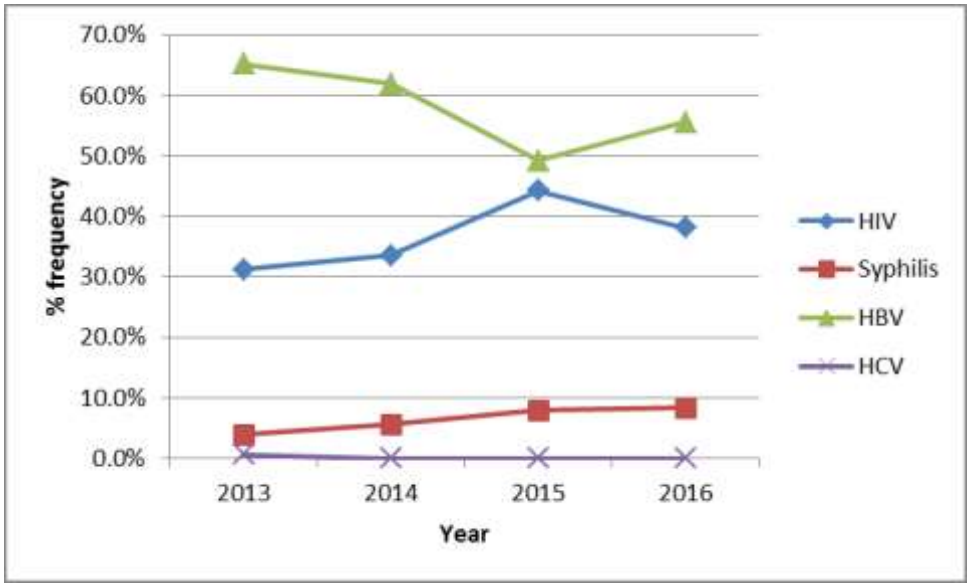

Figure 2: Trends in TTI Prevalence in Males

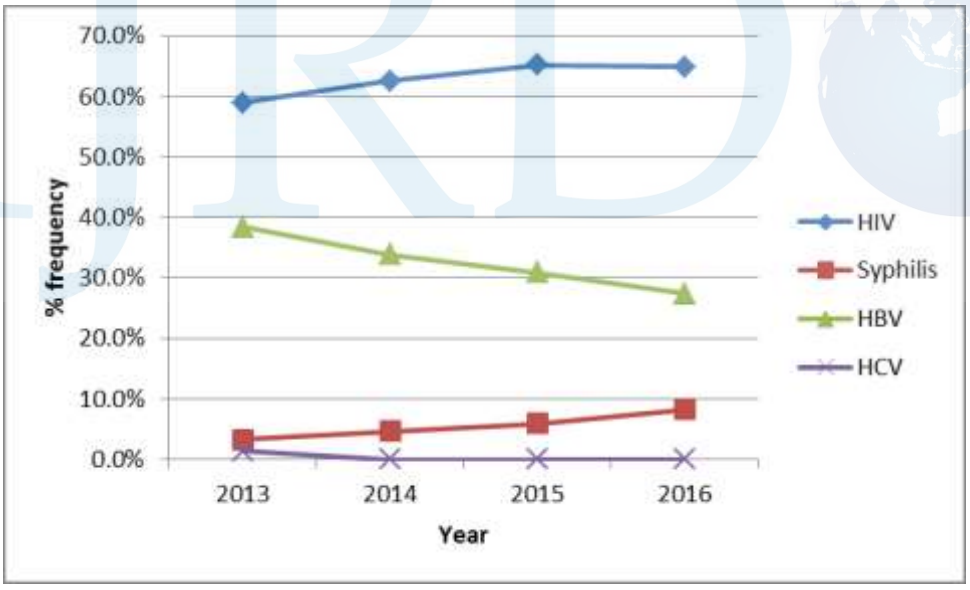

Figure 3: Trends in TTI Prevalence in Females

4.0 Discussion

Provision of safe blood remains the major objective of the NBSZ operations. The current study showed an overall low prevalence of TTIs in voluntary blood donors. A similar study in India showed exactly the same findings (1 *versus* 1.4) (*Ahmed et al., 2016*). It is thought the prevalence of TTIs has been attributed to blood donations collected during the window period

(*Kim et al., 2012*). Despite the noted decline in TTIs, presence of these infections remains a big concern for the safety of blood recipients. Theoretically, the 2555 units from male donors with TTIs could potentially infect more than 13 000 instantly or 52 000 blood recipients in a single year.

More males had TTIs than females. This could be attributed to the fact that, in Zimbabwe, there are more male voluntary blood donors than females. Males have shorter donation intervals (12 weeks) than females (16 weeks). So, males come to donate more frequently than females. Females are often deferred on the basis of low haemoglobin and other issues such as pregnancy and lactation. The same study has also indicated that the low number of women with TTIs could be also attributed to females having discomforts during the donation process and they just avoid blood donation. Another study showed that although there were no significant gender differences, lengthy donations have an effect on female donor participation frequencies (*Misle et al., 2010; Bam et al., 2014*).

The prevalence of TTIs decreased with age groups. The majority of blood donors in Zimbabwe are school children. A previous study at NBSZ showed that a significant number of regular donors of this age group had HIV seroconverted. This trend can also be attributed to practice of unsafe sex in this age group (*Mandisodza et al., 2006*). Individuals are allowed to donate blood up to the age of 65 year. This could be the reason why prevalence of TTIs in blood donors above the age 50 years was not significant.

The prevalence of TTIs was high in new or first time donors than in repeat blood donors. This difference could be attributed to repeat donors' consciousness about donor health requirements through previous donations and tended to practise safe sex than first time blood donors. An Ethiopian study also showed a high prevalence of TTIs in first time blood donors than in repeat donors (*Tessema et al., 2010*)[4].

There was an overall gradual decline in TTIs during the study period with HCV virtually disappearing after 2013. This could be attributed to the use of effective donor selection criteria and intense pre-transfusion testing of donor blood using more sensitive 4th generation kits. A Korean study has showed similar findings. It is thought the disappearance of HCV in Korea was largely associated with improved screening technologies and the implementation of the NAT and tight application donor selection criteria (*Kim et al., 2012; Farshadpour et al., 2016*). Syphilis prevalence was low, but it appeared to increase from 2013. An Indian study showed the same Syphilis prevalence of 0.05% (*Ahmed et al., 2016*). The current study showed an increase to 0.06% from 2014 to 2016. A Nigerian study showed a significant rise in the prevalence of Syphilis and sporadic rises in HIV and HCV from 2009 to 2015. This was thought to be attributed to the use of ineffective donor selection criteria and resurgence of risk life styles (*Fasola et al., 2017*).

The decline and increase in HIV and HBV respectively in male blood donors after 2015 in the study is not clearly understood. The decline trend in HIV infection could be associated with the general awareness of TTIs in the Zimbabwean donor population which is predominantly male. Studies have shown that being male and a history of sexual transmitted infections was associated

with positive HBV markers and the risk of HBV infection has remained high globally (*Kim et al., 2012; Branda et al., 2015*). Although the prevalence of Syphilis has been low before 2013, its resurgence in both male and female blood donors is worrisome. This could be associated to lack of strict donor selection criteria and the practice of unsafe sex by blood donors as indicated in some studies (*Bazie et al., 2015; Fasola et al., 2017*). The increase in HIV in female blood donors is also worrisome. The absence of HCV in this study could be attributed to failure of testing reagents to detect the anti-HCV antibody during the window period of 53.3 days. However, studies have indicated a decline in HCV over the last decade due to application of strict donor selection and improvements in screening reagents (*Kim et al., 2012*). It has been suggested that this was also associated with potential donors' awareness of their status that opted for self-deferment. The population of those born before 1964, before HCV was tested in blood donors, has declined. This has also significantly contributed to the decline in HCV prevalence (*O'brien et al., 2008*). However, a study done in Pakistan has showed a very high prevalence of HCV (4.1%) in the Punjab region (Rahman et al., 2002).

The co-infectivity of the TTIs was more or less according to the mode of infection. HIV/HBV coinfection was the most common because the two are spread in the same manner and their prevalence are the highest among TTIs. However, a previous study has showed HCV/Syphilis to be the most common coinfection due to high degree of their epidemiology and transmission mechanisms. This was followed by the HIV/Syphilis coinfection (*Kumar et al., 2015*).

5.0 Conclusion and Recommendations

It can be concluded that the NBSZ has continued to give priority to safe blood transfusion since 1985 when blood was first tested for HIV before transfusion. The overall seroprevalence of TTIs continued to decline, with HCV virtually disappearing, during the last four years using the 3rd and 4th generations of ELIZA and other technologies to detect HIV, HBV, HCV and Syphilis (*Bhattacharya & Kaur, 2013*). Despite these advanced technological applications in the detection of TTIs, the risk of transfusion transmitted infection remains high. Theoretically, based on the number of voluntary donors who tested positive, the residual TTIs can potentially infect 13000 at once or 52 000 blood and blood product recipients over a period of 12 months. Therefore, efforts should be directed towards radical reduction of TTIs in the country.

It is strongly recommended that implementation of nucleic acid testing (NAT) should be considered in order to reduce the window period to less than 10 days, thereby achieve a markedly reduced rate of transfusion transmitted infections and protect blood recipients in Zimbabwe, despite cost implications. There is also a need to follow up on the switched TTI marker trends for males versus females for HBV. In addition, there is a need to relook at recruitment strategies for new blood donors.

It is also recommended that a follow-up study should be carried out after another 4-5 years for continuous monitoring the prevalence and trends of TTIs in blood donors to further reduce the risk of transfusion transmitted infections.

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