

**TRENDS IN THE SEROPREVALENCE OF TRANSFUSION–TRANSMISSIBLE
INFECTIONS (TTIS) AMONG POTENTIAL BLOOD DONORS IN A TERTIARY
HEALTH FACILITY IN SOUTH–SOUTH NIGERIA**

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ABSTRACT**Background and Objectives**

Transfusion – transmissible infections still pose a formidable threat to blood transfusion safety in Sub-Saharan Africa owing to the endemicity of these infections in the region. Blood donors can be a source of persistent transmission of the infections. This study was conducted to determine the trends and seroprevalence of TTIs amongst prospective donors. **Materials and methods:** The screening records of prospective donors from January 1, 2012 to December 31, 2015 were reviewed with respect to screening outcome for HIV, HBsAg, HCV and Syphilis; age and sex of the donors were also identified. Rapid test kits were used for all screening. All the reactive samples were confirmed using enzyme – linked immunosorbent assay (ELISA). **Results:** A total of 12, 693 prospective blood donors were screened over a 4-year period (2012 – 2015) of which 457 (3.7%), 339(2.7%), 284(2.3%), and 176(1.4%) were positive for HIV, HBsAg, HCV, and Syphilis, respectively. The overall prevalence of TTIs in this study was 10.1%. It declined from 10.7% in 2012 to 10.3% in 2013 but rose slightly to 10.4% in 2014 and reduced to 8.9% in 2015. The infections were more prevalent in males compared to females. The highest HIV, HCV and Syphilis seroprevalence rates were observed among donors aged 36 – 45 years, while for HBsAg, the rate was highest among donors between 26 and 35 years of age. The prevalence of the infections among different age groups was statistically significant ($p < 0.05$). **CONCLUSION:** These results show that TTIs are not uncommon in our blood donors. Thus, there is the urgent need to educate the blood donors on avoiding risky lifestyles while also intensifying voluntary blood donor motivation strategies and increase community surveillance of the infections.

KEYWORDS: Transfusion – transmissible infections, prospective blood donors, HIV, HBsAg, HCV, Syphilis.**INTRODUCTION**

Blood transfusion is an invaluable component of modern healthcare worldwide. It is a veritable therapeutic intervention in many life – saving situations if utilized appropriately and judiciously.^[1] This therapy, however, is not without risks and may lead to the transmission of infectious agents, principally human immunodeficiency virus (HIV), hepatitis B virus (HBV), hepatitis C virus (HCV) and syphilis – causing *Treponema pallidum*. With every one unit of blood transfused, there is a 1% chance of transfusion – related complications including transfusion transmissible infections (TTIs).^[2] The TTIs are a serious threat to blood safety particularly in developing economies such as ours where the existing national blood transfusion services and policies, infrastructure, trained personnel, political structure and financial resources are inadequate. This situation is further exacerbated by the predominance of family replacement and commercially remunerated blood donors, non-prioritization of blood donation from regular,

voluntary and altruistic, non-remunerated donors and lack of stringent screening of donated blood for the transfusion transmissible infectious agents.^[3]

In the quest for global blood safety, the World Health Organization (WHO) recommends universal and quality – assured screening of blood donations for at least the four major transfusion – transmissible infections: human immunodeficiency virus (HIV), hepatitis B virus (HBV), hepatitis C virus (HCV) infections and syphilis.^[4] Undetectable transmission of infectious agents is a major challenge in transfusion medicine. Majority of the risks are due to blood donation during the serologically negative window period. Under this circumstance, blood transfusion is capable of transmitting infection inspite of negative serological screening tests. Providentially, this unnoticeable infection is preventable through application of nucleic acid amplification techniques (NATs) such as polymerase chain reaction (PCR). Currently, NAT has been adopted in many industrialized nations whereas the

developing countries including Nigeria still depend on the traditional antibody screening methods. With the use of the latter method, the risks and implications of TTIs remain a major problem.^[5]

About 35 million people worldwide are living with HIV.^[6] Annually, global infection rate of HIV through blood transfusion alone ranges from 80, 000 to 160,000.^[7] HBV infection affects over 400 million individuals worldwide and is associated with chronic morbidities.^[8] 3% of the world's population is chronically infected with HCV.^[8] According to WHO, there are 12 million new cases of syphilis each year, with more than 90% occurring in developing countries where prevalence can reach 25% among blood donors.^[9]

Sub-Saharan Africa (SSA) has the highest prevalence of blood-borne infections in the world.^[3] The regional prevalence of HIV infection is about 23.5 million which accounts for 69% of the global burden.^[10] Blood transfusion is responsible for 5 – 10% of HIV infection in this region.^[11] Most of sub-Saharan Africa is endemic for HBV infection.^[12] The chronic carriage rate of HBV infection among blood donors ranges between 3% and 22%.^[13] HCV prevalence rate in SSA is 5.3% while the West Africa sub-region has an estimated prevalence of 2.4%.^[14,15] The prevalence of syphilis is one of the highest amongst the TTIs screened in Africa. Existing evidence shows varied reports on the prevalence rates in different countries on the continent.^[16-18]

Multiple studies done within Nigeria have shown a wide variation in the seroprevalence rates of the TTIs.^[19-35] To the best of our knowledge, no similar study has been carried out in Uyo, South-South Nigeria. With this background, the objectives of this study were to determine the prevalence and trends of HIV, HBV, HCV and syphilis among blood donors in South-South Nigeria during a 4-year period from 2012 to 2015. It is hoped that the findings of this study would permit an assessment of the risks of TTIs in the region, evaluate the effectiveness of the blood safety strategies employed in our blood bank as well as engender the formulation and implementation of measures to prevent spread of these infections.

MATERIALS AND METHODS

Study Site

The study was done at the University of Uyo Teaching Hospital, a tertiary referral hospital in Akwa Ibom State, South-South Nigeria. The hospital provides specialized health care services to the indigenes of the oil rich state

of about 4 million people^[36] and neighbouring states of Cross River, Rivers and Abia.

Study Design

A descriptive cross-sectional study design was used to achieve the set objectives.

Study Population

The screening records of 12,693 consecutive prospective blood donors from January 1, 2012 to December 31, 2015 were retrospectively reviewed with respect to screening outcome for HIV, HBsAg, HCV and syphilis.

Laboratory methods

HIV status of blood donors were determined using Determine (HIV - 1/2) (ABBOTT – Japan), an immunochromatographic test kit with 97.96% specificity and 100% sensitivity. Indeterminate results were further tested using UNI-GOLD (Trinity Biotech PLC, Ireland) with 99.70% specificity and 100% sensitivity and /or GENIE II HIV – 1/HIV – 2 (BIO-RAD – France) which has 100% specificity and sensitivity, before being eventually discarded. HBsAg status was determined using commercially available third generation Diaspot HBsAg test strips (Sam – Tech Diagnostics, USA), which is an immunochromatographic test designed for quantitative determination of Hepatitis B surface antigen in plasma and serum. It has a sensitivity of 99.8% and specificity of 100%. Anti-HCV was similarly tested using Diaspot test strips. Antibodies (1gG and 1gM) to Syphilis were tested using Syphilis Ultra Rapid Test Strip (Global strips, USA), which utilizes a double antigen combination of a Syphilis antigen immobilized on the membrane to detect *Treponema pallidum* antibodies (1gG and 1gm) qualitatively in whole blood, serum, or plasma. It has a sensitivity of 99.7% and a specificity of 99.6%. All the reactive samples were confirmed using enzyme – linked immunosorbent assay.

Statistical analysis

The data were analyzed using statistical package for social sciences (SPSS) windows version 20.0 (SPSS Inc; Chicago, IL, USA) and presented in simple tables. The comparison was carried out with chi square test as appropriate and the level of significance was set at 5% ($p < 0.05$).

RESULTS

A total of 12,693 prospective blood donors were screened during the study period (2012-2015) of whom 9579 (75.5%) were males while 3114 (24.5%) were females giving a ratio of 3.1:1 (table 1).

Table 1: Distribution of blood donors with TTIs according to Gender

Variables	Frequency (%) n = 12, 693							
	HIV		HBsAg		HCV		Syphilis	
Gender	Negative	Positive	Negative	Positive	Negative	Positive	Negative	Positive
	Total		Total		Total		Total	
Males	9031 (96.1)	368(3.9)	9244(97.3)	256(2.7)	9185(98.0)	192(2.0)	9446 (98.6)	133(1.4)
	9399		9500		9377		9579	
Females	2999(97.1)	89(2.9)	2899(97.2)	83(2.8)	3022(97.0)	92(3.0)	2862(98.5)	43(1.5)
	3088		2982		3114		2905	
Total	12030(96.3)	457(3.7)	12143 (97.3)	339(2.7)	12207 (97.7)	284(2.3)	12308 (98.6)	176(1.4)
	12487		12482		12491		12484	
X ²	7.04		0.067		8.65		0.14	
P – valve	0.008		0.79		0.003		0.71	

The overall seroprevalence of HIV, HBsAg, HCV, and Syphilis during the study period was 3.7%, 2.7%, 2.3% and 1.4%, respectively (table 2). The prevalence of hepatitis B, hepatitis C and syphilis was higher among females compared to males, while for HIV, it was higher among the females, the difference in prevalence by sex was statistically significant ($p < 0.05$) for HIV and hepatitis C but not for the rest (table 1).

Table 2: Yearly seroprevalence of HIV, HBsAg, HCV and Syphilis from 2012 to 2015

Variables	Frequency (%) n = 12, 693							
	HIV		HBsAg		HCV		Syphilis	
Year	Negative	Positive	Negative	Positive	Negative	Positive	Negative	Positive
	Total		Total		Total		Total	
2012	3019 (96.0)	130(4.0)	3105 (96.6)	108 (3.4)	3140(97.6)	76(2.4)	3188 (99.1)	30(0.9)
	3221		3213		3216		3218	
2013	2845 (95.8)	125(4.2)	2897 (97.5)	75(2.5)	2907 (97.6)	70(2.4)	2935 (98.8)	35(1.2)
	2970		2972		2977		2970	
2014	2936 (96.9)	95(3.1)	2952 (97.4)	78(2.6)	2951 (97.3)	81(2.7)	2969 (98.0)	61(2.0)
	3031		3030		3032		3030	
2015	3158 (87.4)	107(3.3)	3187 (97.6)	78(2.4)	3209 (98.3)	57(1.7)	3216 (98.5)	50(1.5)
	3265		3267		3266		3266	
Total	12030(93.7)	457(3.7)	12143(97.3)	339(2.7)	12207 (97.7)	284 (2.3)	12308(98.6)	176(1.4)
	12487		12482		12491		12484	
X ²	7.56		7.05		6.46		14.71	
P – valve	0.06		>0.05		>0.05		<0.05	

The highest HIV, HCV and Syphilis seroprevalence rates were observed among donors aged 36 – 45 years while for HBsAg, it was highest among donors between 26 and 35 years of age. The prevalence of the infections among different age groups was statistically significant ($p < 0.05$) table 3.

Table 3: Prevalence of the TTIs among different age groups

Variables	Frequency (%) n = 12, 693											
	HIV			HBsAg			HCV			Syphilis		
Age (years)	Negative	Positive	Total	Negative	Positive	Total	Negative	Positive	Total	Negative	Positive	Total
18 – 25	4243 (98.6)	62(1.4)	4305	4303(99.4)	25(0.6)	4328	4297(99.8)	10(0.2)	4307	4352(99.95)	2(0.05)	4354
26 – 35	5212 (98.1)	100(1.9)	5312	4907(95.6)	224(4.4)	5131	4917(96.6)	171(3.4)	5088	4973(98.0)	100(2.0)	5073
36 – 45	1814(96.8)	276(13.2)	2090	2436(96.8)	80(3.2)	2516	2475(96.1)	100(3.9)	2575	2473(97.2)	72(2.8)	2545
46 – 55	741(97.6)	18(2.4)	759	488 (98.0)	10(2.0)	498	503(99.4)	3(0.6)	506	492(99.6)	2(0.4)	494
56 – 65	20(95.2)	1(4.8)	21	9(100)	0(0)	9	15(100)	0(0)	15	18(100)	0(0.0)	18
Total	12030(96.3)	457(3.7)	12487	12143(97.3)	339(2.7)	12482	12207(97.7)	284(2.3)	12491	12308 (98.6)	176(1.4)	12484
X ²	651.5			130			144			110.5		
p-value	<0.001			<0.001			<0.001			<0.001		

DISCUSSION

Acquisition of transfusion – transmissible infections in the course of therapeutic blood transfusion is a pervasive global health challenge in transfusion medicine; thus all hands must be on deck to eliminate or reduce this complication to its lowest ebb. This is particularly important because of the chronic morbidity and mortality associated with these infections. It is therefore utterly expedient to continue to monitor the trends in the prevalence of transfusion transmissible infections in order to evaluate the risk of TTIs in our prospective blood donors, and by extrapolation, the risk in the general population receiving such blood, taking into cognizance the peril of bleeding donors during the “window period” when they may be negative for the offending antigens or antibodies being screened for.

The overall prevalence of HIV, HBsAg, HCV, and Syphilis during the period under review was 3.7%, 2.7%, 2.3% and 1.4%, respectively. The prevalence of HIV observed in this study is higher than the estimated national HIV seroprevalence which is put at 3.4% but lower than the 6.5% found in the general population.^[37] It is however consistent with a 3.5% prevalence rate reported by Chukwuurah and Nneil^[19] in Enugu. Conversely, our figure is at variance with other figures reported in the country; Hassan and Colleagues in Kaduna (2.8%), Ejele and Colleagues^[21] in Port Harcourt, South-South, Nigeria (1%), Offor and Colleagues^[22] in Benin City (0.5%), Musa and Colleagues^[23] in Osogbo (3.1%), Irena et al^[24] in Lagos Island (8%), Amadi et al^[25] in Abia State (10.6%) and Baba et al^[26] in Maiduguri (5.5%). In other countries, 3.1% has been reported from Ghana^[28] and 2.92% from the United States.^[39] In Saudi Arabia, El-Hazmi^[40] observed a zero percent HIV prevalence among their cohort of 24,173 blood donors, while in Egypt, El-Gilany and associates^[41] observed HIV seroprevalence of 6.9% among 1, 257 voluntary donors. A study of 213,666 blood donors in Brazil^[42] yielded an overall HIV prevalence of 0.149%. The variation in prevalence rates reported in different studies might be attributed to the differences in geographical locations, age range of donors, sample sizes, the period of time the studies were conducted, ethno-religious and socio-cultural factors. The socio-cultural and religious practices implicated in the risk of HIV transmission include indiscriminate sexual relations, handling of childbirth by unskilled birth attendants outside health facilities (churches/mosques), use of unsterilized instruments for circumcision, scarification and tattoo and obnoxious practice like female genital mutilation.

A reduction in the aforementioned practices through motivational and educational campaign and pretest counseling for donors to allow them to self-defer might have accounted for the declining infection rate observed in our work. It is also possible that improvement in technology might have made current screening reagents more specific and sensitive. However, we observed a

higher prevalence rate in 2015 compared to 2014. The trend might probably be a reflection of a surge in incidence in our society due to the prevailing economic recession which may push some unemployed persons to source for money through selling their blood as has been reported earlier by Durosinni^[43] and which calls for continuous stringent and meticulous measures at donor recruitment. The rise might also suggest a laxity in activities and programmes to stem the spread of HIV. It may also be due to an increase in the number of new infections in the general population. It is pertinent to note that the use of HIV – P24 antigen testing has reduced the residual risk of HIV infection from 0.38 to 0.24 per million^[44] in industrialized nations. Regrettably, this is not the case in developing economies like Nigeria that still depend on antibody screening methods. Therefore, as long as the resource – constrained economies continue to transfuse HIV infected blood which may be HIV negative as a result of antibody screening during the “window phase of infection”, the residual risk of HIV may continue to rise in our environment.

The 2.7% seroprevalence of HBsAg found in this study is much higher than figures reported by Polizzotto et al^[45] in Australia (0.01%), Gupta et al^[46] in India (0.66%), Amini et al^[47] in Iran (0.56%), El-Hazmi^[40] in Saudi but similar to that reported by Gulia et al^[48] (2.48%). However, our rate is lower than prevalence rates reported by Uneke et al in Ilorin, Nigeria (21.70%), Baba et al^[26] in Maiduguri, Nigeria (14.0%) Mustapha et al^[28] Buseri et al in Osogbo, Nigeria (18.6%), Ampofo et al^[38] in Ghana (15.0%), Glynn et al^[39] in the United States (10.4%) and Diro et al^[49] in Ethiopia (8.2%). Differences in sexual behaviour and practices, cultural practices, geographical variation, test methods employed for HBV detection and the level of health education on prevention of HBV infection, may all play significant roles in the wide variations of HBsAg seroprevalence noted in the literature.

Furthermore, in order to mitigate the residual risk of transfusing hepatitis B virus during the window period, many advanced economies have adopted the nucleic acid amplification test (NAT). By contrast, the developing economies are yet to add this highly sensitive screening test to their donor screening menu. With the use of NAT, low levels of HBV-DNA are detected in serum and liver tissues of some patients who cleared HBsAg following acute self-limiting infection^[50] and can cause overt hepatitis especially when immunocompromised patients are transfused with such blood.^[51] The use of NAT could have probably been responsible for the decline in the prevalence of the TTIs in the industrialized world as shown by the significantly low rates reported.

The prevalence of HBsAg observed in this study is one of the lowest ever reported from Nigeria. This is a testament to the fact that efforts of both government agencies and non-governmental organizations at

reducing the scourge of hepatitis B virus infection are yielding impressive results. The incorporation of HBV vaccination in the childhood immunization schedule in the last 15 years, education and public enlightenment campaign on the importance of HBV vaccination might have accounted for the reduction in the infection rate in the general population which is being reflected in the donor population.

Sub-Saharan Africa has some of the highest reported global rates of HCV seroprevalence, ranging from 2.1% to 2.8%, with the highest in West Africa, approximately 2.8%.^[28] However, studies on HCV prevalence among blood donors in this region showed that blood donors consistently had lower prevalence (1.9%) than the general population.^[53] A prevalence of 0.8 to 12.3%^[23,29-32] has been reported among blood donors in Nigeria. The seroprevalence of 2.3% obtained from our study is comparable with the 2.8% and 2.9% found among blood donors in Ghana^[54] and Port Harcourt,^[33] Nigeria, respectively, though much higher than the figure obtained in a study done in USA (0.072%).^[55] Higher rates than ours have been recorded among blood donors in Tanzania (8.0%),^[56] Ghana (8.4%),^[38] Central African Republic (5.0%)^[57] and Egypt (15.8%).^[58] The reduction in the prevalence rate from 2.7% in 2014 to 1.7% in 2015 in the present study is a desirable development. Hopefully the decline will be a sustained downward trend in infection rate of the blood donors. Such decline could be as a result of a combination of Factors including a change in screening reagent used, diminution in population risks, or effectiveness of prospective donor screening measures. In the absence of NAT screening method for HCV, efforts should be geared towards reducing false negative anti-HCV cases to the barest minimum through stringent donor selection criteria and excluding high – risk subjects as studies have shown that the most efficient mode of transmission of HCV is blood to blood contact,^[59,60] less efficiently through sexual route unlike HBV and HIV infection.^[61,62]

The finding of 1.4% seroprevalence for syphilis observed in this study is similar to the observation made by Buseri and others^[23] from Osogbo, the South-West region of Nigeria who reported a value of 1.1% in their blood donors. However, higher values have been reported in other parts of Nigeria and some African countries including Maiduguri (12.8%)^[17] and Tanzania (12.7%).^[16] In more advanced economies, Syphilis seroreactivity is lower,^[63-67] being less than 1.0% in many of the reports. Similar lower value (0.1%) has been reported by Ejele *et al*^[21] in Port Harcourt, Nigeria. The wide variation in the Syphilis infection rate among the blood donors reported in multiple studies may be due to differences in the testing methodologies, sample sizes, geographical locations and socio-cultural practices such as sexual behaviour and conjugal practices which are peculiar to some parts of the world. The risk of contracting Syphilis is closely related to risk factors in the prospective blood donor, particularly sexual habits

since the disease like the other TTIS are primarily transmitted by the sexual route. Risky lifestyles such as prostitution, homosexuality, lesbianism, bisexuality, intravenous drug abuse and skin scarification (tattooing, blood rituals), have been known to heighten the risk of syphilis transmission.^[68]

Majority of our study population were males (75.5%), with females representing a proportion of 24.5%. This observation shows that more males donate blood than females in our environment. The reason for this gender imbalance may, in part, be cultural where men in Africa are perceived as being healthier than women,^[69] as well as physiological where iron deficiency anaemia from monthly menstrual flow, pregnancy and lactation preclude women from joining the donor pool.^[7] It could also be due to lack of proper public health awareness (education) on the essence of blood donation. Similarly, male dominated donor pool was noted by Okocha^[71] and Matee^[56] in studies done in South-East Nigeria and Tanzania, respectively. In contrast, a study in China showed higher rate of female donors (44.5%).^[72]

The present study observed that the male donors had a higher prevalence of all the TTIs than their female counterparts. This is consistent with a study done by Matee *et al*^[56] in Tanzania. The explanation for this male gender – related predisposition to TTIs is not far-fetched. Socio-cultural practices and beliefs may play a significant role. In most African settings, men are culturally permitted to have multiple sexual partners, mistresses and concubines, whereas it is a taboo for women to follow suit. Men are also more sexually active and more likely to adopt high-risk lifestyles (having unprotected sexual intercourse, intravenous drug abuse, tattooing or engaging in blood rituals) that put them potentially at risk for acquiring HIV, HBsAg, HCV and Syphilis.^[73]

The highest prevalence of HIV, HCV and Syphilis was found in the 36-45 years age group, while HBsAg infection was more common in donors aged 26 – 35 years. Our finding is in agreement with previous results reported by Baba and associates,^[26] Ejele and colleagues,^[21] Buseri, *et al*^[23] and Karmakar *et al*^[74] in which highest prevalence rates were observed among blood donors within these age brackets. The high prevalence of HIV, HBsAg, HCV and syphilis observed among these donors in this present study could be as a result of lack of adequate educational enlightenment about the modes of transmission and prevention of these infections. It may also be due to prevalence of high risk behaviour among these persons. This observation is appalling since the most productive and economically viable age group of the population are afflicted. There is the fervent need for renewed intensification of prevention programmes targeted at changing high-risk behaviour in our society.

CONCLUSION

This study has shown that transfusion – transmissible infections are not uncommon in our blood donors and that HIV infection is the most common and syphilis the least common TTI. A declining trend in prevalence of all the infections occur during the years under study. Lower seroprevalence rates of the TTIs in our work compared to previous studies in other centres, particularly in sub-Saharan Africa, lends credence to the effectiveness of our donor screening measures. However, education of the blood donors on avoiding risky lifestyles, voluntary blood donor motivation strategies and community surveillance of the infections should be intensified and in addition, efforts should be geared towards adding NAT to the donor screening menu to further reduce the number of blood donors likely to donate during the window period and by extension improve the access to safe blood.

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