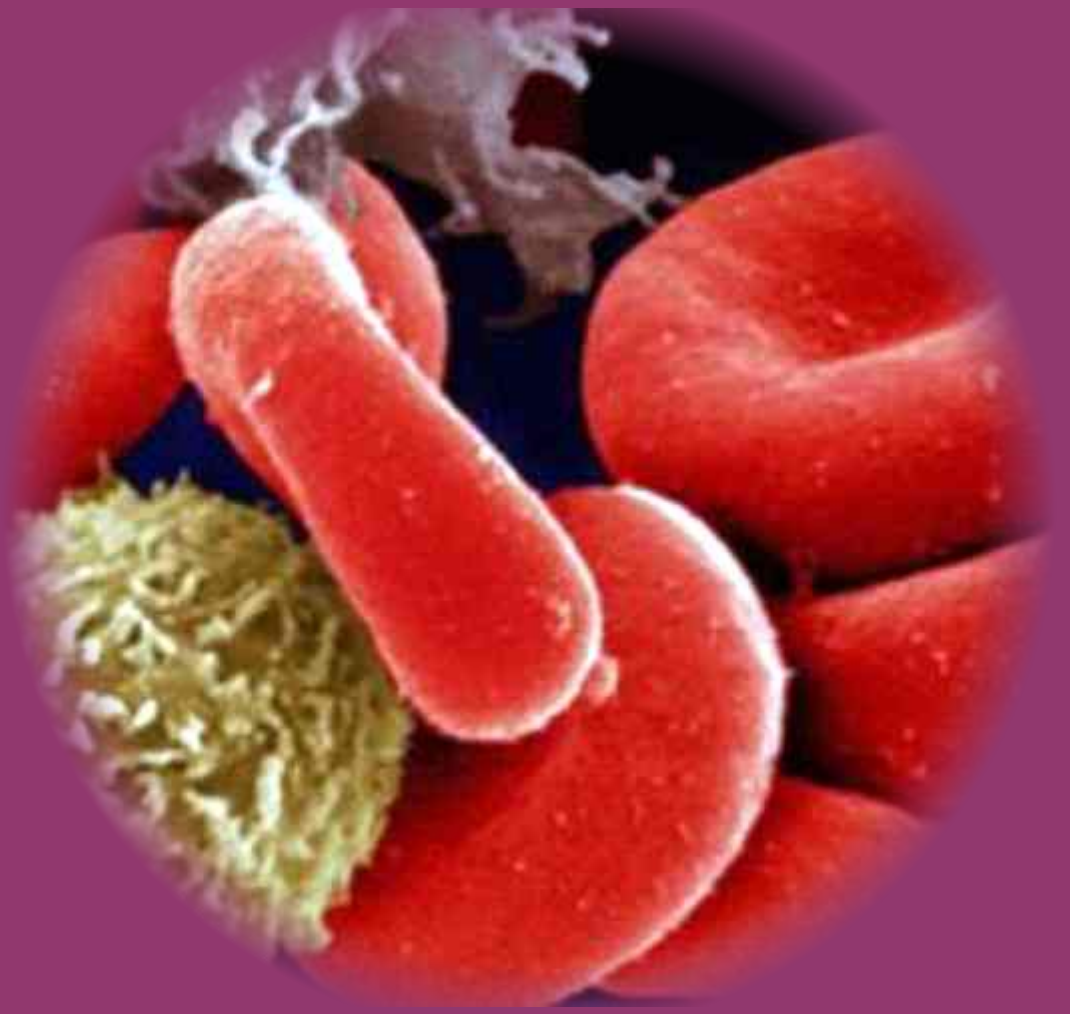
N S H B T

NIGERIAN J OURNAL OF HAEMATOLOGY

Journal of the Nigerian Society for Haematology & Blood Transfusion



ISSN: XXX - XX - XXX

VOL. 1 NO 1, AUGUST, 2017

ORIGINAL RESEARCH ARTICLE

Transfusion Transmissible HIV Infection: How Reliable are Rapid Screening as Pre-Donation Tests?

IN Ibrahim [1,2], AI Mamman[1], MS Balogun[2], A Hassan[1], S Awwalu[1], IU Kusfa[1,2]

[1]Department of Haematology and Blood Transfusion, Ahmadu Bello University, Zaria - Nigeria and
[2] Department of Nigeria Field Epidemiology and Laboratory Training Programme, Abuja

Corresponding Author:
Dr. Ismaila N Ibrahim,
Department of Haematology, ABUTH, Zaria, Nigeria
Email: dribronda@yahoo.com

ABSTRACT

Background:
Blood transfusion is the most efficient mode of transmission of human immunodeficiency virus (HIV) infection; resulting in up to 96% of seroconversion in recipients following receipt of HIV-infected blood. In developing countries transfusion-transmissible HIV infections (TTHI) are fueled by reliance on replacement blood donation and quality-compromised pre-donation screening of blood donors with rapid diagnostic tests (RDTs).

Aims and Objectives:
The objective of this study was to assess the false negative rates of pre-donation screening of HIV using RDTs in state government-owned hospital blood donation units in Kaduna, North-West Nigeria.

Materials and Methods:
Between January and March 2016, blood samples from 264 HIV RDT seronegative blood donors were collected in three government-owned hospitals in Kaduna metropolis and retested at the North-west zonal national blood transfusion service

Kaduna using 4th generation sandwich ELISA. The ELISA positive samples were subjected to confirmatory tests using nucleic acid testing (NAT).

Results:
The false negative rates of pre-donation RDT for HIV against ELISA was 10(3.8%). However, 7 out of 10 ELISA reactive samples were positive for HIV with NAT. Thus RDT that was used for donor screening had missed 7(2.7%) of HIV positive blood donors' samples.

Conclusion:
Pre-donation screening of blood donors for HIV using RDT can lead to false negative results which could lead to TTHIs. We therefore recommend ELISA test as the minimum standard in Kaduna, Nigeria.

Keywords: blood donors, pre-donation screening, HIV, rapid diagnostic tests (RTDs).

INTRODUCTION

In the developed countries, the risk of transfusion transmissible infections (TTIs) has been progressively declining over the last few decades as a result of coordinated blood safety strategies; recruitment of low-risk regular voluntary non remunerated blood donors and screening of donated blood in a quality-assured manner using highly sensitive laboratory methods. [1-3] In the USA, the residual risk of transmitting HIV is 1 in 3.1 million, and this is usually for donations during window periods. [4]

Recently, there has been a paradigm shift from the long held estimates that 5% to 10% of new HIV infections in sub-Saharan Africa were due to transfusion of unwholesome blood and blood products.[5] However, blood and blood products still account for up to 1.1% of TTHIs; and remain the most efficient mode of HIV infections resulting in about 96% of seroconversion in recipients following one unit of HIV-infected blood. [6] Quality-assured screening of blood has been difficult to implement and sustain in sub-Saharan Africa due to lack of infrastructure, inadequate skilled manpower and financial constraints. [7] This is further compounded by the dwindling support for blood screening by international donor agencies such as the President's Emergency Programme for HIV/AIDs Relief (PEPFAR). The

hospital-based blood transfusion services which provide the bulk of blood requirements for Nigerians, rely mainly on family replacement or commercial donors. [8] In addition, the use of pre-donation rapid diagnostic tests (RDTs) for TTIs is a common practice in these settings. Kaduna State with a population of over 8 million people in 2016 is the third most populous state in Nigeria and has the highest HIV prevalence in the North-western geo-political zone with a regional prevalence of 3.2%. [9] We therefore aimed to retest the blood samples of blood donors by ELISA method after previously being screened for HIV using RDTs. In addition, all the reactive samples after ELISA test were confirmed by NAT using polymerase chain reaction (PCR) technique to exclude any false positives.

MATERIALS AND METHODS

Study area: The study was carried out in three main hospitals in Kaduna metropolis from January to March, 2016.

Study design and sampling technique: This was a cross-sectional study. The hospitals' laboratories that housed the blood donation units were selected because they had cold chain facilities for blood sample preservation. All the 264 donor samples collected and screened using RDT during the study period were negative for HIV 1 and 2 antibodies.

Laboratory methods: Five milliltres (mls) of blood was collected into EDTA containing vacutainer bottles from the prospective blood donors for routine screening for TTIs. The HIV 1 and 2 antibodies screening was carried out using Alere® Determine HIV-1/2 at the blood donation units. After centrifugation, plasma from each of the blood samples was separated into well-labeled plain sample bottles and stored at -20 ℃. They were transported in cold boxes to the National Blood Transfusion Service (NBTS) Kaduna for retesting with ELISA in a quality-assured manner. The assay was carried out with Genscreen Ultra HIV antigen/antibody combination fourth generation ELISA by Bio-rad. The laboratory personnel who conducted the retest were unaware of the results of HIV antibody-based screening from the health facilities. Confirmatory testing were carried out on ELISA positive samples using NAT.

Ethical considerations: Ethical approval for this study was granted by the Kaduna State Ethical Review Committee and authorities of the participating hospitals. The Kaduna State ministry of health and the managements of the three hospitals were notified of HIV false negative results with RDTs against ELISA. The affected blood donors were referred to the antiretroviral clinics of the respective hospitals to seek further evaluation.

RESULTS

Two hundred and sixty-four donor blood samples were analyzed in this study: 117 from hospital I, 97 from hospital II and 50 from hospital III. All the 264 samples screened using RDT were HIV 1 and 2 antibodies negative, and thus the units were certified suitable for transfusion if they were also nonreactive to hepatitis B surface antigen, hepatitis C antibody and syphilis. However, on retesting of the 264 samples for HIV using fourth generation sandwich ELISA, 10(3.8%) were reactive (discordant results).

Table: False negative rates of HIV antibody RDT compared with fourth generation ELISA antigen-antibody combination and NAT assays

Health facility	RDT HIV Neg.	ELISA HIV Pos.	NAT HIV Pos.	RDT False Neg. (%)	ELISA False Pos. (%)
Hospital I	117	4	3	3(2.6)	1(0.9)
Hospital II	97	3	2	2(2.1)	1(1.0)
Hospital III	50	3	2	1(2.0)	1(2.0)
Total	**264**	**10**	**7**	**7(2.7)**	**3(1.1)**

Key: Pos = Positive, Neg = Negative

Of the 10 HIV ELISA reactive samples, 7(70%) were confirmed HIV positive using NAT (See table below). Thus, the RDT screening missed 7 HIV positive samples from blood donors, giving a false negative rate of 2.7%. All the 254 samples that had concordant negative results for HIV with both RDT and 4th generation ELISA (antigen-antibody combo) were considered HIV negative. Hospital I had 3(2.6%), hospital II 2(2.1%) and hospital III 1(2.0%) false negative rates for RDT. The 4th generation ELISA produced an overall 1.1% (range: 0.9-2.0) false positive rates compare with PCR.

DISCUSSION

Transfusion of safe blood has been an issue of concern in transfusion medicine, and with the emergence of HIV/AIDS pandemic in the 1980s, particular attention has been focused on preventing transfusion-transmitted infections (TTIs) through the use of sensitive tests. [10]

The World Health Organization (WHO) recommends ELISA method for TTIs screening because of its greater sensitivity and specificity compared with RDTs. [11] ELISA is not widely available as a screening test for TTIs in most hospital blood transfusion units in Nigeria due to high financial costs and lack of skilled manpower coupled with equipment and infrastructural deficits. In addition, most units do not have or follow standard operating procedures (SOPs) for conducting RDTs. Similarly, a low blood inventory due to scarce regular voluntary non-remunerated blood donors and poorly funded NBTS limit the use of more sensitive screening methods, [11] as targeted blood donations on emergency basis for immediate release are often the practice.

This study found pre-donation screening for HIV using RDT producing a 7(2.7%) false negative results; that is, the test failed to detect HIV in people who are actually infected with the virus. Though not a validity test, false negative results using RDT for screening donated blood have been reported in similar studies in North Central Nigeria, Cameroon, South Africa and India. [12-16]

Factors that could be responsible for this poor performance of RDT for HIV range from the intrinsic properties of the test kits to external factors such as poor training of personnel on test performance, lack of implementation of quality-assurance programmes, and poor storage conditions of the test kits. It has been observed in some studies that the same RDT may perform differently under different field conditions. [15,17]

This study also noted that there were no quality systems in place for kits procurement and, screening of donor blood samples for HIV in the three facilities. The false-negative RDT results could be due to procurement of poor-quality RDTs, or due to being compromised as a result of poor transport and storage conditions. In addition, SOPs were not routinely followed during the analytic phase of HIV testing in the facilities.

We found that ELISA had better outcome for screening blood donors for HIV in this study. This superior outcome might be due to the use of HIV ELISA kit with antigen-antibody combination that is capable of detecting HIV antigen before the antibody seroconversion could have occurred. However, Chaurasia *et al* [18] have reported in India that fourth generation ELISA testing for HIV could generate false positive results due to its potential for nonspecific reactivity. In this study, 3(1.1%) of ELISA results were false positives following confirmatory testing using NAT.

The HIV RDT detects only HIV 1 and 2 antibodies, not HIV antigens (P24) that 4th generation used in the retest detects. Thus this marker of early HIV infection could have been missed by RDT kit.

CONCLUSION

The present strategy of pre-donation RDT screening of blood donors is not adequate in preventing TTHI in Kaduna. Thus, the state ministry of health should put in place a coordinated state-wide blood transfusion service with ELISA screening as a minimum benchmark.

Acknowledgement:

We would like to thank Dr. Ijeoma Ogbue, the then North-West Zonal Director of National Blood Transfusion Service for help with the storage and testing of the blood samples in her laboratory.

Conflict of Interest:

No conflict of interest was declared by the authors.

Contribution of Authors:

All authors contributed significantly to the study design, collection of data and the writing of this paper.

REFERENCES

1. Kleinman SH, Lelie N, Busch MP. Infectivity of human immunodeficiency virus-1, hepatitis C virus, and hepatitis B virus and risk of transmission by transfusion. *Transfusion* 2009; 49(11): 2454-2489. doi:10.1111/j.1537-2995.2009.02322.x.
2. Scheiber GB, Bush MP, Kleiman SH, Korelitz, JJ. The risk of transfusion-transmitted viral infections. *N Engl J Med.* 1996; 334(26):1685-90. Available at: http://www. nejm.org [Accessed 1st May 2016].
3. Zou S, Stramer SL, Dodd RY. Donor testing and risk: current prevalence, incidence, and residual risk of transfusion-transmissible agents in US allogeneic donations. *Transfus Med Rev.* 2012; 26: 119-128. doi:http://dx.doi.org/10.1016/j.tmrv.2011.07.007.
4. Stramer SL, Glynn SA, Kleinman SH, Strong M, Caglioti S, Wrght DJ, *et al*. Detection of HIV-1 and HCV infections among antibody-negative blood donors by nucleic acid-amplification testing. *N Engl J Med.* 27265BC:760-768. doi:10.1056/NEJMoa 040085.
5. Morar MM, Pitman JP, McFarland W, Bloch EM. The contribution of unsafe blood transfusion to human immunodeficiency virus incidence in sub-Saharan Africa: reexamination of the 5% to 10% convention. *Transfusion* 2016; 56, 12, p. 3121-3132 12 p. doi:10.1111/trf.13816. [Accessed 28th December, 2016]
6. Joint United Nations Programme on HIV/AIDS. UNAIDS 2012. *Modeling the expected Short-term distribution of new HIV infections by modes of transmission.* ISBN 978-92-9173-997-4. [Accessed 30th May, 2017]
7. Moore A, Herrera G, Nyamongo J, Lackritz E, Granade T, Nahlen B, *et al*. Estimated risk of HIV transmission by blood transfusion in Kenya. Lancet 2001; 358: 657-660.
8. National Blood Transfusion Service (Federal Ministry of Health). NBTS 2006. *The Nigerian National Blood Policy.* Available at: http://googlesearch.com [Accessed 5th April, 2015].
9. Federal Ministry of Health (Nigeria). FMOH 2013. *National HIV & AIDS and Reproductive Health Survey 2012 (NARHS Plus).* NARHS-Plus-2012-Final-18112013.pdf [Accessed on 27th September, 2015]
10. Kaadan A, Angrini M. Blood transfusion in history. JISHIM 2010; 8-9. ISSN: 1303-667x. [Accessed 26th October, 2016]
11. World Health Organization. WHO 1-73:2012. *Screening Donated Blood for Transfusion Transmissible Infections*. WHO 2010.ISBN 978 92 4 154788 8 [Accessed on 5th April, 2015]
12. Orkuma J, Egesi J, Banwat E, Ejele OA, Orkuma JH, Bako IA, *et al*. HIV screening in blood donors: rapid diagnostic test versus enhanced ELISA. *Niger J Med* 2014; 23(3):192-200. Available at: http://www. goole.com [Accessed 8th May 2016].
13. Wolpaw BJ, Mathews C, Chopra M, Hardie D, de Azevedo V, Jennings K, *et al*. The failure of routine rapid HIV testing: a case study of improving low sensitivity in the field. *BMC Health Services Research.* 2010; 10: 73. doi: 10.1186/1472-6963-10-73. [Accessed 30th May, 2017]
14. Aghokeng AF, Mpoudi-Ngole E, Dimodi H, Atem-Tambe A, Tongo M, Butel C, *et al*. Inaccurate diagnosis of HIV-1 Group M and O is a key challenge for ongoing universal access to qntiretroviral treatment and HIV prevention in Cameroon. *PLoS ONE* 4(11):e7702. doi:10.1371/journal.pone.0007702. [Accessed 30th May, 2017]
15. Mehra B, Bhattar S, Bhalla P, Rawat D. Rapid tests versus ELISA for screening of HIV infection: Our experience from a voluntary counselling and testing facility of a tertiary care centre in North India. *ISRN AIDS.* 2014; Apr 7; 2014: 296840. http://dx.doi.org/10.1155/2014/

296840.

16. Torane V, Shastri J. Comparison of ELISA and rapid screening tests for the diagnosis of HIV, Hepatitis B and Hepatitis C among healthy blood donors in a tertiary care hospital in Mumbai. *Indian J Med Microbiol.* 2008; 26(3): 284-285. Available at: http://www.googlescholar.com [Accessed 9th May 2016].
17. Urassa W, Nozohoor S, Jaffer S, Karama K, Mhalu F, Biberfeld G. Evaluation of an alternative confirmatory strategy for the diagnosis of HIV infection in Dar Es Salaam, Tanzania, based on simple rapid assays. *J Virol Methods* 2002; 100:115-20.
18. Chaurasia R, Zaman S, Das B, Chatterjee K. Screening donated blood for transfusion transmitted infections by serology along with NAT and response rate to notification of reactive results: an Indian experience. *Journal of Blood Transfusion*. 2014; (2014): 1-6. Available at http://dx.doi.org/10.1155/2014/412105. [Accessed 6th June, 2015]

KALCOGEN®

Filgrastim 300 mg

for better outcome

Simplifies Choice

- ✓ **Prevents** : infection, neutropenia
- ✓ **Modicies** : biological responses
- ✓ **Stimulates** : granulocyte production
- ✓ **Saves Life** : reduces time of neutropenia

Dose: 5 mg/kg body weight daily

KALBE

signet® NIG.
08034251438