Original Research

Screening for Syphilis Among Blood Donors in Nigeria: Application of General Quality Principles

Dépistage de la Syphilis chez les Donneurs de Sang au Nigéria: Application des Principes Généraux de Qualité

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ABSTRACT

Background: Safety of blood for transfusion is a global concern. WHO and Africa Society for Blood Transfusion require a minimum of antibodies to *Treponema pallidum* or VDRL or RPR test on all donated blood units before transfusion. Application of general quality principle in screening for Transfusion Transmissible Infections, syphilis inclusive is a major determinant of safety of blood transfusion.

Methods: Forty-eight health care facilities were recruited for the study between January and June 2018. A self-administered structured questionnaire, physical interactions and telephone calls were employed to collect all relevant data on quality measures, types of blood donors, total number of blood units screened and reactivity to syphilis screening tests.

Results: Venereal Disease Research Laboratory method was used to screen all donations for syphilis at 81.3% of the facilities screened. Twenty seven of the 39 facilities that screened for syphilis validated their test kits, 24 facilities had written SOPs and quality control system while 33 and 6 facilities procured syphilis screening reagents through Hospital Managements and Departments. A total of 98 478 blood units were collected and screened for syphilis. Of the 831 samples found reactive, 405, 408 and 18 were obtained from tertiary, secondary and private hospitals and 384, 381 and 66 of the samples were from family replacement, paid and voluntary non-remunerated blood donors respectively.

Conclusion: Majority of the facilities studied screened for syphilis using non-specific method and most employed general quality

RÉSUMÉ

Contexte: La sécurité transfusionnelle est une préoccupation mondiale. L'OMS et la Société Africaine de Transfusion Sanguine recommandent au minimum le dépistage d'anticorps anti-Treponema palladium par le VDRL ou RPR sur toutes les unités de sang provenant de dons avant la transfusion. La mise en œuvre du principe général de la qualité dans le dépistage des infections tranmissibles par tsransfusion, y compris la syphilis, est un facteur déterminant de la sécurité des transfusions sanguines.

Méthodes: Quarante-huit établissements de santé ont été recrutés pour l'étude entre Janvier et Juin 2018. Un questionnaire structuré auto-administré, des interactions physiques et des appels téléphoniques ont été utilisés pour recueillir toutes les données pertinentes sur le système de la qualité, les types de donneurs de sang, le nombre total d'unités de sang dépistées et le taux de réactivité aux tests de dépistage de la syphilis.

Résultats: Une méthode de laboratoire de recherche sur les maladies vénériennes a été utilisée pour dépister tous les dons pour la syphilis dans 81,3% des installations dépistées.Vingt-sept des 39 établissements qui dépistaient la syphilis ont validé leurs kits ; 24 disposaient de procédures opératoires standardisées et d'un système de contrôle de la qualité, tandis que 33 et 6 établissements avaient acheté des réactifs pour le dépistage de la syphilis par l'intermédiaire des directions et des services hospitaliers. Au total, 98 478 unités de sang ont été collectées et testées pour la syphilis. Sur les 831 échantillons trouvés réactifs, 405, 408 et 18 provenaient d'hôpitaux tertiaires, secondaires et privés respectivement, et 384, 381 et 66 des échantillons provenaient respectivement

principles that conform to National and Africa Society for Blood Transfusion guidelines. Syphilis sero-prevalence of 0.84% was recorded in this study.

de donneurs de remplacement familial, de donneurs de sang payés et de donneurs volontaires.

Conclusion La majorité des établissements dépistaient la syphilis en utilisant une méthode non spécifique et la plupart des principes de qualité généraux employés étaient conformes aux directives de la AfSBT. Une prévalence de 0.84% pour la syphilis a été enregistrée dans cette étude.

INTRODUCTION

Safety of blood and blood products for transfusions has being a concern globally and particularly for African countries. The HIV/AIDS pandemic has awaken attention on the importance of preventing transfusion-transmitted infections (TTIs). Up to 3% of HIV infections worldwide are transmitted through transfusions of contaminated blood and blood products. Many more recipients of blood products may have been infected by hepatitis B and C viruses, syphilis and other infectious agents. The global burden of diseases due to unsafe blood transfusions can be eliminated or substantially reduced through several integrated strategies for blood safety.[1]

Appropriate recruitment and selection of blood donors together with pertinent and precise laboratory screening for TTIs are major determinants of blood safety. WHO recommends screening tests for TTIs including syphilis to be done according to the quality system requirements.[2] Immunological test for syphilis is part of the mandatory recommended tests for blood donors in Nigeria.[3] Screening for syphilis is used as either a surrogate of viral TTI which are regularly transmitted sexually in the general population or, to actually prevent transfusion of *Treponema pallidum*-contaminated blood and blood products[4]. The serological tests that are available for blood donor screening may detect antibodies against treponema antigens (specific) such as Treponema Pallidum Haemaglutination Assay (TPHA) and Treponema Pallidum Particle Agglutination Assay (TPPA) or non-treponema antigens (non-specific) such as Venereal Disease Research Laboratory (VDRL) and Rapid Plasma Reagin (RPR). Those that are *T. pallidum*-specific require infrastructure that may not be available in some laboratories in remote areas of some African countries and, therefore, rapid, non-specific methods are used. Both non-specific and specific assays detect antibodies but not the infectious treponemes. Rapid non-specific tests have also been reported to be highly sensitive and specific.[5] The WHO reported sensitivities of 84.5-97.7% and specificities of 92.8-98% for eight syphilis rapid screening tests (VDRL inclusive) when compared to the TPHA/TPPA reference standard.[6,7] Rapid non-specific syphilis tests have advantages of minimal cost, minimal training and equipment requirements and results availability within 15-20 minutes.

Because of the serious implications of screening tests, blood transfusion services need to eliminate potentials for false positive or false negative results. Application of quality principles like standard operating procedures, adequate in-laboratory quality controls, correct reagents storage, handling and application, training laboratory personnel and avoidance of clerical errors are measures that contribute to correct screening results.

Screening for syphilis as recommended by WHO has been questioned by so many authors.[8] This is because of the belief that *Treponema pallidum* does not survive the cold storage temperature of blood bank (2-6^{O}C) and many syphilis antibodies found in most donors are as a result of previous infections or an unspecific reaction.[9] This theory may not be applicable in developing countries where blood bank storage temperature can hardly be maintained and also because transfusion of Fresh Whole Blood (FWB) units has completely replaced transfusion of platelets concentrate and Fresh Frozen Plasma due to lack of facilities to prepare these blood products.[10] To compound the problem, family replacement (FRDs) and paid blood donors (PDs) constitute 75-80% of blood donors in developing countries, Nigeria inclusive.[11]

Studies done locally and internationally, have indicated varying prevalence levels for syphilis among healthy blood donors.[12,13] The prevalence was reported to be as low as 0.1%[14] and as high as 3.6%[15] among blood donors in Nigeria, hence the need for routine screening for syphilis among blood donors. The last case of syphilis acquisition through blood and blood products transfusion in the developed world was in the United State in 1966[16] while the developing world still battles with the scourge.[3]

In Nigeria as in other developing countries, hospital-based blood transfusion services still predominate where blood for transfusions are collected from all types of blood donors. The largest percentage of these blood donors in Nigeria are FRDs and PDs,[11,17,18] despite reported higher syphilis sero-prevalence among FRDs[19]. This contrast with what obtains in centralized blood transfusion services where voluntary non-remunerated blood donors (VNRDs) predominate. Also in hospital-based transfusion services, equipment and reagents are procured by individual hospitals based on their availability and affordability as against central or regional procurement recommended by WHO for its cost effectiveness and safety. There

is a strong but unsubstantiated believe that screening for syphilis in Nigeria may be poorly regulated and may lack general quality principles.

It was in the light of these that we decided to study the mode of screening for syphilis in our health facilities in all the six geo-political regions of the country with a view to assessing our compliance with Nigerian National Blood Transfusion Service (NBTS) guidelines [20] and Africa Society for Blood Transfusion (AfSBT) Step-Wise Accreditation Standard[21]. National syphilis sero-reactivity amongst blood donors was also determined.

METHODOLOGY

Study Location:
Health care facilities (HCF) that are involved in blood transfusion services in all the six geo-political regions of the country were selected for this study.

Study Population:
The Heads of Department (HOD) of Haematology and/or the Chief Medical Laboratory Scientists of the selected blood banks.

Study Size:
Forty-eight HCFs completed the questionnaires and responded to telephone calls within the study period of 6 months and were recruited for the study. This included 18 tertiary HCFs, 18 secondary HCFs and 12 private HCFs. Tertiary HCFs comprises of Teaching Hospitals and Federal Medical Centers, while secondary HCFs are State government owned General Hospitals.

Inclusion Criteria:
Health Care Facilities that were involved in the collection, processing and transfusion of blood and blood products.

Exclusion Criteria:
Health Care Facilities that rely wholly on NBTS for supply of blood and blood products for transfusions and those that did not give consents.

Methods:
A self-administered and structured questionnaire, physical interactions and telephone calls to the aforementioned study population were employed to collect all relevant data which included kit validation, existence of standard operating procedures, use of quality control programs and methods of reagent procurement as proxy indicators of global best practice, methodologies used for syphilis screening and laboratory results among blood donors. Most of the target population was approached at national conferences and meetings. Communications through telephone calls and sending the questionnaire through e-mail, which were cost effective, were also employed to get all the data where the target population was not met at conferences and meetings.

Data Analysis:
This was done using Software Package for Social Sciences version 20. Results were presented as proportions and analyzed by Chi square tests. Level of significance was set at $p \leq 0.05$.

Funding: This study was funded by the researchers.

RESULTS

Forty-eight HCFs, 18 each of tertiary and secondary and 12 private HCFs participated in the study, out of which, 39 (81.3%) screened for syphilis in all donated blood units. Twenty-seven (69.2%) [12 each of tertiary and secondary and 3 private] of the 39 facilities that screened for syphilis validated their test kits. Twenty-four (61.5%) [12 tertiary, 9 secondary and 3 private] of the 39 facilities had written Standard Operating Procedures (SOPs). Twenty-four (61.5%) [9 tertiary, 12 secondary and 3 private] of the facilities had quality control. Thirty-three (84.6%) [12 tertiary, 9 secondary and 12 private] of the health facilities procured syphilis screening reagents through hospital management, while 6 [secondary health facilities] procured reagents through their departments. All the blood units collected were screened using non-specific (Venereal Disease Reference Laboratory) syphilis screening method, **Table 1**.

A total of 98 478 blood units were collected and screened for in the study period. Tertiary HCFs collected the largest number, 56 061 (56.9%), followed by secondary, 41,133 (41.8%) and private, 1 284 (1.3%). Family replacement blood donors constituted the largest percentage of all blood donors in all the facilities 84%, followed by VNRDs, 14.6% and PDs, 1.4%. A total of 831 samples (0.84%) were reactive to syphilis, of which 405 (0.72%), 408 (0.99%) and 18 (1.4%) were obtained from tertiary, secondary and private HCFs respectively, **Table 2**.

Of the 831 samples that were found reactive to syphilis, 384 (46.2%), 381 (45.8%) and 66 (7.9%) were from FRDs, PDs and VNRDs respectively. Overall sero-reactivity was higher amongst PDs (28.8%) than FRDs (0.46%) and VNRDs (0.46%). Sero-reactivity was significantly higher amongst PDs (33.7%) at tertiary compared with that of private (2.9%) HCFs, $p<0.05$. Significantly higher sero-reactivity was also noticed amongst FRDs at private (1.12%) and secondary (0.98%) than in tertiary HCFs (0.05%), $p<0.05$. Likewise sero-reactivity was significantly less amongst VNRDs at tertiary (0.10) than in secondary HCFs (1.0), $p<0.05$, **Table 3**.

Table 1. Result of Screening Survey for all HCFs.

		HCFs			
		Tertiary	**Secondary**	**Private**	**Total**
Screening Methods	VDRL RPR TPHA	12/66.7 - -	15/83.- - -	12/100 - -	39/81.3 - -
Facilities that validated test kits (n/%)		12/66.7	12/66.7	3/25	27/69.2
Facilities with written SOP (n/%)		12/66.7	9/50	3/25	27/69.2
Facilities with Quality Control Measures (n/%)		9/50	12/66.7	3/25	24/61.5
Methods of reagents procurement (n/%)	HOSP DEPT	12/66.7 0/0	9/50 6/33.3	12/100 0/0	33/84.6 6/7.7
Total samples screened with specific method		0/0	0/0	0/0	0/0
Total samples screened with non-specific method (VDRL) (n/%)		56 061/100	41 133/100	1 284/100	98 478/100

Abbreviations: HCFs (Health Care Facilities), VDRL (Venereal Disease Research Laboratory), RPR (Rapid Plasma Reagin), TPHA (Treponema Pallidum Haemagglutination Assay), HOS (Hospital), DEP (Department).

Table 2. Results of Syphilis Screening Survey 2017 for all HCFs.

		HCFs			
		Tertiary	**Secondary**	**Private**	**Total**
Number of sites studied		18	18	12	48
Number of sites that screened for syphilis (n/%)		12/66.7	15/83.3	12/100	39/81.3
Total samples screened.		56 061	41 133	1 284	98 478
Number of samples screened according to donor type (n/%)	VNBD FRD PD	8 952/16 45 996/82 1 113/2	5 448/13.2 35 685/86.8 0/0	0/0 1 074/83.6 210/16.4	14 400/14.6 82 755/84 1 323/1.4
Number of samples reactive to syphilis (n)		405	408	18	831
Sero-prevalence		0.72	0.99	1.4	0.84

Abbreviations: HCFs (Health Care Facilities), VNBD (Voluntary non remunerated blood donor), FRD (Family replacement donor), PBD (Paid blood donor), VDRL (Venereal Disease Research Laboratory).

Table 3. Comparing sero-reactivity of syphilis amongst types of blood donors and HCFs.

Facilities	VNBD				FRD				PD			
	TD	TR	Sero-P	p-value	TD	TR	Sero-P	p-value	TD	TR	Sero-P	p-value
Tertiary	8.952	9	0.10	<0.05	45.996	21	0.05	<0.05	1.113	375	33.7	<0.05
Secondary	5.448	57	1.0		35.685	351	0.98		0	0	0	
Private	0	0	0		1.074	12	1.12		210	6	2.9	
Total	14.400	66	0.46		82.755	384	0.46		1.323	381	28.8	

Abbreviations: HCFs (Health Care Facilities), VNBD (Voluntary Non-remunerated Blood Donor), FRD (Family Replacement Donor), PD (Paid Donor), TD (Total units donated), TR (Total units found reactive), Sero-P (Sero-prevalence).

DISCUSSION

Blood transfusion practice still appears poorly regulated in Nigeria, despite establishment of NBTS since 2004. Presently there are seventeen NBTS Centers in Nigeria, with headquarter/ demonstration center at Abuja. The center supplies safe blood and blood products to all HCFs in the country. It also has policy and guidelines for blood transfusion practice in Nigeria. At the centers, testing for antibodies to HIV I and II, Hepatitis B surface antigen (HBsAg), antibodies to Hepatitis C virus, immunological VDRL tests for syphilis and p24 HIV antigens are performed using Enzyme Linked Immuno-sorbent Assay method with all the quality principles in place according to WHO recommendations.

Unfortunately, because the demand for blood and blood products out-stripped supply from NBTS, most health facilities still operate hospital-based blood transfusion service where equipment and reagents are procured by individual hospitals based on their availability and affordability as against central or regional procurement recommended by WHO for its cost effectiveness and safety. Hence screening for syphilis in particular and other transfusion transmissible infections may be compromised and in actual fact it is erroneously perceived as being poorly regulated with no internal and external quality control measures.

Our study revealed that most HCFs (more than two thirds) validated their test kits before being used, have Standard Operating Procedures and have both internal and external quality control measures as recommended by WHO[2] and all employed VDRL screening method. Most of the facilities in this study, 84.6%, procured syphilis screening reagent centrally through Laboratory Revolving Fund of the hospitals. Although this is not as acceptable as national or regional procurement, it is better than procurement by individual or by the departments.

A low syphilis sero-reactivity of 0.84% was recorded in this study which is similar to the findings of other researchers in Nigeria[13,14]. Although all facilities that screened for syphilis in this study used *T. pallidum*-nonspecific screening method, VDRL, it is in keeping with AfSBT recommendations.[21] Africa Society for Blood Transfusion requires a minimum of antibodies to *T. pallidum* or VDRL or RPR test and that non reactive blood donor to non-specific screening method could be considered negative for syphilis infection and the donation be released for transfusion provided it meets all other requirements. Overall syphilis sero-reactivity was highest amongst PDs in tertiary HCFs. This is not unexpected as most PDs are found in tertiary facilities. Family replacement blood donors and VNRDs have the same overall sero-reactivity but lower than that of PDs in this study in contrast with the findings of previous studies that indicated higher sero-prevalence amongst FRDs.[19,22-24]

CONCLUSION

Majority of the facilities studied screened for syphilis using *T. pallidum*-non specific, VDRL screening method. Also most of the facilities conformed to the standard by Nigerian NBTS and AfSBT in terms of test kits validation, use of Standard Operating Procedures, quality control measures and central method of reagents procurement. Low syphilis sero-reactivity was recorded in this study despite widespread practice of hospital-based blood transfusion service. Blood transfusion safety in Nigeria can be improved further if all HCFs adopt centralized blood transfusion service.

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