Original Article

Towards 2030 Target for Hepatitis B and C Viruses Elimination: Assessing the Validity of Predonation Rapid Diagnostic Tests versus Enzyme-linked Immunosorbent Assay in State Hospitals in Kaduna, Nigeria

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Abstract

Introduction: Sub-Saharan Africa accounts for 25% of the estimated global 325 million people with chronic hepatitis B and C virus infections. Weak blood transfusion systems facilitate the spread of both hepatitis B and C virus infections. This is worsened by the absence of sustainable quality assurance programs and perennial shortage of sensitive screening kits. We aim to compare the validity of rapid diagnostic tests (RDTs) with the World Health Organization-recommended quality-assured enzyme-linked immunosorbent assay (ELISA) screening method for these viruses. **Materials and Methods:** We conducted a cross-sectional study on consecutive blood donor samples. Two hundred and sixty-four blood donor samples screened for hepatitis B and C viruses using RDTs were retested at a National blood transfusion service, Kaduna, Nigeria. Data were analyzed using OpenEpi version 3.01 to determine the sensitivity, specificity, and predictive values of RDTs versus ELISA. **Results:** The sensitivities of the RDTs at 95% confidence interval (CI) were low – 40% (19.8–64.3) and 50.0% (18.8–81.2) – for hepatitis B surface antigen (HBsAg) and hepatitis C virus (HCV) antibody, respectively. The specificities and 95% CI were high – 99.9% (97.8–99.9) and 100.0% (98.5–100) for HBsAg and HCV antibody, respectively. **Conclusion:** Predonation RDTs screening of blood donor samples for hepatitis B virus and HCV in hospital donation units performed poorly compared to quality-assured ELISA screening in Kaduna. The risk of transmitting viral hepatitis through blood transfusion still exists. We recommend quality-assured ELISA screening of all donated units for HBsAg and HCV antibody to reduce the risk of these transfusion-transmitted infections.

Keywords: Blood donors, hepatitis B and C virus, rapid diagnostic tests, validity

Introduction

Africa has keyed into the global strategy for eradication of both hepatitis B and hepatitis C virus (HCV) infections by the year 2030.[1] However, transfusion-transmissible viral hepatitis has posed a significant obstacle to achieving this target. Therefore, the elimination of viral hepatitis in rests on harmonizing other strategies with minimizing transfusion transmissible hepatitis, especially in resource-poor countries where the provision of safe blood is still a major challenge.

The introduction of hepatitis B vaccine in routine immunization is reducing the incident of hepatitis B in under-five children; however, chronic infection still exists in about 257 million mainly adults born before the introduction of this strategy.[1]

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Recent data from the World Health Organization (WHO) revealed that 25% of 325 million persons living with chronic hepatitis B virus (HBV) and HCV are in Sub-Saharan Africa.[2] The natural history of hepatitis was altered by the development of agents that either cure the infection or suppress viral replication for the long-term preservation of quality of life. Treatment failure has been reported for hepatitis C due to the emergence

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of drug resistance and the suboptimal activities of antiviral agents.[3] Unfortunately, these drugs are not readily affordable to the vast majority of people in sub-Saharan Africa making their clinical utility difficult. Thus, the risk still exists for disease progression to chronic liver disease, including hepatocellular carcinoma with attendant morbidity and mortality.[4,5] Spread of both viruses in blood and blood products is facilitated by the high prevalence and weak blood transfusion programs. Studies have shown a higher prevalence of HBV and HCV infections among multiply transfused patients with conditions such as sickle cell disease.[6,7] Several methods have been deployed to screen donated blood or blood components to mitigate the risk of transfusing bloodborne pathogens and these include rapid diagnostic tests (RDTs), enzyme-linked immunosorbent assay (ELISA), and nucleic acid test (NAT).[8] The effectiveness of these tests at detecting viral markers depends on the length of the window period of the infectious agent.[9] The window period is the time interval from infection to detection of serological or nucleic material by serological or NAT assays, respectively.[10] Infrastructural challenges alongside the absence of quality-assured methods are limitations in the battle against transfusion transmissible hepatitis B and C viruses in Nigeria. Although ELISA and NAT are the recommended screening tests, most hospital blood transfusion units in resource-poor countries lack the capacity and resources to apply them and thus resort to the use of RDTs although poor-quality assurance measures.[11,12] We aim to assess the validity of RDTs against the WHO recommended quality-assured ELISA screening method for transfusion-transmissible infections in secondary health facilities in Kaduna metropolis, Northwest Nigeria, in the era of global strategy to eradicate hepatitis B and C infections.

Materials and Methods

Study area

The study was carried out at blood donation centers of three State Government Hospitals in Kaduna metropolis from January 2016 to March 2016.

Study design and sampling technique

This was a cross-sectional study of consecutive replacement blood donor samples irrespective of the screening outcomes with RDTs at the donors' units.

Laboratory methods

Predonation screening for hepatitis B surface antigen (HBsAg) and HCV antibody of donor blood samples was carried out using RDTs (Skytec® HBsAg and Skytec® anti-HCV test strips by Skytec Diagnostics) at the selected blood donation units. Plasma from each of the blood sample was separated into well-labeled sample bottles and stored at −20°C. They were transported in cold boxes to the National Blood Transfusion Service (NBTS), Northwest zonal center in Kaduna, for retesting based on the principle of sandwich ELISA with Monolisa HBsAg ULTRA® by BIO-RAD and HCV Ab® by DIA. PRO Diagnostic (Marnes-la-Coquette - France). Data obtained were analyzed using OpenEpi version 3.01 (Sesto San Giovanni (Milano) – Italy).

Ethical considerations

Ethical approval was granted by the Kaduna State Ethical Review Committee to conduct this research. In addition, approval was obtained from the authorities of the three hospitals that were selected for the study. Informed consents were obtained from the participants to carry out further screening on their blood samples. The cost of further screening was bored by me with support from the Nigeria Field Epidemiology and Laboratory Training Programme.

Results

All the 264 samples were tested for HBsAg and HCV antibody using RDT (Skytec® HBsAg and Skytec® anti-HCV) as part of the routine screening of blood donors at the facilities. Seven samples were reactive for HBsAg with RDT, but one was false-positive after retesting the 264 samples at the NBTS using ELISA (Monolisa HBsAg Ultra by BIO-RAD®). However, 15 samples were reactive for HBsAg with ELISA. This indicates that nine reactive samples were missed (false-negative) by RDT [Table 1]. Similarly, of the 264 samples, three were reactive for HCV using RDT (Skytec® anti-HCV) while ELISA (DIA. PRO HCV Ab) detected six; the RDT failing to detect three reactive samples [Table 2]. Table 3 shows the calculated sensitivity, specificity, positive predictive value (PPV), and negative predictive value at 95% confidence intervals of RDTs.

Discussion

In this study, we found sensitivity and specificity with Bio-rad® HBsAg having values of (40.0% and 99.6%) and DIA. PRO® HCV Ab (50.0% and 100.0%), respectively. These sensitivities

Table 1: Diagnostic accuracy of predonation rapid diagnostic tests compared to enzyme-linked immunosorbent assay screening for hepatitis B virus

RDT (Skytec® HBsAg)	ELISA Monolisa HBsAg Ultra (BIO-RAD)		Total
	Reactive	Nonreactive	
Reactive	6	1	7
Nonreactive	9	248	257
Total	15	249	264

RDT – Rapid diagnostic tests; ELISA – Enzyme-linked immunosorbent assay; HBsAg – Hepatitis B surface antigen

Table 2: Diagnostic accuracy of rapid diagnostic tests compared to enzyme-linked immunosorbent assay in screening for hepatitis C virus

RDT (Skytec anti-HCV)	ELISA (DIA.PRO HCV Ab)		Total
	Reactive	Nonreactive	
Reactive	3	0	3
Nonreactive	3	258	261
Total	6	258	264

RDT – Rapid diagnostic tests; ELISA – Enzyme-linked immunosorbent assay; HCV – Hepatitis C virus

Table 3: Validity of rapid diagnostic tests compared to enzyme-linked immunosorbent assay in the screening of blood donor samples for hepatitis B and hepatitis C viruses in Kaduna, Nigeria (*n*=264)

Parameters	HBV (%)	HCV (%)
ELISA positive	15 (5.7)	6 (2.3)
False-negative by RDT	9 (60.0)	3 (50.0)
ELISA negative	249 (94.3)	258 (97.7)
False-positive by RDT	1 (0.4)	0 (0.0)
Sensitivity of RDT	19.8-64.3 (40.0)	18.8-81.2 (50.0)
Specificity of RDT	97.8-99.9 (99.9)	98.5-100 (100.0)
PPV of RDT	48.7-97.4 (85.7)	43.9-100 (100.0)
NPV of RDT	93.2-97.9 (96.5)	96.7-99.6 (98.9)

RDT – Rapid diagnostic tests; ELISA – Enzyme-linked immunosorbent assay; HCV – Hepatitis C virus; HBV – Hepatitis B virus; PPV – Positive predictive value; NPV – Negative predictive value

are below the sensitivity level of at least 99.5% recommended for any assay to be used for blood screening.[13] These findings are consistent with earlier studies in Nigeria. Orkuma *et al*.[14] reported low sensitivity of RDTs in the screening of blood donors for HIV in northcentral Nigeria, whereas Erhabor *et al*.[15] working on HBsAg screening using RDTs among blood donors found a similar sensitivity. Studies in India[16,17] also showed a low sensitivity compared to ELISA. In a developing country like Nigeria, where hospital blood transfusion units greatly rely on replacement blood donors, and to some extent, commercial blood donation, coupled with a high prevalence of transfusion-transmitted infections (TTIs), the need for quality blood screening as an effective strategy to reduce TTIs, including hepatitis cannot be overemphasized. The WHO-recommended quality-assured screening of donated blood for TTIs with ELISA screening as the minimum benchmark due to their better validity and thus better outcome compared to RDTs for blood screening and their manufacturer more reliable.[13]

Despite the drawbacks of RDTs, they often remain convenient methods for predonation screening of blood donors in resource-limited settings. During the conduct of this research, all the state government-owned hospitals were using RDTs for predonation TTIs screening of prospective blood donors. The most important factor that determines the use of RDTs rather than ELISA or nucleic acid testing in the screening of donated blood for TTIs is the resources available at the testing site; and this includes cost, infrastructure, skilled personnel, and the ease of use.[8,18]

Reasons put forward for the low sensitivity of the RDTs range from poor compliance with the WHO manufacturing standards, rather long window periods to a demand for high antigen or antibody required to match the low detection rates.[17-19] Other studies have shown that certain mutants of these viruses are not readily detected by some conventional RDTs in use, hence, the need for validation of all rapid tests to meet the local standard before they are deemed suitable as screening assays.[8,18] The implication of low sensitivity of RDTs is that the kits will be unable to detect the presence of TTIs; these false-negative results pose a threat of transmission of viral hepatitis through blood transfusion in Kaduna State. Therefore, in resource-poor setting where ELISA is unavailable, practice of using rapid kits for blood banks may lead to spread of the pathogens due to residual infectious risk.

In this study, interestingly, we observed a high specificity which was 99.6% for HBsAg RDT and 100% for HCV antibody RDT and varying PPVs. This study, unlike others,[8,17] produced one false-positive result for HBV and none for HCV. Thus, where predonation screening is practiced, false-positive results will lead to wrongful permanent deferral of potential blood donors, consequently of decreasing blood availability. In addition, false-positive potential donors are referred for sensitive and expensive investigations, which is a burden on the health-care system. There is also the psychological burden on the person; that is, the anxiety and worry induced as a result of the person been told of a positive result.

This study has some limitations. First, using ELISA as a gold standard could have reduced the validity of the study. False-positive results have been reported with the 4th-generation ELISA due to its high sensitivity,[20] requiring confirmation with nucleic acid testing. To mitigate this, the ELISA screening was carried out by experienced personnel using quality-assured protocol with positive and negative quality controls included during the test running. Second, the study was carried out among blood donor population, with the outcome of the screening showing much more negative results. This could affect the validity of the test.

Conclusion

Our study has shown that predonation RDT screening of blood donors for HBV and HCV in hospital blood donation units performed poorly compared to quality-assured ELISA screening in Kaduna. The risk of transmitting hepatitis through blood transfusion still exists. The health authorities in Kaduna State need to urgently introduce quality-assured ELISA screening of donated blood for hepatitis B and C viral infections to reduce the risk of their transmission through blood transfusion.

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Conflicts of interest

There are no conflicts of interest.

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