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ORIGINAL ARTICLE

The prevalence of antibodies to Hepatitis B core antigen among blood donors in a tertiary institution in Nairobi County, Kenya

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ABSTRACT

Background: Infections linked to blood transfusion or tissue transplants prove to be a major challenge globally because of the serological window period (WP) and a latent stage exhibited by most viral infections. The objective of this study was to determine the prevalence of anti-HBc antibodies in HBsAg negative donors at Aga Khan University Hospital Nairobi.
Methods: The current project was a cross-sectional study in which 76 donor samples that tested negative for HBsAg marker were reevaluated with an anti-HBc ELIA kit (Elecsys reagent kit) following Cobas 601(Roche, Stuttgart, Germany) machine operation manual. Anti-HBc positive samples were confirmed for positivity using polymerase chain reaction (PCR). Donor demography and risk factors such as age; gender, marital status, employment status, and donor type were reviewed and documented from the archived questionnaires.
Results: In total, 76 archived samples were screened during the period of the study. The study population had an average age of 32 ± 8 years which male donors dominating at n=61 (79.2 %) and female n=16 (20.8 %). The prevalence rate of anti-HBc Total was 13 % during the period of the study. On further analysis of the 10 anti-HBc positive samples with PCR, there was no detectable HBV-DNA. The majority (63.6 %) of Anti-HBc positive cases were first-time donors and blood donors aged between 25–45 years being the majority.
Conclusions: The introduction of anti-HBc as a routine screening tool is recommended to all potential blood donors and even in other medical procedures such as dialysis. These support the need for a duo approach when screening potential donors to rule out occult infection.

Key words: Antibodies, Hepatitis B virus, anti-Hepatitis B core total, Transfusion, Blood donor, Window period

INTRODUCTION

Transfusion of blood and tissue transplants is one of the channels in which disease causing pathogens to get transmitted to the blood or tissue recipients if the donors were not screened for infectious diseases[1]. Hepatitis B virus infection is characterized by the detection of HBV-DNA, anti-HBc, anti-HBs, and HBsAg among other seromarkers, while seronegative is described by undetectability of both HBV-DNA, anti-HBc, HBsAg and anti-HBs[2]. Hepatitis B surface antigen (HBsAg) was the first marker introduced for the purpose of screening donor tissues for HBV infection since the early 1970s and is currently in use in most blood banks to date. Eventually, this sows a reduction in the number of post-transfusion HBV infection after a blood transfusion or tissue transplant[3].

Infections associated with blood transfusion or tissue transplant is still a global challenge in transfusion science and organ transplant[4,5]. Different modalities have been put in place all over the world to minimize the risk of transfusion-transmitted infections (TTIs)[6]. Some of these modalities include the use of voluntary blood donation, coming up with donor recruitment guidelines, incorporation of the quality control program in blood donor screening, and minimize blood usage by requesting clinicians[7].

A prevalence of 5.4 % anti-HBc (IgM) for instance was reported from donors with undetectable levels of HBsAg negative blood donors in a remote region of Nigeria posing a higher risk to blood recipients[8]. Immunoglobulins to hepatitis B virus core antigen (IgM) are detectable in individuals with acute hepatitis B virus (HBV) infection or with reactivation of disease in chronic carriers[9]. Total

hepatitis B core antibodies (anti-HBc IgM and IgG) immunoglobulins, on the other hand, are detected in chronic HBV infection, individuals with the previous exposure, or in the acute stage of the infection[10]. A systematic review from various countries has shown that in 2017, about 1.1 million people were newly infected with chronic HBV infection globally[11,12]. This review reported a bigger difference in the total estimates of HBV prevalence across countries; this in itself explains the difference in risk levels and mode of transmission HBV across continents. Prevalence estimated at a regional level indicated a significant burden of infection in most of the Africa countries and some countries in the Western Pacific region in particular. These reviews highlighted a continuous need for prevention strategies on HBV transmission[13,14].

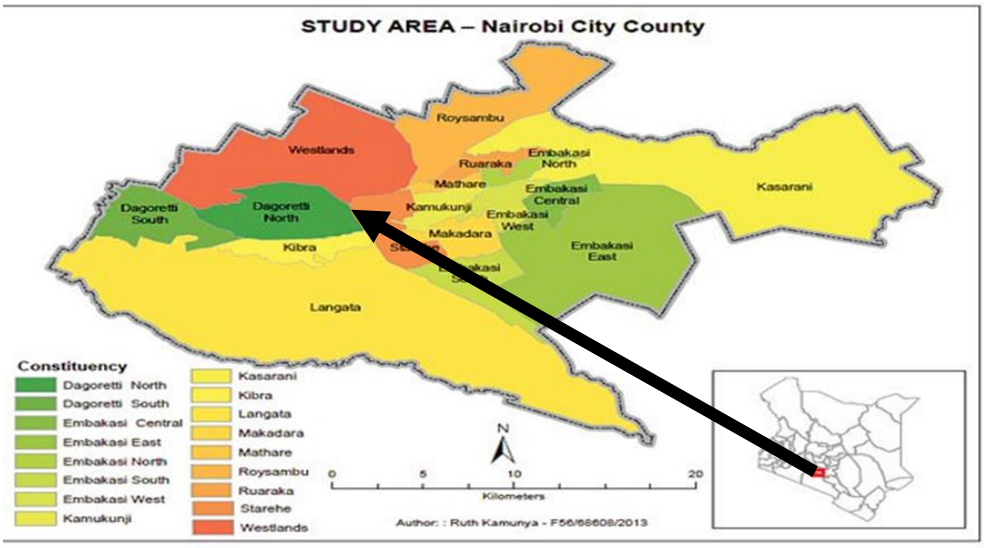
The hepatitis B virus and hepatitis C virus are the leading cause of infectious diseases that leads to higher mortality and morbidity in many communities, draining families financially and destroy economies of most countries which therefore has become a major global health burden[15]. In Sub-Saharan Africa for instance, 12.5% of recipients who receive blood transfusion are at greater risk of post-transfusion hepatitis infection[16,17]. In Kenya and other Sub Saharan Africa (SSA) countries, blood donated is screened for HIV 1 and 2, syphilis, Malaria parasite, hepatitis C virus (HCV) and HBV alone[18]. The only intervention to the prevention of transmission of HBV infection and other infectious diseases during blood transfusion is through blood screening[19]. Several scientific publications have reported the existence of HBV infection in individuals who tested
negative for HBsAg but having a detectable amount of HBV virion in their hepatic cells or blood circulation[20–24]. Some of these publications have reported HBV infections as a result of transfusion of blood screened and found to be HBsAg negative[25,26]. There is strong evidence that HBsAg-negative blood donation still poses a risk of inducing post-transfusional hepatitis in recipients[27,28]. With this uncertainty of HBV screening in mind, the purpose of this study was to determine the prevalence of seropositivity of anti-HBc among healthy Kenyan blood donors and highlight its risk in blood transfusion.

METHODS

Study area

The study was carried out in Nairobi County ***(Figure 1)*** at the Aga Khan University teaching hospital (AKUHN), Parklands Sub County. Aga Khan University Hospital, Nairobi is a private not-for-profit teaching hospital that provides tertiary and secondary level healthcare services to the vast population of Nairobi County. The University Hospital has been providing high-quality care for the people of East Africa and beyond for several years now. The laboratory has a transfusion service that includes a blood bank and apheresis. In this laboratory, blood is routinely screened for malaria, syphilis, HBV, HCV, and HIV. screening of HBV is routinely done by using HBsAg assay on the Architect 1000SR. Any positive results are then confirmed on the Roche Cobas e601 (Roche, Stuttgart, Germany). Any discrepant result between the two HBsAg assays is considered indeterminate. All pints with a positive or indeterminate result for any of the TTIs screened are usually discarded.

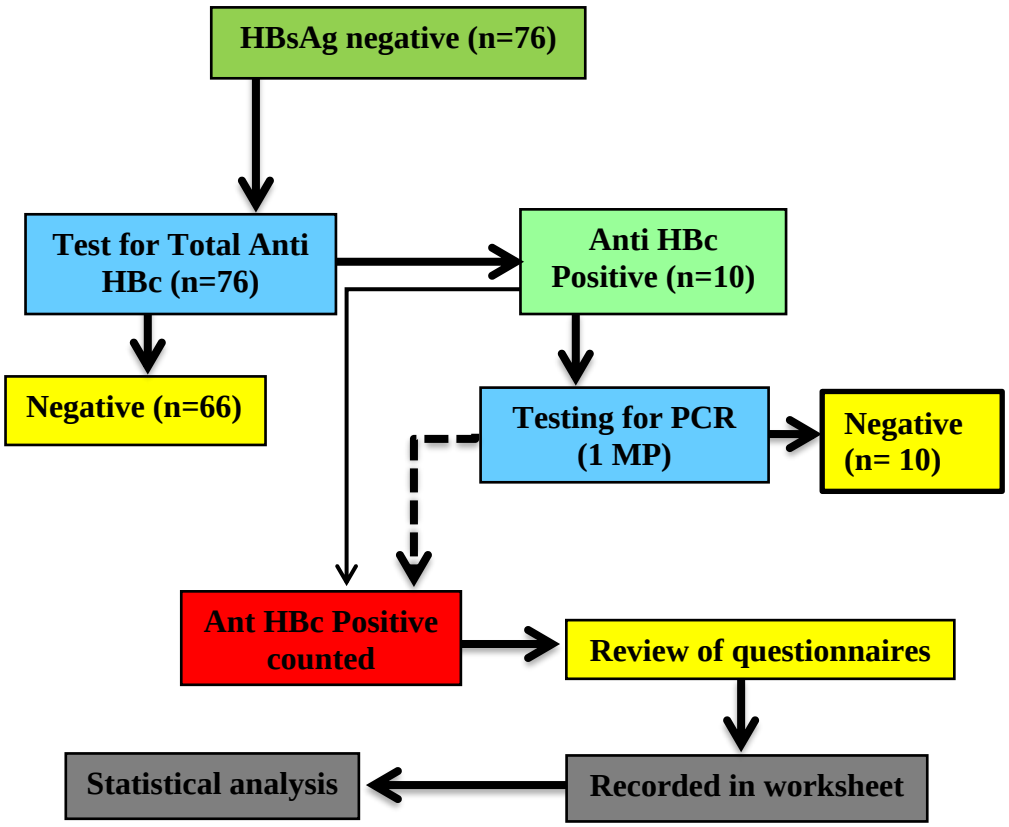
FIGURE 1. ***Study Area***



Study design

This was a laboratory-based cross-sectional study ***(Figure 2)*** design, where all serum samples screened for HBsAg during the initial blood testing of respective donors at the Aga Khan University hospital Nairobi donor unit were re-analyzed using anti-HBc Total as a marker for HBV. All samples that screened positive for Anti-HBc, plasma samples were obtained and aliquoted and were further screened by Polymerase Chain Reaction (PCR) to confirm anti-HBc positivity. Donor demography and risk factors such as age; gender, marital status, employment status, and history of blood transfusion for positive samples were reviewed by examining archived donor questionnaires stored at the donor unit.

FIGURE 2. ***Prevalence of antibodies to hepatitis B core antigen among blood donors in Nairobi City-County, Kenya***



Study population, Inclusion and Exclusion criteria

The study population included all archived samples from healthy blood donors that were initially recruited at the Aga Khan university hospital blood transfusion unit. All HBsAg negative samples collected between April 2019 to May 2019 were eligible for the study. On average, the blood bank receives 300 donors per month thus we were able to achieve the desired sample size within the specified period. All HBsAg negative blood archived samples with no signs of deterioration were included in the study. However, samples that were found to be positive for HBsAg and that showed visible deterioration were excluded from this study.

Sample Size

The minimum sample size (n= 76) was determined using the Cochran formula[29] required to

allow for adequate statistical power: $n = \frac{z^2pq}{e^2}$

where z is 1.96 at 95% confidence interval; e^2 the level of desired precision (0.05); p is prevalence of occult hepatitis B infection (0.6%)[30]; q is (1-p).

Sampling procedure

Seventy-seven serum archived samples negative for HBsAg were purposively sampled for three weeks and reanalyzed for hepatitis B virus core immunoglobulins using ELIA kit (Elecsys reagent kit) following Cobas 601(Roche, Stuttgart, Germany) machine operation manual. Plasma samples for

the positive anti-HBc total were obtained from the respective donor pack, aliquoted in 1.8 ml vials and stored at -20 ^{0}C till they were analyzed. The corresponding blood questionnaires were retrieved from the blood bank storage archives. Donor demography and risk factors such as age; gender, marital status, employment status, and donor type were reviewed and documented from the archived questionnaires.

Testing for Anti-HBc

Hepatitis B core antibodies Total were analyzed using a commercial kit (Elecsys, Stuttgart, Germany) by following the manufacturer's instructions for Cobas 601.[31] At the main laboratory, the samples were allowed to attain room temperature before analysis using the immunoassay technique on Cobas 601(Roche, Stuttgart, Germany) following a written and approved SOP. Before processing, the selected samples were provided with a unique code for easier identification. The results were entered on a laboratory sheet bearing the unique code for the sample. The report was either read reactive for anti-HBc Total or non-reactive for anti-HBc Total.

Ethical consideration

Because the study was dealing with archived samples no consent was sort from the donors, but an approval was granted by the AKU research ethical Committee (REC)- Ref: 2019/REC-27 (VL).

Data analysis

The data generated was cleaned and entered into an excel worksheet then analyzed using IBM SPSS version 20 (IBM Corporation, New York, USA). Chi-square was applied to determine if there was any association between donor socio-demographic characteristics, exposure to risk factors and antiHBc positivity. Where p <0.05 was of statistical significance. The prevalence of HBV was then calculated and expressed in percentage.

RESULTS

From the beginning of April 2019 to the end of May 2019, 76 we purposively selected blood donor archived samples and reevaluated them see if Total antiHBc was present. The study population had a mean age of 32 ± 8 years with the majority of the samples coming from the male donors at n=61 (79.2 %) and female n=16 (20.8 %) ***(Table 1)***. At the conclusion of the study, the prevalence rate of anti-HBc Total was 10/76 (13 %) ***(Figure 3)***. We further analyzed the 10 anti-HBc positive samples with PCR to confirm the seropositivity, there was no detectable HBV-DNA in the positive samples. We also noted that the majority (63.6 %) of Anti-HBc positive cases were mostly first-time blood donors ***(Table 2)*** and aged between 25–45 years ***(Figure 4)***.

TABLE 1. ***Socio-demographic characteristics of 76 hepatitis B surface antigen negative blood donors***

Characteristics		Frequencies (n)	Percentages (%)
Age(years)	16-24 yrs.	12	15.6
	25-45 yrs.	58	75.3
	46-55 yrs.	6	7.8
	56-65 yrs.	1	1.3
Sex	Male	61	79.2
	Female	16	20.8
Marital status	Single	35	45.5
	Married	41	53.2
	Widowed	1	1.3
Employment	Self-employed	54	70.1
	Employed	15	19.5
	Unemployed	8	10.4
Type of donor	First time donor	40	51.9
	Repeat Donor	31	40.3
	Regular Donor	6	7.8

FIGURE 3. ***Prevalence of anti-HBc Total in the study samples***

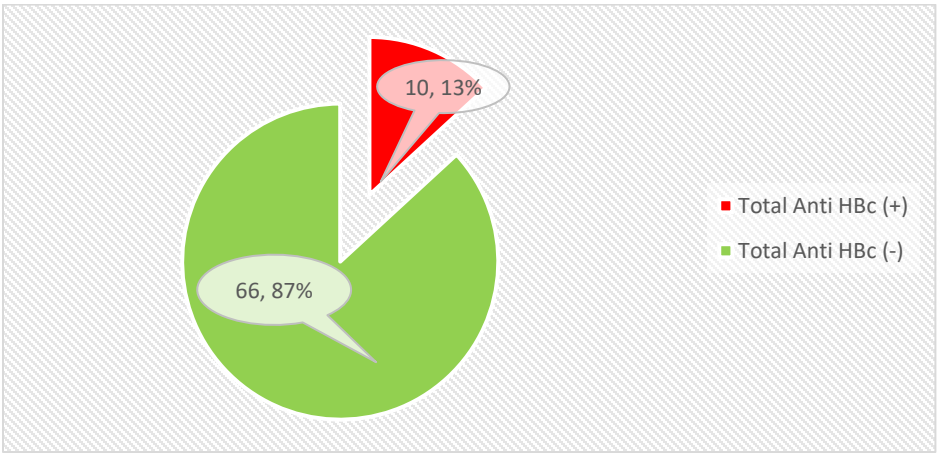


TABLE 2. Socio-demographic characteristics of 76 hepatitis B surface antigen negative blood donors

Characteristics	Exposed	Not exposed	X^2	P value
Age (years)				
16-24	2 (2.6 %)	10 (13.2%)	1.294	0.731
25-45	9 (11.8%)	49 (64.5%)		
46-55	0	6 (7.9%)		
56-65	0	1 (1.3%)		
Gender				
Male	10 (13.1%)	51 (67.1%)	1.065	0.301**
Female	1 (1.3%)	15 (19.7%)		
Marital status				
Single	6 (7.9%)	29 (38.2%)	6.920	0.031**
Married	4 (5.3%)	37 (48.7%)		
Widowed	1(1.3%)	0		
Employment				
Self-employed	9(11.8%)	45(59.2%)	0.982	0.612
Employed	1(1.3%)	14(18.4%)		
Unemployed	1(1.3%)	7(9.2%)		

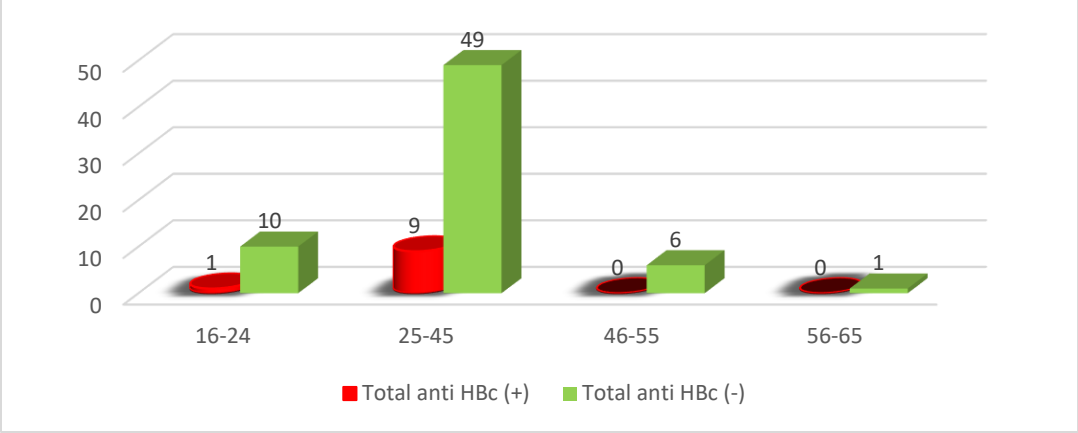
Prevalence of Anti-HBc in the Study Population

In total we analyzed 76 HBsAg negative samples on various during the study period. A total of *n*=10 samples were reactive for anti-HBc representing a 13% prevalence rate ***(Figure 3)***. The current picture indicates that apart from the study donors being negative for HBsAg, at one point they had exposure to the hepatitis B virus. These might present a donor with previous exposure or a donor who is recovering from hepatitis B infection. Such information is missed out if a donor is screened for HBsAg alone, a situation that endangers the respective blood recipient. The 87% represents individuals lacking the two serological markers (that is HBsAg and Total antiHBc), though this in itself does not rule out the existence of other HBV markers especially if the infection is in its initial stages.

Prevalence of Anti-HBc across age groups

The study also sorted to evaluate the distribution of anti-HBc marker among the blood donors. The results described in ***Figure 4*** shows that blood donors between the age of 25 to 45 had the highest reactivity to Total anti-Hbc at 11.7%. The other reactivity was seen between the age of 16-24 years at 2.6%. There were no cases reported in individuals above the age of 46 years.

Figure 4. ***Prevalence of anti-HBc Total in the study samples***



Characteristics of the Selected Archived Samples

A total of 76 archived samples at Aga Khan University Hospital in Nairobi County were selected into this study. The donor's socio-demographic characteristics are presented below.

Age of the Donors

The average age of the blood donors selected for the study samples was 32 *(SD* = 8; range 19-71) years. There were two age group peaks; of which 75.3 % of the donors were aged 25 to 45 years and 15.6 % were aged between 16 to 24 years. Other age categories included 7.8 % aged between 46 to 55 years (7.8%) and aged above 56 years (1.3%) being the list aged group ***(Table 1)***.

Gender of the Donors

In the current study, 61 (79.2%) were male donors while less than a quarter of 16 (20.8%) were female donors. Across all age groups, the majority of the participants were males. Among those aged 25-45 years' male was 44 (75.9%) while females were 14 (24.1%); those aged 16 to 24 years' male were 11 (91.7%) while females were 1 (9.3%). Among those aged 46 - 55 years (83; 69.7%) were females while (36; 30.3%) were males. For those aged 41 to 50 years 5(83.3%) were males while 1 (16.7%) were female. Those aged ≥ 55 years we had only 1 male as shown in ***Table 1***.

Occupation and Marital status of the donors

About 70.1 % of the donors were self-employment, 19.5 % were engaged either in formal or informal employment follow by 10 % donors who were students. Half of the donors (53.2%) were married, 45.5 % were single and only 1.3% widowed. Most of the donors in this study we self-employed and half of them were married ***(Table 1)***.

Risk Factors Associated with Occult Among Blood Donors

Table 2 summaries the socio-demographic characteristics of selected donors and the risk factors associated with anti-HBc positivity. Most of the donors were males 79.2 % and the female 16 % (X^2= 1.065, p = 0.301). we performed a statistical analysis to see if the was any association between the donor's socio-demographics and anti HBc seropositivity. On performing a Chi-square statistical analysis, there was no significant association between gender and anti-HBc positivity. However, this study showed that the male donors had the highest prevalence rate of 12.1 % (n=9) as compared to female donors with a prevalence rate of 1.3% (n=1).

Around 11.8 % of the anti HBc Total reactive donors were aged 25 to 45 years versus 1.3 % aged < 24 years (p = 0.731). Donors who were currently single (7.9%) were with the highest prevalence of anti-HBc Total, followed by the married donors at 5.3%. There was a significant difference between those who were single and married regarding anti-HBc positivity with a p value of 0.031. This was statistically significant, showing a strong association between marital status and anti-HBc reactivity. There was no association between donor's type (p = 0.500); age (p= 0.731), presence of a tattoo (p= 0.471); occupation (p= 0.621) and anti HBc positivity.

DISCUSSIONS

There is an increased risk of blood recipients getting infected with HBV from blood donors if blood screening is not done properly and the existence of occult hepatitis B infection in donors with HBsAg negative results. Therefore, these results show that the anti-HBc positivity was probably due to previous exposure that had resolved. Blood safety is among the major challenges encountered in blood transfusion practice today. As outlined in most blood transfusion guidelines HBsAg detection is the number one serological marker utilized for the detection of HBV in most blood transfusion centres in Kenya[32].The study also revealed that the selected samples were positive for total anti-HBc an indication that the donors had an initial exposure to HBV. However, this finding was found to be higher than the 4% described by Kisangau *et al*, in (october 2018) among the health care workers in Makueni county[33]. Similarly, it was also different to a 4.4 % prevalence rate as described in a study by Salawu *et al,* (2011) in Nigeria for anti-HBc among blood donors[34]. On a global comparison, the current study had a higher prevalence as compared to 6.3% and 8% in Saudi Arabia and Iran among potential blood donors respectively[35,36].

Nonetheless, other studies reported a higher prevalence. For instance, there was a higher prevalence rate of anti-HBc of 16.6% from Egyptian donors as described by Said *et al*, (2013).[37] Similar findings of 10.5% were reported by Lavanya *et al*, (2012) in India[38]. The distinguishing factors between this study and other studies that were done in other global regions could be attributed to varying levels of endemicity of HBV infection and differences in societal dynamics across geographical regions[39]. This lower endemicity seen in developed countries could be attributed to various factors which include; the geographical location, cultural practices regarding marriage, the availability of highly sensitive test kits, and stringent donor selection procedures, literacy levels among their population, voluntary donations, and differences in their level of civilization from the study settings[40]. The current study was carried out in a country that is still developing and facing a lot of societal issues that predispose individuals to be more vulnerable to hepatitis B infection.

In Kenya, the seroprevalence of anti-HBc is low as shown from this study in comparison to other African countries, and consequently, screening of donor blood for either anti-HBc IgM or total anti-HBc may be used in some circumstances especially if there is a historical suspicion of a donor being exposed. However, the lack of HBsAg detection as seen from the current study in itself does not guarantee blood safety because there is evidence of post-transfusion HBV infection in recipients who receive blood reactive for anti-HBc alone as reported by other researchers[41–43]. There is a compelling existence of HBV genome in blood donors reactive for only anti-HBc among the other viral markers from previous studies[44,45]. Therefore, screening for HBsAg does not rule out the possibility of HBV transmission, as the donor might be in the window phase, and detection of anti-HBc would serve as a convenient serologic marker during this period[46,47]. In Kenya, testing for HBsAg forms the initial laboratory diagnostic tool applied to confirm HBV infection in potential donors, but it does not give information on previous exposure to HBV[48]. In the current Kenya blood transfusion service (KBTS) guidelines, anti-HBc is not applied as a screening test for HBV. Therefore, as shown in this study, the safety of blood products and tissue organs should be a major priority in transfusion practice and organ transplants[49,50]. Hepatitis B surface antigen is the only diagnostic marker used in most blood transfusion centres in African countries including Kenya and it does not offer protection against HBV infection[51,17].

The current study findings have exhibited a significant association between anti-HBc positivity and some sociodemographic characteristics of the donors. There was a clear association of anti-HBc reactivity with factors such as marital status, type of donor, age and gender of the donors. From the current study people who were single were more likely to have been exposed to HBV as compared to the married or widowed an observation also reported by other authors[52]. Other studies have also reported a significant association between anti-HBc positivity with factors such as gender, age, educational level, intravenous drug use and men having sex with men activity[53,54]. From the current study, most of the positive samples were from individuals aged between 25-45 years of age. According to Alves *et al*., (2014) they showed that HBV infection was significantly associated with age between 25 and 50 years[55]. Therefore, the current research findings were in agreement with previous studies, which highlighted that middle age was associated with a higher risk of HBV exposure[56,57]. This may be because individuals in this age group are more sexually active and with a lot of risky social behaviours that expose them to HBV infection.

In this study, females were less likely to be anti-HBc positivity. A similar finding was also described by Antar *et al*., (2010) in Egypt showing that HBV infection was significantly associated with the male gender.[58] Being male was a factor for HBV exposure as reported in this study and similar finding has also been reported previously in other studies possibly due to high-risk social behaviours the makes them vulnerable to HBV infection[59]. History of using the drug of abuse and hypersexuality infection within this age bracket has been attributed to being male, and especially to those still single[60].

In this study, all the anti-HBc reactivity occurred among donors who reported not having involved themselves in risky social behaviour. This is in contradiction with other studies undertaken in southern Brazil in the years 2009 and 2010 pinpointed that tattooing, multiple sex partners, ear piercing and use of IDU increase the chance of one getting infected by HBV during adulthood[61]. Other factors that are associated with anti-HBc positivity that we either did not measure, included a history of hepatitis in the family of the donor, visiting barbershops and homosexual behaviour[62].

CONCLUSION

Following evidence of exposure to HBV infection, there is a significant chance of HBV transmission irrespective of a donor testing negative for HBsAg, and this is an important message for medical practitioners in deciding whether to transfuse blood or not. The introduction of anti-HBc as a routine screening tool is recommended to all potential blood donors and even in other medical procedures such as dialysis.

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Conflict of Interest

The authors declare no conflict of interest related to this study

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