



## Residual Risk of HBV in African Blood Banks: Systematic Review and Meta-Analysis

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### Authors' contributions

*This work was carried out in collaboration among all authors All authors read and approved the final manuscript.*

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## ABSTRACT

**Background:** Blood transfusions carry the risk of transmitting blood-borne infections. A precise estimate of the transfusion risk of viral infection will help to determine the effect of new and current safety measures in sub-Saharan Africa. This study proposes to estimate the residual risk of HBV in blood banks in African countries and to compare them to other countries in the South.

**Methods:** The study followed the Preferred Reporting Items for Systematic Reviews and Meta-Analysis guidelines. PubMed, Medline, Google Scholar and Zotero were accessed. The eligibility criteria were based on published studies that had blood donors as participants, looking at the residual risk of HBV in developing countries and the technique was based on the search for HBsAg or Hepatitis B Core Antibodies or Nucleic Acid (DNA) testing. The Cochrane tool was used to assess the risk of bias.

**Results:** Twelve articles comprising 71,207 allogeneic and hepatitis B surface antigen (HBsAg)-negative blood donations were included in the meta-analysis. A total of 4912 HBsAg negative African donation including (51.0%) new donors and (49.0%) from regular donors. 80.8% of them were male and the median age was 28 years. Of 1225 HBV strains (47% and 53.4% incident cases) were frequencies in sub-Saharan Africa and in other Southern countries respectively.

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Considering the twelve participating blood centres as a whole, the incidence rate of new infections was high (4905.1) in sub-Saharan Africa than (869.7) in other Southern countries per 100,000 person-years. In contrast, the estimated residual risk in sub-Saharan Africa (5913 in 1 million donations) was five times higher than estimated in other Southern countries (1048.4 in 1 million donations).

**Conclusion:** Blood donations with HBsAg undetectable by routine testing and low levels of HBV DNA are extremely common in sub-Saharan Africa, at a rate of 5913 per 1 million donations. Given that at least several of these samples could reflect contamination or a false negative result, elimination of infection by a test limited to HBsAg does not prevent transmission.

*Keywords: HBV; Blood transfusion; Residual risk; sub Saharan Africa.*

## ABBREVIATIONS

*HBV-DNA: Hepatitis B viral DNA*  
*HBsAg : Hepatitis B Surface Antigen*  
*Anti-HBc : Hepatitis B Core Antibodies*  
*PCR : Polymers Chain Reaction*  
*NAT : Nucleic Acid Testing*  
*OBI : Occult B Infection*

## 1. INTRODUCTION

The most important risks to recipients in industrialized countries are mainly volume overload, bacterial contamination and errors in transfusion of the blood product. In contrast, sub-Saharan Africa has high post-transfusion infection rates and high residual viral infection risk resulting in high prevalences of blood-borne diseases [1,2,3,4]. Transfusion transmitted infections are still a major global public health concern confronting worldwide [5].

Over the past 20 years, there has been a significant increase in the safety of the blood supply in wealthy countries marked by deferral of donors from at-risk donors, continuous improvement in serological screening tests and HBV DNA testing by viral genomic screening in mini-pool [6,7,8]. The risk of HBV transmission by blood transfusion in the United States is currently extremely low among recipients [9].

In developing countries outside Africa, nucleic acid testing for HBV blood screening has not been nationally implemented in any developing countries. A partial screening has been implemented and reported in China, India and Brazil among others [10,11,12].

In low-income and middle-income countries, particularly countries in sub-Saharan Africa, Hepatitis B virus residual risk remains the single most transmitted infectious pathogenic disease

passed on from blood donors to their recipients through transfusion. In Africa, the screening of blood donations for HBV was introduced in 2002, before which time screening was performed in only a few African Blood bank. Under these conditions, it is anticipated that HBV safety for recipients of a blood transfusion might remain compromised even after routine blood testing for HBsAg. Approximately 12.5% of HBV infections are due to blood donation in SSA [13,4,14,15].

It is important to introduce epidemiologic observatories in developing countries where high levels of viral diversity are generally observed.

This study proposes to estimate the residual risk of HBV in blood banks in African countries and to compare them to other countries in the South.

## 2. METHODS

### 2.1 Study Design

Our study is a systematic review with a meta-analysis of summary data from several studies available online. These studies focused on the residual risk of HBV in blood banks in sub-Saharan African and other Southern countries. The data for this study were retrieved from full-text or full-text articles and obtained by reading the articles that provided all the information necessary for this study. Relevant studies published from 1 January 2013 to 31 December 2018 reporting information on the residual risk of HBV in African and other Southern countries' blood banks were searched.

### 2.2 Research Strategy

A systematic manual search of Medline, Pubmed and Google Scholar databases for studies on residual HBV risk in sub-Saharan

African and other Southern countries. The search strategy was based on the use of the following literature search equations: « HBV OR residual risk OR blood donors OR HBsAg seronegative OR positive NAT », « HBV OR risk of transmission OR blood donors OR positive anti-HBc» and « Residual risk OR HBV OR blood transfusion OR negative HBsAg OR positive HBsAg OR Africa »

### 2.3 Selection Criteria

The preferred reporting elements for systematic reviews and meta-analyses (PRISMA) from the 2020 guidelines were used as a template for the report of this review [16]. Full-text articles including titles and abstracts were included in the review after independent analysis by two individuals from the research team. Any discrepancies in the analysis required a third

opinion to discriminate. Of the two thousand and four studies that were retrieved from the databases, only twelve met the eligibility criteria, namely published studies with blood donors as participants, with a risk focus on residual HBV risk and with a methodology based on the detection of HBsAg, ant-HBc and/or nucleic acid (HBV DNA). On the other hand, for the non-inclusion criteria, one thousand nine hundred and ninety-two articles were excluded for multiple reasons, namely, studies with a small size of fewer than one hundred participants, studies with a duration of more than 10 years were excluded, studies that did not include all the keywords, studies with non-exploitable results and other reasons that did not allow us to associate these studies with our meta-analysis study (Fig. 1).

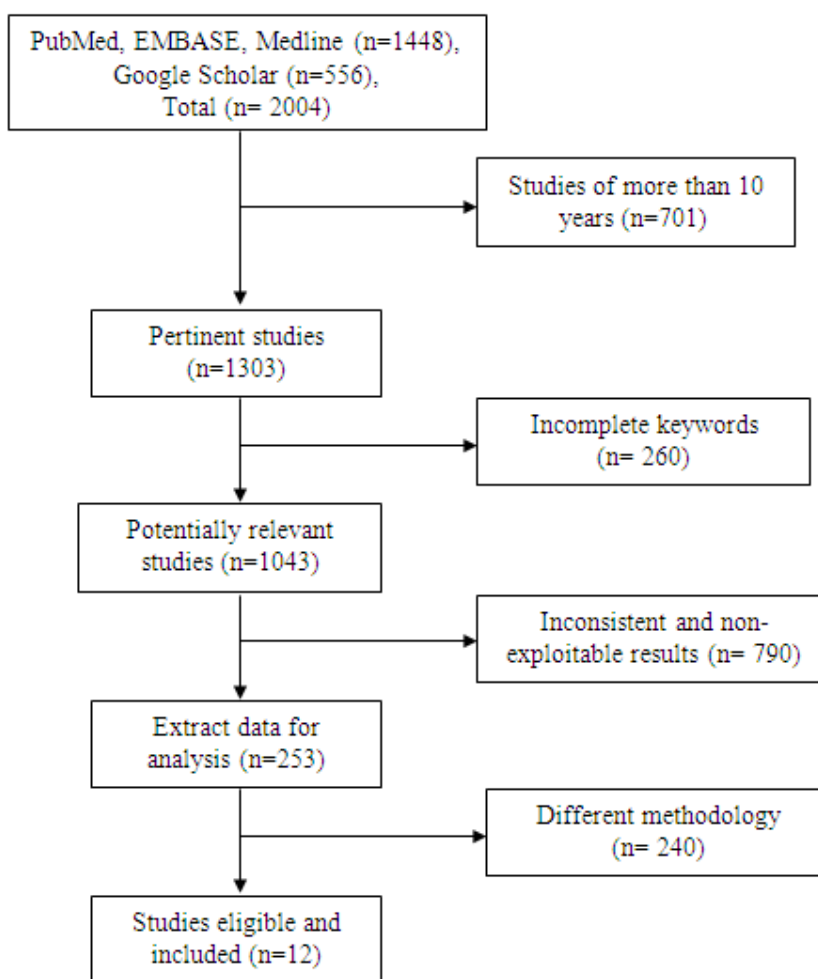


Fig. 1. Flow Diagram for the selection of studies

## 2.4 The Quality of the Studies Included

The 9-point scoring system developed by Stanifer was used to assess the quality of the included studies. The scoring criteria also assessed sample size, sampling and representativeness of participants. For a study associated with a score of 1-3; 4-6; 7-9 was low, medium or high respectively. We only included moderate and high-quality studies.

## 2.5 Data Abstraction

Data extraction was done independently to maintain statistical comparability. Any discrepancies were referred to a third opinion to reach a consensus. All data from eligible studies were extracted. These data included the HBsAg status at first (HBsAg negative) and second donation (Hepatitis B Core Antibodies positive), the number of NAT or PCR positive donors at first donation.

All socio-demographic data from these eligible studies were also extracted. All members of the research team checked the calculations and abstractions performed in this study. All studies with unpossessed or miscalculated data were excluded.

## 2.6 Atypical Serological Profiles in Hepatitis B Virus Infection

Hepatitis B surface antigen (HBsAg) is the main marker for the diagnosis of acute and chronic hepatitis B. Although HBsAg assays have been continuously improved, gaps remain in the detection of early and late acute infection and occult hepatitis B infection (OBI). During hepatitis B virus (HBV) infection, the observation of at least four antigen-antibody systems: HBsAg and anti-HBs; preS antigen and anti-preS antibodies; HBcAg and anti-HBc; and HBeAg and anti-HBe. The examination of these antigen-antibody systems allows the diagnosis of hepatitis B infection and the observation of the disease course. Although the serological results that allow both the diagnosis of HBV infection and the assessment of its clinical course are already well established, the dynamics of viral protein expression and antibody production may vary during the natural course of the infection. As a result, HBV infection is sometimes associated with the presence of unusual serological profiles, which may lead to doubts in the interpretation of

results or the suspicion of an incorrect serological result. Hepatitis B virus (HBV) causes a variety of clinical manifestations, ranging from asymptomatic carriage to fulminant or chronic hepatitis. Serological tests are widely used in the diagnosis of HBV infections to detect viral markers. However, encountering atypical serological profiles in some patients leads to problems in interpreting results and managing patients. Antibodies to hepatitis B virus (HBV) core antigen (anti-HBc) are thought to be the most reliable serological markers of HBV infection. However, chronic HBV infection can be manifested by an atypical serological profile, such as anti-HBc antibody negativity with the presence of hepatitis B surface antigen (HBsAg). Anti-HBc antibody negativity during HBV infection has been observed in a few different circumstances, such as infections with HBV variants, in children born to hepatitis B envelope antigen-positive mothers and in immunocompromised patients [17,18,19,20,21].

## 2.7 Profile of Residual HBV Risk

HBV infection is a threat to the safety of the blood supply. While most infectious blood units are eliminated by screening for hepatitis B surface antigen (HBsAg), there is clear evidence that transmission through HBsAg negative components occurs, in part, during the negative window period, but mostly during the late stages of infection.

In the case of our study, all those who were considered incident cases had a profile of HBsAg negative at first donation and Ac-anti-HBc positive at second donation or HBsAg negative but NAT or PCR positive at first donation. Voluntary blood donors (new or regular donors) are a self-selected group of healthy individuals who have been screened for potential risk factors such as homosexuality, intravenous drug use and multiple sexual partners.

Incident infections among HBV DNA-positive donors were defined as samples that were anti-HBc-reactive and HBsAg-negative (HBV DNA-positive/anti-HBc-reactive/HBsAg-negative) or HBsAg-negative (HBV DNA-positive/HBsAg-negative). HBsAg positive samples from repeat donors with a previous negative donation (1st donation) were also included as incident cases.

## 2.8 Genetic Diversity of the Hepatitis B Virus

The genetic diversity of incident infections in donor blood and plasma affects the safety of blood and diagnostic tests commonly used in blood banks. HBV screening and diagnosis of HBV-related liver disease in low- and middle-income countries differ significantly from those in developed countries in terms of access to resources and expensive technologies requiring highly specialised personnel. These resource-limited settings include mainly countries in Africa, Asia and Latin America where the prevalence of blood-borne viral infections is high. Detection of the incidence of hepatitis B virus infection is done by testing for anti-HBc antibodies or DNA for units of blood that are not reactive for hepatitis B surface antigen (HBsAg) or are not detected by routine testing. The first marker to appear in plasma is HBV DNA, followed by hepatitis B surface antigen (HBsAg) during acute HBV infection. After resolution of the infection or in the absence of HBsAg, anti-HBc antibodies remain detectable in acute, chronic or old infections. Thus, occult hepatitis B virus infection (OBI) is defined as the persistence of hepatitis B virus (HBV) genomes (with detectable or undetectable HBV presence) in the liver of HBsAg-negative individuals. It represents the negative phase of the natural history of HBV infection in individuals with self-limited acute hepatitis B or in HBsAg carriers or patients with chronic hepatitis B who lose HBsAg either naturally or after antiviral treatment and maintains a lifetime serum level of anti-HBc (with or without anti-HBs and/or anti-HBe). In rare cases, this may be a primary "occult" infection caused by tiny amounts of virus unable to induce a humoral immune response. The risk of false-negative results for hepatitis B surface antigen (HBsAg) can be partially reduced in some cases by introducing additional procedures such as anti-HBc antibody testing and nucleic acid (HBV DNA) testing. The effect of genetic variability, when HBsAg is the only marker sought in donor populations, represents a major challenge for blood banks and recipients of blood and blood products [22,13,23,24,25].

## 2.9 Statistical Analysis

A meta-analysis was used to compile data on the residual risk of HBV in African and other Southern countries' blood banks. Study-specific estimates were pooled using the random-effects

meta-analysis model to obtain an overall, synthetic estimate of the residual risk of HBV in blood banks in African and other developing countries. Inter-rater agreement for study inclusion and data extraction was assessed using Cohen's kappa ( $\kappa$ ) coefficient. Residual risks (RRs) for each eligible study were determined using Schreiber's method ( $RR = \text{Incidence Rate (IR)} \times \text{Serum Window Duration (DSW)} / 365$ ) [26]. The duration of the window period was 44 days [27]. IRs for each study was calculated by dividing the number of incident cases during the study period by the total number of person-years (PY). Person-years are calculated by multiplying the study population by the study duration. Similarly, the percentages of male and female donors were calculated. The statistical threshold was defined as  $P \leq .05$ .

## 3. RESULTS

Our search yielded 2004 citations. Twelve articles were included after applying exclusion criteria, including 10 cross-sectional studies, 1 Case-control and 1 Cohort studies (Fig. 1). The participating blood organizations screened 71 207 allogeneic donations. A total of 4912 HBsAg negative African donation including (51.0%) new donors and (49.0%) from regular donors. 80.8% of them were male and the median age was 28 years (Table 1). Of 4912 HBsAg-negative African donations, 571 were incident cases and available (Table 2). However, only 124 of these possible incident infections were HBV DNA positive, whereas 1802 tested HBV DNA negative, indicating either false-negative HBsAg ELISA results or do not use sensitive tests.

While in the other Southern countries region (Pakistan, Malaysia, Colombia, Laos, Indonesia, Saudi Arabia), of 66295 HBsAg-negative donations, 654 were incident cases (Table 2) and only 108 of these incident infectious were HBV DNA positive and 66 187 tested HBV DNA negative.

Table 3 shows the estimated incidence rate of HBV infection in the donor population. Of 1225 HBV strains (47% and 53.4% incident cases) were frequencies in sub-Saharan Africa and other Southern countries respectively.

The incidence of new infections was 4905.1 in sub-Saharan Africa and 869.7 in other Southern countries per 100,000 person-years respectively.

**Table 1. Socio-demographic data of African donors**

Socio-demographic characteristics	N	%	Total
Sex			
Female	941	19.2	4912
Male	3971	80.8	
Median age (years)	28.0		
Status of donor			
New donors	2506	51.0	4912
Regular donors	2406	49.0	

**Table 2. Summary of data extracted from all included studies from African and other developing countries**

Authors/Years	Origin	Study design	Study duration	Serological Test		Molecular Test	
				HBsAg negative(1st donation)	Ab-HBc positive (2nd donation)	PCR/NAT Negative	PCR/NAT Positive
Hudu et al. 2016	Malaysia	Cross sectional	1 year (J- Dec 2016)	1000	NA	945	55
Moiz et al. 2014	Pakistan	Cross sectional	1 year (J- Dec 2012)	41259	NA	41252	7
Jutavijittum et al. 2014	Laos	Cross sectional	1 year (J-Dec 2006)	819	75	807	12
Rios-Ocampo et al. 2014	Colombia	Cross sectional	1 year (J-Dec 2011)	14316	302	14310	6
Mardian et al. 2017	Indonesia	Case-control	2 years (2013-2014)	456	17	445	11
Alshayea et al. 2016	Saudi Arabia	Cross-sectional	2 years (2011-2012)	8445	198	8428	17
Diarra et al. 2017	Burkina faso	Cross-sectional	4 year (2014- 2017)	219	NA	163	56
Shambesh et al. 2015	Libya	Cross sectional	1 year (J-Dec 2015)	979	38	978	1
Olotu et al. 2016	Nigeria	Cross sectional	1 years (J-Dec 2014)	502	354	483	19
Kishk et al. 2015	Egypt	Cross sectional	1 years (J-Dec 2015)	126	44	116	10
Mahmoud et al. 2013	Sudan	Cross sectional	2 years (2011-2012)	100	42	62	38
Kabinda Maotela et al 2014	DR Congo	Cohort	3 years (2010-2012)	2986	37	NA	NA

NAT : Nucleic Acid Test ; Ab : Antibody ; HBsAg : HBsAntigen ; NA : Not Achieved

**Table 3. Incidence rate and residual risk of HBV transmission by transfusion in African countries**

<b>African countries</b>	<b>Study duration</b>	<b>PY</b>	<b>Number of incidence case</b>	<b>IR per 100 000 per person-year</b>	<b>RR per 1 million of donation</b>
Diarra et al. 2017	4 year (2014-2017)	876	56	6392.7	7706.3
Shambesh et al. 2015	1 year (J-Dec 2015)	979	38	3881.5	4679.1
Olotu et al. 2016	1 years (J-Dec 2014)	502	354	70517.9	85007.9
Kishk et al. 2015	1 years (J-Dec 2015)	126	44	34920.6	42096.1
Mahmoud et al. 2013	2 years (2011-2012)	200	42	21000	25315.1
Kabinda Maotela et al 2014	3 years (2010-2012)	8958	37	413	497.9

*RR : Residual Risk ; IR : Incidence Rate ; PY : Person-Year*

**Table 4. Incidence rate and Residual risk of HBV transmission by transfusion in other countries of South**

<b>Other developing countries</b>	<b>Study duration</b>	<b>PY</b>	<b>Number of incident cases</b>	<b>IR per 100 000 per person-year</b>	<b>RR per 1 million of donation</b>
Hudu et al. 2016	1 year (J- Dec 2016)	1000	55	5500	6630.1
Mardian et al. 2017	2 years (2013-2014)	912	17	1864	2247.1
Alshayea et al. 2016	2 years (2011-2012)	16890	198	1172.3	1413.2
Jutavijittum et al. 2014	1 year (J-Dec 2006)	819	75	9157.5	11039.2
Rios-Ocampo et al. 2014	1 year (J-Dec 2011)	14316	302	2109.5	2543
Moiz et al. 2014	1 year (J- Dec 2012)	41259	7	16.9	20.5

*IR : Incidence Rate ; RR : Residual Risk PY : Person-Year*

The overall residual risk for HBV amounted to 5913 per 1,000,000 donations in African countries and 1048.4 per 1,000,000 donations in other Southern countries (Table 4).

#### 4. DISCUSSION

The purpose of this study was to assess the residual risk of HBV in African blood banks and to compare them to other countries in the South countries by a meta-analysis using published papers. In this systematic review, the estimated residual risk for HBV in sub-Saharan Africa (5913 per 1,000,000 donations) was 5 times higher than in other Southern countries (1048.4 per 1,000,000 donations). This observation was also reported in other African countries [28,26,29]. These residual risk rates in our study were significantly higher than those reported in others developing countries [11,30]. The reasons for the relatively higher rate of residual risk of HBV in Africa blood-transfusion services as compared to others in the South might be the improvement in diagnostic technology might make current screening reagents to be more specific and reliable; the economic status of the country and the geographical differences in prevalence.

Incidence rates per 100,000 PY were estimated at 4905.1 for African sub-Saharan. In contrast to the incidence rate was the highest compared to other countries in the South (869.7). This observation was also reported in a recent study [31]. This may be due to the long window period. In addition, serological HBsAg tests without confirmation tests have led to large proportions of false-negative results [32].

In our study majority of the donors (80.8%) were males which are similar to the study done by previous studies [33,34,35,36,37]. These may be due to fewer females donating blood; hence fewer females are screened compared to males.

New donors are predominant (51%) were new donors which is similar to the study done by previous studies [38,39,40,41,42]. This may be due to motivation. There are also cultural beliefs surrounding blood donation that prevent donors from coming forward. There is also the recruitment of volunteer donors from the community is complex and costly and depends on regular education programmes, collection teams, vehicles and cold stores.

Our meta-analysis study had several limitations, including the original articles that met the

eligibility criteria. Most articles did not contain demographic information. Furthermore, in this meta-analysis, HBV infection was defined as positive for serum anti-HBc or HBV DNA. Studies using different HBsAg ELISA kits or HBV DNA quantification tests with different sensitivities could potentially affect the results of the analysis.

#### 5. CONCLUSION

Through this meta-analysis, we have shown that the residual risk of HBV remains high in sub-Saharan Africa compared to other countries in the South. Blood donations with HBsAg undetectable by routine testing and low levels of HBV DNA are extremely common in sub-Saharan Africa, the residual risk rate per 1 million donations was estimated at 5913 for HBV. Given that at least several of these samples could reflect contamination or a false negative result, elimination of infection by a test limited to HBsAg does not prevent transmission. We believe that the implementation of additional procedures such as sensitive NAT and continued anti-HBc testing.

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#### COMPETING INTERESTS

Authors have declared that no competing interests exist.

#### REFERENCES

1. Yooda AP, Soubeiga ST, Yacouba Nebie K, Diarra B, Sawadogo S, Ouattara AK, et al. Impact of multiplex PCR in reducing the risk of residual transfusion-transmitted human immunodeficiency and hepatitis B and C viruses in burkina faso. *Mediterr J Hematol Infect Dis.* 2018;10:e2018041. DOI : 10.4084/mjhid.2018.041
2. Ware AD, Jacquot C, Tobian AAR, Gehrie EA, Ness PM, Bloch EM. Pathogen reduction and blood transfusion safety in Africa: strengths, limitations and challenges of implementation in low-resource settings. *Vox Sanguinis.* 2017;113:3–12. DOI: 10.1111/vox.12620



3. Oluyinka OO, Tong HV, Bui Tien S, Fagbami AH, Adekanle O, Ojurongbe O, et al. Occult hepatitis B virus infection in nigerian blood donors and hepatitis B virus transmission risks. Roques P, editor. PLOS ONE [Internet]. Public Library of Science (PLoS). 2015;10(7):e0131912. DOI: 10.1371/journal.pone.0131912
4. Nambei WS, Rawago-Mandjiza D, Gbangbangai E. Seroepidemiology of HIV, syphilis and hepatitis B and C viruses among blood donors in Bangui, Central African Republic. Médecine et Santé Tropicales [Internet]. John Libbey Eurotext. 2016;26(2):192–8. DOI: 10.1684/mst.2016.0553
5. Busch MP, Bloch EM, Kleinman S. Prevention of transfusion-transmitted infections. Blood [Internet]. American Society of Hematology. 2019; 133(17):1854–64. DOI: 10.1182/blood-2018-11-833996
6. Candotti D, Boizeau L, Laperche S. Occult hepatitis B infection and transfusion-transmission risk. Transfusion Clinique et Biologique [Internet]. Elsevier BV. 2017 ;24(3):189–95. DOI: 10.1016/j.tracli.2017.06.014
7. O'Brien SF, Yi QL, Fan W, Scalia V, Goldman M, Fearon MA. Residual risk of HIV, HCV and HBV in Canada. Transfusion and Apheresis Science [Internet]. Elsevier BV. 2017;56(3):389–91. DOI: 10.1016/j.transci.2017.03.010
8. Rosenthal P. Faculty opinions recommendation of detection of hepatitis B virus infection in German blood donors 2008-2015. Faculty Opinions – Post-Publication Peer Review of the Biomedical Literature [Internet]. Faculty Opinions Ltd; 2020. DOI: 10.3410/F.737325603.793571057
9. Dodd RY, Crowder LA, Haynes JM, Notari EP, Stramer SL, Steele WR. Screening blood donors for HIV, HCV, and HBV at the American Red Cross: 10-Year Trends in Prevalence, Incidence, and Residual Risk, 2007 to 2016. Transfusion Medicine Reviews [Internet]. Elsevier BV. 2020;34(2):81–93. DOI: 10.1016/j.tmr.2020.02.001
10. Rajput MK. Automated Triplex (HBV, HCV and HIV) NAT assay systems for blood screening in India. Journal of Clinical and Diagnostic Research [Internet]. JCDR Research and Publications ; 2016. DOI: 10.7860/jcdr/2016/16981.7319
11. Corrêa AS de M, Lamarão LM, Vieira PCM, de Castro RBH, de Almeida NCC, de Castro JAA, et al. Prevalence, incidence and residual risk of transfusion-transmitted HBV infection before and after the implementation of HBV-NAT in northern Brazil. Khudyakov YE, editor. PLOS ONE [Internet]. Public Library of Science (PLoS). 2018;13(12): e0208414. DOI: 10.1371/journal.pone.0208414
12. Ye X, Li T, Shao W, Zeng J, Hong W, Lu L, et al. Nearly half of ultrio plus NAT non-discriminated reactive blood donors were identified as occult HBV infection in South China. BMC Infectious Diseases [Internet]. Springer Science and Business Media LLC. 2019;19(1). DOI: 10.1186/s12879-019-4215-9
13. Roberts DJ, Field S, Delaney M, Bates I. Problems and approaches for blood transfusion in the developing countries. Hematology/Oncology Clinics of North America [Internet]. Elsevier BV; 2016;30(2):477–95. DOI:10.1016/j.hoc.2015.11.011
14. Candotti D, Tagny-Tayou C, Laperche S. Challenges in transfusion-transmitted infection screening in Sub-Saharan Africa. Transfusion Clinique et Biologique [Internet]. Elsevier BV; 2021;28(2):163–70. DOI: 10.1016/j.tracli.2021.01.007
15. Lelie N, Bruhn R, Busch M, Vermeulen M, Tsoi W, Kleinman S, et al. Detection of different categories of hepatitis B virus (HBV) infection in a multi-regional study comparing the clinical sensitivity of hepatitis B surface antigen and HBV-DNA testing. Transfusion [Internet]. Wiley; 2016 ;57(1):24–35. DOI: 10.1111/trf.13819
16. Page MJ, McKenzie J, Bossuyt P, Boutron I, Hoffmann T, mulrow cindy d, et al. Updating guidance for reporting systematic reviews: Development of the PRISMA 2020 statement. Center for Open Science ; 2020. DOI: 10.31222/osf.io/jb4dx
17. Albuquerque I de C, Sousa MT, Santos MDC, Nunes JDC, Moraes MJD, Gomes-Gouvêa MS, Pinho JRR, Carrilho FJ, Fonseca LMB, Ferreira A de SP, et al. Mutation in the S gene a determinant of the hepatitis B virus associated with concomitant HBsAg and anti-HBs in a

- population in Northeastern Brazil. *Journal of Medical Virology*. 2017;89(3): 458-462.  
DOI: 10.1002/JMV.24653
18. Hou W, Huo Z, Du Y, Wang C, Syn WK, et al. Characteristics of amino acid substitutions within the “a” determinant region of hepatitis B virus in chronically infected patients with coexisting HBsAg and anti-HBs. *Clinics and Research in Hepatology and Gastroenterology*. 2020;44(6):923-931.  
DOI:10.1016/J.CLINRE.2019.08.005
  19. Pondé RAA. Acute hepatitis B virus infection or acute exacerbation of chronic hepatitis B infection: The differential serological diagnosis. *European Journal of Clinical Microbiology & Infectious Diseases*. 2016;35(1):29-40.  
DOI: 10.1007/S10096-015-2522-7
  20. Malve B, Eschlimann M, Galgey S, Fenaux H, Zoulim F, Goehringer F, Rabaud C, May T, Jeulin H, Schvoerer E, et al. Impact of deletions and mutations in hepatitis B virus envelope proteins on serological profile and clinical evolution. *Virus Research*. 2017;238:141-147.  
DOI: 10.1016/J.VIRUSRES.2017.06.028
  21. Adetunji SO, Donbraye E, Alawode-Obabiyi L, Akinniyi O, et al. Serological profile of HBV infection among apparently healthy hospital attendees. *Journal of Immunoassay and Immunochemistry*. 2019;40(3):237-249.  
DOI: 10.1080/15321819.2018.1555764
  22. Allain JP, Opare-Sem O. Screening and diagnosis of HBV in low-income and middle-income countries. *Nature Reviews Gastroenterology & Hepatology [Internet]*. Springer Science and Business Media LLC. 2016;13(11):643–53.  
DOI: 10.1038/nrgastro.2016.138
  23. Chulanov V, Pshenichnaya N, Leblebicioglu H. Genetic diversity of the hepatitis B virus and its epidemiological significance. *Viral Hepatitis: Chronic Hepatitis B [Internet]*. Springer International Publishing. 2018;41–50.  
DOI: 10.1007/978-3-319-93449-5\_4
  24. Revill PA, Tu T, Netter HJ, Yuen LKW, Locarnini SA, Littlejohn M. The evolution and clinical impact of hepatitis B virus genome diversity. *Nature Reviews Gastroenterology & Hepatology [Internet]*. Springer Science and Business Media LLC. 2020;17(10):618–34.  
DOI: 10.1038/s41575-020-0296-6
  25. Candotti D, Laperche S. Hepatitis B virus blood screening: need for reappraisal of blood safety measures? *Frontiers in Medicine [Internet]*. Frontiers Media SA. 2018;5.  
DOI: 10.3389/fmed.2018.00029
  26. Wongjarupong N, Oli S, Sanou M, Djigma F, Kiba Koumare A, Yonli AT, et al. Distribution and Incidence of blood-borne infection among blood donors from regional transfusion centers in burkina faso: A comprehensive study. *The American Journal of Tropical Medicine and Hygiene [Internet]*. American Society of Tropical Medicine and Hygiene. 2021;104(4):1577–81.  
DOI: 10.4269/ajtmh.20-0601
  27. Dodd RY, Nguyen ML, Krysztof DE, Notari EP, Stramer SL. Blood donor testing for hepatitis B virus in the United States: Is there a case for continuation of hepatitis B surface antigen detection? *Transfusion [Internet]*. Wiley. 2018;58(9):2166–70.  
DOI: 10.1111/trf.14784
  28. Attia A, Elmetwalli A. Screening of occult hepatitis B virus infection among egyptian blood donors. *Medical Journal of Viral Hepatitis [Internet]*. Egypts Presidential Specialized Council for Education and Scientific Research. 2021;5.2(2):27–31.  
DOI: 10.21608/MJVH.2021.158276
  29. El-Nabi SH, El-Garawani I, Ismail F, Abdelsameea E. Anti-HBc and hepatitis B virus DNA among HBsAg-negative blood donors from the main central blood bank units in Eastern Libya. *Transfusion Medicine [Internet]*. Wiley. 2020;30(5):401–5.  
DOI: 10.1111/tme.12711
  30. Grubyte S, Urboniene J, Nedzinskiene L, Jelinskaite A, Zagminas K, Ambrozaitis A, et al. Prevalence, incidence and residual risk of transfusion transmitted viruses (HBV, HCV and HIV infections) in Lithuanian blood donors from 2004 to 2018: The incidence/window-period model study. Chemin I, editor. *PLOS ONE [Internet]*. Public Library of Science (PLoS). 2021;16(2):e0246704.  
DOI: 10.1371/journal.pone.0246704
  31. Seri B, Minga A, Gabillard D, Dembele B, Konate S, Le Carrou J, et al. Twenty-year evolution of hepatitis B virus and human immunodeficiency virus prevalence and incidence in voluntary blood donors in Côte d'Ivoire. *Open Forum Infectious*

- Diseases [Internet]. Oxford University Press (OUP). 2018;5(4). DOI: 10.1093/ofid/ofy060
32. Seed CR. Screening and confirmatory testing strategies for the major transfusion-transmissible viral infections. ISBT Science Series [Internet]. Wiley. 2014;9(1):6–13. DOI: 10.1111/voxs.12060
33. Aluora PO, Muturi MW, Gachara G. Seroprevalence and genotypic characterization of HBV among low risk voluntary blood donors in Nairobi, Kenya. Virology Journal [Internet]. Springer Science and Business Media LLC. 2020;17(1). DOI: 10.1186/S12985-020-01447-2
34. Osei E, Lokpo SY, Agboli E. Seroprevalence of hepatitis B infection among blood donors in a secondary care hospital, Ghana (2014): A retrospective analysis. BMC Research Notes [Internet]. Springer Science and Business Media LLC. 2017;10(1). DOI: 10.1186/S13104-017-2733-3
35. Yambasu EE, Reid A, Owiti P, Manzi M, Sia Murray MJ, Edwin AK. Hidden dangers-prevalence of blood borne pathogens, hepatitis B, C, HIV and syphilis, among blood donors in Sierra Leone in 2016: opportunities for improvement: a retrospective, cross-sectional study. Pan African Medical Journal [Internet]. Pan African Medical Journal. 2018;30. DOI: 10.11604/PAMJ.2018.30.44.14663
36. Okoroiwu HU, Okafor IM, Asemota EA, Okpokam DC. Seroprevalence of transfusion-transmissible infections (HBV, HCV, syphilis and HIV) among prospective blood donors in a tertiary health care facility in Calabar, Nigeria; an eleven years evaluation. BMC Public Health [Internet]. Springer Science and Business Media LLC. 2018;18(1). DOI: 10.1186/S12889-018-5555-X
37. Kabemba BH, Kasendue EP, Shiku MA, Mukena TS, Kasolva TC, Kabingie NG, et al. Seroprevalence of hepatitis B virus infection (HBsAg) in rural blood donors, moba, tanganyika province, Democratic Republic of Congo (2014 to 2016). OALib [Internet]. Scientific Research Publishing, Inc. 2017;04(03):1–5. DOI: 10.4236/oalib.1103434
38. Mohammed S, Essel HB, et al. Motivational factors for blood donation, potential barriers, and knowledge about blood donation in first-time and repeat blood donors. BMC Hematology, 2018; 18(1):36. DOI: 10.1186/S12878-018-0130-3
39. Asamoah-Akuoko L, Hassall OW, Bates I, Ullum H, et al. Blood donors' perceptions, motivators and deterrents in Sub-Saharan Africa – a scoping review of evidence. British Journal of Haematology. 2017;177(6) :864-877. DOI: 10.1111/BJH.14588
40. Teklemariam Z, Mitiku H, Weldegebreal F, et al. Seroprevalence and trends of transfusion transmitted infections at Harar blood bank in Harari regional state, Eastern Ethiopia: Eight years retrospective study. BMC Hematology. 2018;18(1):24. DOI: 10.1186/S12878-018-0115-2
41. Kasraian L, Hosseini S, Dehbidi S, Ashkani-Esfahani S, et al. Return rate in blood donors: A 7-year follow up. Transfusion Medicine. 2020; 30(2):141-147. DOI: 10.1111/TME.12647
42. Mremi A, Yahaya JJ, Nyindo M, Mollel E, et al. Transfusion-transmitted infections and associated risk factors at the Northern zone blood transfusion center in Tanzania: A study of blood donors between 2017 and 2019. PLOS ONE. 2021;16(3):e0249061. DOI: 10.1371/JOURNAL.PONE.0249061

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