Annals of Health Research
Volume 4, Issue No 1: 68-74
January-June 2018
DOI: 10.30442/ahr.0401-1-09

ORIGINAL RESEARCH

Socio-demographic and other risk factors associated with HBV potential infectivity among Hepatitis B Surface Antigen Negative blood donors

Busari OE[1], Ojo OT*[2], Aken'Ova YA[3]

[1]Department of Haematology, Afe Babalola University, Ado Ekiti, Ekiti State, Nigeria
[2]Department of Haematology and Blood Transfusion,
Olabisi Onabanjo University Teaching Hospital, Sagamu, Ogun State, Nigeria
[3]Department of Haematology, University College Hospital, Ibadan, Oyo State, Nigeria

*Correspondence: Dr. OT Ojo, Department of Haematology and Blood Transfusion, Olabisi Onabanjo University Teaching Hospital, Sagamu, Ogun State, Nigeria. Tel: +2348023426641; Email: fiyinfola02@gmail.com; ORCID – http://orcid.org/0000-0002-7211-650X

Abstract

Background: There have been cases of post-transfusion hepatitis in spite of transfusion of hepatitis B surface antigen negative blood unit.
Objective: To determine the socio-demographic and risk factors associated with positivity of anti-HBc among Hepatitis B surface antigen negative blood donors.
Methods: A cross-sectional study was carried out among 490 HBsAg negative blood donors. The participants were tested for anti-HBc using ELISA kits. A structured questionnaire was used to obtain socio-demographic data and other possible risk factors.
Results: The mean age of the participants was 32.5 ± 9.5 years with male predominance of 462 (94.3%) while 375 (76.5%) were first time donors. Of the 490 HBsAg negative blood donors, 89 (18.2%) were positive for anti-HBc.
The highest prevalence of anti-HBc occurred in the 26-34 years age group. Independent risk factors associated with the presence of anti-HBc included age ($p = 0.049$), marital status ($p = 0.003$), dental and surgical procedure ($p<0.001$), traditional practices such as tattoo, body piercing and scarification ($p<0.001$) and previous blood transfusion ($p = 0.016$).
Conclusion: Age, marital status, traditional and cultural practices like scarifications, tattoo and body piercing and history of blood transfusion were risk factors associated with HBV infection despite HBsAg negativity.

Key words: Anti-HBc, Blood donors, HBsAg, Hepatitis, Risk factors, Socio-demographics.

Introduction

The demonstration of Hepatitis B surface antigen (HBsAg) in the blood is the mainstay in the diagnosis and screening for Hepatitis B Virus (HBV) infection in most developing countries, including Nigeria.. [1] Therefore, subjects who are sero-negative for HBsAg are labeled as free of HBV infection. However, patients who have been transfused with blood from HBsAg-negative blood donors had been reported to develop post-transfusion hepatitis from HBV infection. [2]
Acute HBV infection is characterized by the presence of HBsAg in serum and the development of IgM class antibody to the core protein (IgM anti-HBc). [3] Anti-HBc (IgG anti-HBc) is developed during convalescence from HBV infection. The Hepatitis B core antigen (HBc) is an intracellular antigen that is not detectable in serum, but it is the most accurate index of HB viral replication. The anti-HBc, which is the antibody against HBc, indicates a prior exposure to HBV, irrespective of the current HBsAg status.

Immunoassays for the detection of total anti-HBc involve both IgM and IgG class antibody to the core protein and these indicate current or past exposure to the HB virus and viral replication. [4] The clinical manifestations of infectivity with HBV among HBsAg negative donors, which range from general

fatigue to hepatic dysfunction cannot be over emphasized. Therefore, this study was designed to determine the socio-demographic and other risk factors associated with positivity of anti-HBc among HBsAg negative blood donors.

Methods

This was an analytical cross-sectional study. Consenting blood donors who were HBsAg negative by ELISA method and donated blood in the blood bank at the University College Hospital, Ibadan, Nigeria were studied. The blood donors who were positive for Human Immunodeficiency Virus (HIV), Hepatitis C Virus (HCV) and syphilis were excluded from the study.

Ethical approval was obtained from the Joint Ethical Committee of the University of Ibadan and University College Hospital Ibadan before the commencement of the study. A semi-structured, self-administered questionnaire was used to obtain the attributes of the subjects which were considered as risk factors for HBV.

Five millimeters (5mls) of venous blood were collected from consenting blood donors after a written informed consent was obtained. All the blood samples were screened, using a sandwich third generation Enzyme Linked Immunosorbent Assay (ELISA) for HBsAg. All the laboratory tests were carried out according to the manufacturer's instructions as outlined in the package inserts. Furthermore, all the blood samples found to be negative for HBsAg were further tested for anti-HBc. For the purpose of this study, HBsAg-negative participants who are HBc-positive were referred to as the exposed participants.

The data obtained were subjected to descriptive and inferential statistical analysis using the SPSS version 20 (SPSS Inc, Illinois, USA) software. Quantitative variables were summarized using means and standard deviations while qualitative variables were summarized in frequencies and proportions. The level of statistical significance was set at 5% (p less than 0.05). Subgroup analysis was done and the differences were compared using Chi-Square test. Bivariate logistic regression analysis was performed to identify independent predictors of Hepatitis B infectivity from the variables considered (socio-demographic, behavioural and medical risk factors).

Results

A total number of 490 blood donors who tested negative for Hepatitis B surface antigen (HBsAg) were recruited into the study. Four hundred and sixty-two (94.3%) were males while 28 (5.7%) were females. Their ages ranged from 18 years to 60 years with a mean of 32.5 ± 9.5 years. More than half (290; 59.2%) were married while the remaining were single. Other socio-demographic characteristics are as illustrated in Table I.

Table I: Socio-demographic characteristics of 490 Hepatitis B surface antigen negative blood donors

Characteristics		*Frequencies*	*Percentages*
Age (Years)	<25	119	24.3
	25-34	178	36.3
	35-44	132	27.0
	>45	61	12.4
Sex	Male	462	94.3
	Female	28	5.7
Marital status	Married	290	59.2
	Single	200	40.8
Education	Primary	42	8.6
	Secondary	237	48.4
	Tertiary	210	43.0
Employment	Employed	201	41.0
	Unemployed	71	14.5
	Others*	218	44.5

Others included students and housewives

Three hundred and seventy five (76.5%) of the study participants were first time donors while 115 (23.5%) had previously donated blood. The donors consisted predominantly of family replacement donors (452; 92.2%), 33 (6.7%) were voluntary donors and the remaining 5 (1%) were commercial donors. A majority, 485 (98.8%) had never been transfused with blood. Thirty-one (6.3%) of the blood donors gave history of Hepatitis B vaccination but only six completed the vaccination.

The sero-prevalence of anti-HBc was 18.6% (89/490). As shown in Table II, although most of the exposed group were males (86/89), the male sex was not significantly associated with exposure (p = 0.217). The mean age of the exposed group was 34.5 ± 8.5 years and about half of them [49.4%; 44/89] were older than 25 years. Older age was significantly associated with the presence of anti-HBc (p = 0.026). Seventy (78.7%) of the exposed group were married, with a significant association with exposure to HBV infection (p<0.001). The level of education and employment status had no association with the likelihood of exposure to HBV.

Table III shows factors that were significantly associated with exposure to HBV included previous history of blood transfusion (p = 0.044), dental/surgical procedure (dental procedure, caesarian section, abortion and previous injections) (p<0.001), ear piercing and tattoo including scarification marks (p<0.001). The risk factors were assessed for their association with exposure to HBV infection using multivariate logistic regression. Table IV shows that marriage, exposure to dental or surgical procedure, tattoo and or ear piercing and previous history of blood transfusion were significantly associated with detection of anti-HBc.

Table II: Association of socio-demographic characteristics with infectivity of Hepatitis B Virus

Characteristics	*Exposed*	*Not exposed*	χ^2	*P values*
Age (Years)				
<25 (n = 119)	11 (9.2)	108 (90.8)	9.265	0.026
25-34 (n = 178)	34 (19.1)	144 (80.9)		
35-44 (n = 12)	30 (22.7)	102 (77.3)		
>45 (n = 61)	14 (23.0)	47 (77.0)		
Gender				
Male (n = 462)	86 (18.6)	376 (81.4)	1.109	0.217
Female (n= 28)	3 (10.7)	25 (89.3)		
Marital status				
Married (n = 290)	70 (24.1)	220 (75.9)	17.063	<0.0001
Single [a] (n = 200)	19 (9.5)	181 (90.5)		
Education				
Primary (n = 42)	9 (21.4)	33 (78.6)	0.654	0.721
Secondary (n = 237)	40 (16.9)	197 (83.1)		
Tertiary (n = 211)	40 (19.0)	171 (81.0)		
Employment				
Employed (n = 201)	35 (17.4)	166 (82.6)	2.416	0.299
Unemployed (n = 71)	9 (12.7)	62 (87.3)		
Others [b] (n = 218)	45 (20.6)	173 (79.4)		

a = includes single, widowed and divorced, b = others include students, house wife.
Figures in parentheses are percentages of the total in the respective rows.

Table III: Association of behavioral and medical risk factors with HBV infectivity

Factors	*Exposed*	*Not exposed*	χ^2	*P values*
Tattoo/Ear piercing/Scarifications				
Yes (n = 10)	9 (90.0)	1 (10.0)	35.441	<0.001
No (n = 480)	80 (16.7)	400 (83.3)		
History of blood transfusion				
Yes (n = 5)	3 (60.0)	2 (40.0)	5.948	0.044
No (n = 485)	86 (17.7)	3399 (82.3)		
Vaccination				
Yes (n = 31)	6 (19.4)	25 (80.6)	1.603	0.52
No (n = 459)	83 (18.1)	376 (81.9)		
Dental/Surgical Procedures				
Yes (n = 12)	10 (63.3)	2 (16.7)	35.148	<0.001
No(n = 478)	79 (16.5)	399 (83.5)		

Figures in parentheses are percentages of the total in the respective rows.

Discussion

It is not unexpected that there was a male predominance in this study as it is a common experience in many countries and particularly, in the Nigerian setting, as previously documented. [5, 6] This has been ascribed largely to socio-cultural beliefs and required minimum donor haemoglobin levels.

The detection of HBV infection among Nigerians, in many studies, has mostly been performed using the presence of only HBsAg. [7, 8] Therefore, many subjects who were sero-negative for HBsAg have been labeled as free of HBV infection. [8] However, the screening of blood donors for HBsAg does not totally eliminate the risk of transmission of HBV. [9] It has been reported that the transmission of HBV infection through blood transfusion still occurs in a proportion of cases even when the transfused blood tested negative for HBsAg using highly sensitive assays. [10-12]

Table IV: Logistic regression analysis of risk factors of exposure to HBV infection

Variables	*B*	*OR*	*P values*	*95%CI*	
				Lower	*Upper*
Age (Years)					
<25 Ref					
25-34	1.134	3.01	0.049	1.000	9.637
35-44	0.616	0.85	0.335	0.529	6.480
>45	0.107	1.11	0.883	0.269	4.610
Marital status					
Married	1.231	3.42	0.003	1.517	7.731
Single Ref					
Dental/Surgical Procedures					
Yes	1.374	7.19	<0.001	5.385	58.265
No Ref					
Tattoo/Ear piercing/Scarifications					
Yes	4.666	16.28	<0.001	10.576	168.146
No Ref					
History of blood transfusion					
Yes	2.707	14.99	0.016	1.668	134.744
No Ref					

B – Regression Coefficient; OR – Odd Ratio; CI – Confidence Interval; Ref – Reference variable

Therefore, the Hepatitis B virus (HBV) remains a major risk for transfusion-transmitted infection due to pre-seroconversion window period, infection with immunovariant viruses and with occult carriage of HBV infection (OBI). Occult HBV infection is currently defined as the absence of circulating HBsAg in individuals who are positive for serum or tissue (liver) HBV DNA, irrespective of other HBV serological markers. [13] Seropositive occult hepatitis B virus infection is characterized by the presence of anti-HBc and/or anti-HBs, while neither of the two markers is detected in sero-negative OBI. [14] HBV Nucleic Acid Testing combines the ability to significantly reduce the window period and to detect occult HBV.

The antibody to Hepatitis B core antigen is a marker of acute, chronic or resolved infection. [15] In this study, 18.2% of HBsAg negative blood donors were found positive for antibody to hepatitis B core antigen (anti-HBc). This observation agreed with different values which have been reported in various studies, ranging from 0.4% to 70%. [16-19] The presence of IgM anti-HBc with high index value, usually indicates a recent HBV infection and this antibody usually disappears within six months. [20] Among individuals with acute Hepatitis B disease, IgG anti-HBc appears shortly after HBsAg and persists for life. [21] Recent studies have also indicated that isolated IgG anti-HBc may suggest an occult or silent HBV infection. [22]

Anti-HBsAg antibody is a neutralizing antibody and its presence suggests recovery from hepatitis B infection and confers a long-term protective immunity against HBV infection. In addition, it is the only detectable serological marker in those who

successfully respond to hepatitis B immunization. [23] Several studies have shown the effectiveness of hepatitis B vaccination in the prevention of HBV infection. [24-26] In the present study, 6.3% of the HBsAg negative blood donors gave a history of previous hepatitis B vaccination but only six completed the vaccination.

Analysis of the variables considered as risk factors for the presence of anti-HBc in the studied population revealed that age, marital status, history of blood transfusion, previous exposure to surgical or dental procedures, history of tattoo, scarification and ear piercing were significantly associated with the presence of anti-HBc. All these variables remained significant following multivariate logistic regression. The older age was significantly associated with the detection of anti-HBc. A higher frequency of anti-HBc was found in the age groups 25-34 years (38.2%) and 35-44 years (33.7%) compared to the youngest age group of < 25 years (12.4%). This finding was in agreement with the reports of Dettori *et al.* [27] in Italy and Matos *et al.* [28] in Brazil. This could be due to the greater number of years of potential exposure, lack of awareness of HBV infection in early life and infrequent HBV vaccination among adults. Marital status was observed in the present study to be a significant risk factor for exposure to HBV. The high frequency of anti-HBc among married participants was similar to the reports of El-Beltagy *et al.* [(29] and El-Ghitany *et al.* [30] reported in Saudi Arabia and Egypt respectively. This may be due to the relatively older age of the participants and greater sexual exposure.

The presence of cosmetic alterations in the form of body piercing or tattooing, traditional and cultural practices which are associated with scarification marks as well as unsafe injection practices, dental and surgical procedures by quacks should be taken into consideration when assessing the risk of an individual for anti-HBc. Dettori *et al.* [27], Matos *et al.* [28], and El-Ghitany *et al.* [30] all gave concordant reports. However, El-Beltagy and colleagues [29] reported no significant association with anti-HBc. The presence of these risk factors is associated with procedures practiced under poor hygienic conditions with the sharing of instruments such as scissors, needle and syringe without adequate sterilization. In the light of these, public enlightenment must be intensified to increase awareness of the danger in such practices, both in the rural and urban settings. Previous blood transfusion was significantly associated with the presence of anti-HBc in the present study similar to the report by El-Ghitany *et al.* [30] but was at variance with the report of El-Beltagyy *et al.* [29] This observation could be due to improper blood screening procedure which is practised in some laboratories within the country.

Limitation of the study

Hepatitis B virus DNA was not examined among the subjects due to limited resources.

Conclusion

Age, marital status, traditional and cultural practices like scarifications, tattoo and body piercing and the history of blood transfusion were risk factors for exposure to HBV. There is a need for public health education on the risk factors associated with infectivity for Hepatitis B Virus. Socioeconomic development, public and well structured adult immunization programs should also be initiated or intensified in places where it is already in existence.

Authors' Contributions: BOE **and A'OYA** conceived and designed the study and wrote the initial draft of the manuscript. **OOT participated in drafting the manuscript. All the authors approved the final version of the manuscript**
Conflict of Interest: None
Funding: Self-funded
Publication History: **Submitted** 13-December 2017; **Revised** 24-March 2018; **Accepted** 13-April 2018.

References

1. Salawu L, Adegoke AO, Aboderin AO, Huraina HA. Hepatitis B viral markers in surface antigen negative blood donors: The need to look beyond antibody Negativity. West Afr J Med 2011; 30(4): 292-295.

2. Behzad-Behbahani A, Mafi-Jenad A, Tabei SZ, Lankarani KB, Torab A, Moaddem A. Anti-HBc and HBV DNA detection in blood donors negative for hepatitis B virus surface antigen in reducing the risk of transfusion associated HBV infection. Indian J Med Res 2006; 123: 37-42.

3. Kaneko S, Feinstone SM, Miller RH**.** Rapid and sensitive method for the detection of serum hepatitis B virus DNA using the polymerase chain reaction technique. J Clin Microbiol 1989; **27**(9): 1930-1933.

4. Schuurs AHWM, Kacaki J. Reversed haemagglutination test for the detection of hepatitis B antigen. Vox Sang Basel 1974; 27: 97-114.

5. Norder H, Courouce AM, Magnius LO. Complete genomes, phylogenetic relatedness, and structural proteins of six strains of the hepatitis B virus, four of which represent two new genotypes. Virology 1994; 198: 489–503.

6. Kao JH. Hepatitis B viral genotypes: clinical relevance and molecular characteristics. J Gastroenterol Hepatol 2002; 17: 643-650.

7. Ola SO, Otegbayo JA, Odaibo GN, Olaleye OD, Olubuyide OI. Serum hepatitis C and hepatitis B surface antigenaemia in Nigerian patients with acute icteric hepatitis. West Afr J Med 2002; 21: 215-217.

8. Ajayi AO, Komolafe AO Ajumobi K. Seroprevalence of hepatitis B surface antigenaemia among health care workers in a Nigerian tertiary health institution. Niger J Clin Pract 2007; 10: 287-289.

9. Badru S, Akgun A. Diagnosis of hepatitis B infection and monitoring of treatment. J Clin Virol 2001; 21: 229-237.

10. Zervou EK, Dalekos GN, Boumba DS, Tsianos EV. Value of anti-HBc screening of blood donor for prevention of HBV infection: results of 3-year prospective study in Northwestern Greece. Transfusion 2001; 41: 652-658.

11. Kaviani MJ, Behbahani B, Mosallaii MJ, Sari-Aslani F, Taghavi SA. Occult hepatitis B virus infection and cryptogenic chronic hepatitis in an area with intermediate prevalence of HBV infection. World J Gastroenterol 2006; 12: 5048-5050.

12. Custer B, Sullivan SD, Hazlet TK, Iloeje U, Veenstra DL, Kowdley KV. Global epidemiology of hepatitis B virus. J Clin Gastroenterol 2004; 38: 158-168.

13. Ching-Lung L, Daniel S, Anna SL, Ting-Tsung C, Hugo C, Zachary G, *et al*. Entecavir versus Lamivudine for Patients with HBeAg-Negative Chronic Hepatitis B. N Engl J Med 2006; 354: 1011-1020.

14. Ekwere TA, Ino-Ekanem M, Motilewa OO, Iquo AI.Pattern of blood donor deferral in a tertiary hospital, South-South, Nigeria: A three-year study review. Int J Blood Transfus Immunohematol 2014; 4: 7-12.

15. Damulak DO,Ogbenna AA, Adediran AO, Samuel E, Rufai O, Bolorunduro SA, *et al*. The pattern of blood donation in the National Blood Transfusion Service in North- Central Nigeria. Highland Med Res J 2014; 14(2): 80-84.

16. Jafarzadeh A, Arababadi MK, Mirzaee M, Pourazar A. Occult hepatitis B virus infection among blood donors with antibodies to hepatitis B core antigen. Acta Medica Iranica 2008; 46: 27-32.

17. Comanor L, Holland P. hepatitis B virus blood screening: unfinished agendas. Vox Sanguinis 2006; 91: 1-12.

18. Ola SO, Otegbayo JA, Odaibo GN, Olaleye OD, Olubuyide OI, Summerton CB, *et al*. Occult HBV infection among cohort of Nigeria. J Infect Dev Ctries 2009; 3(6): 442-446.

19. Ashim M, Ali R, Khan LA, Hussain SA, Singla R, Kar P. Significance of anti-HBc screening of blood donors and its association with occult hepatitis B virus infection: Implications for blood transfusion. Indian J Med 2010; 132: 312-317.

20. Chu CJ, Lok AS. Clinical utility of quantifying serum HBV DNA levels using PCR assays. J Hepatol 2002; 36: 549-551.

21. Raimondo G, Allain JP, Brunetto MR, Buendia MA, Chen D, Colombo M, *et al*. Statements from the Taormina expert meeting on occult hepatitis B virus infection. J Hepatol 2008; 49: 652-657.

22. Schuurs AH, Kacaki J. Reversed haemagglutination test for the detection of hepatitis B antigen. Vox Sang Basel 1974; 27: 97-114.

23. Abraham. Evaluation of a new recombinant DNA hepatitis B vaccines. Vaccine 1999; 17: 1125-1129.

24. Salama II, Sami SM, Said ZNA, El-Sayed MH, El-Etreby LA, Rabah TM, *et al*. Effectiveness of hepatitis B virus vaccination program in Egypt: Multicenter national project. World J Hepatol 2015; 7(22): 2418–2426.

25. Damme PV. Long-term Protection After Hepatitis B Vaccine. *J Infect Dis* 2016; 214(1): 1–3.

26. Liang S, Bi S, Yang W, Wang L, Cui G, Cui F, *et al*. Epidemiological serosurvey of hepatitis B in China–declining HBV prevalence due to hepatitis B vaccination. Vaccine 2009; 27: 6550–6557.

27. Dettori S, Candido A, Kondili LA, Chionne P, Taffon S, Genovese D, *et al*. Identification of low HBV-DNA levels by nucleic acid amplification test (NAT) in blood donors. J Inf 2009; 59(2): 128-133.

28. Matos MA, Reis NR, Kozlowski AG, Teles SA, Motta-Castro AR, Mello FC, *et al*. Epidemiological study of hepatitis A, B and C in the largest Afro-Brazilian isolated community. Trans R Soc Trop Med and Hyg 2009; 103(9): 899-905.

29. El-Beltagy KE, Al Balawi IA, Almuneet M, Memish ZA. Prevalence of hepatitis B virus markers among blood donors in a tertiary hospital in Tabuk, northwestern Saudi Arabia. Int J Inf 2008; 12: 495-499.

30. El-Ghitany EM, Farghaly AG. Serological pattern of hepatitis B virus among HBsAg negative blood donors in Alexandria, Egypt. East Meditt Health J 2013; 19(7): 600-607.