

The effect of Anti-HBc Detection in Egyptian Blood Donors Negative for HBsAg in Reducing the Risk of Transfusion Associated HBV Infection

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Abstract

Background: In spite of the progress made in the prevention of transfusion transmitted infections over the last few years, transmission of hepatitis B virus (HBV) infection through transfusion of hepatitis B surface antigen (HBsAg) negative blood has been documented.

Objective: To study the seroprevalence of antibody to hepatitis B core antigen (anti-HBc) in healthy blood donors negative for HBsAg and to evaluate whether anti-HBc detection could be adopted in Egypt as a screening assay for HBV in addition to HBsAg.

Methods: In across sectional study, a total of 3043 blood donors were screened in 2009 for the following viral markers: hepatitis C virus antibody (anti-HCV), hepatitis B surface antigen (HBsAg), and human immunodeficiency virus I / II (anti-HIV I / II). Nine hundred and four samples negative for HBsAg (323 samples with elevated ALT level and 581 with normal ALT level) were tested for the presence of anti-HBc.

Results: One hundred and sixty two samples (17.92 %) were reactive for anti-HBc. The present study showed 20.12 % and 16.7 % anti-HBc positivity for samples with elevated and normal ALT level respectively.

Conclusion: Anti-HBc should be tested routinely in blood-donor volunteers. Rejection of anti-HBc positive units will be beneficial in decreasing the risk of HBV transmission with its potential consequences.

Keywords: Anti-HBc; HBsAg; HBV; Blood Donors

Introduction

Hepatitis B virus (HBV) infection is a serious global health problem affecting two billion people worldwide, and 350 million people suffer from chronic HBV Infection^(1,2). Regardless of all efforts to guarantee the safety of blood, hepatitis B residual risk is the highest among transfusion-transmitted diseases^(3,4). Hepatitis B surface antigen (HBsAg) is the primary diagnostic marker used for screening blood products in hospitals and health care facilities⁽⁵⁾. Several studies have demonstrated that some HBsAg negative individuals and those reactive for the antibody to hepatitis B core antigen (anti-HBc) continue to replicate HBV^(2,6). Thus the absence of HBsAg in the blood of apparently healthy individuals may not be sufficient to ensure lack of circulating HBV⁽²⁾. The strategy of combined HBsAg and anti-HBc screening virtually eliminates blood-transmitted HBV with the rare exception of donations in the window period where serological

markers are still negative^(3,7). Currently, a number of countries including the United States screen all donations for anti-HBc, which is not mandatory in other countries⁽⁸⁾. Blood donors in Egypt are not screened for anti-HBc. Therefore, the residual risk of transmission of HBV from HBsAg negative donors remains considerable in the transfused groups⁽⁹⁾. In this study, we aim to evaluate whether anti-HBc detection could be adopted in Egypt as a screening assay for HBV in addition to HBsAg to improve the safety of blood transfusion.

Material and Methods

Study Population: The 3043 blood samples used in this study were collected between January and August 2009 at the blood donation center a of the Teaching Hospital of Suez Canal University. Donors were interviewed and medically examined before transfusion. The blood samples were centrifuged briefly and serum sample were stored at -80C ° until use.

Biochemical tests for liver function: For all collected samples, the alanine aminotransferase (ALT) test was carried out by an enzymatic method.

Serological studies: All blood specimens were examined for blood bank routine serological tests using commercially available ELISA, HBsAg and anti-HCV (DiaSorin, Saluggia, Italy) and anti-HIV I/II (TETRA, Biotest, Germany). The blood unit, which tested negative for the aforementioned routine screening test, were thus considered eligible for transfusion. Then total anti-HBc was performed for all accepted samples with elevated ALT level and for a selected group with normal ALT level using commercially available ELISA (DiaSorin, Saluggia, Italy).

Statistics: the GraphPad software (Quick Calcs online calculators for scientists at <http://www.graphpad.com/quickcalcs/index.cfm>) were used to perform the Chi-square and Fisher's exact two-tailed tests.

Results

Blood donations from 2865 males (94.15%) with a median age of 27 years, and 178 females (5.85%) with a median age of 27 years were included in this study.

The concentration of ALT was determined for all samples. The mean average of ALT level was 28.29 ± 6.83 IU/L. Table (I) shows the distribution of ALT intervals among the blood donors.

Donations from 192 males and 6 females were found reactive and were rejected. HBsAg was detected in 59 samples (1.94%) (58 males and a single female) while HCV Ab was detected in 140 samples (4.6%) (135 males and 5 females). HIV I/II Ab was not detected in any blood donation.

Nine hundred and four samples negative for all routine serological assays were tested for the presence of anti-HBc. These samples were categorized according to ALT level (Figure 1). Three hundred and twenty three samples with elevated ALT level (> 30 IU/L) were examined; Sixty five samples were reactive (20.12%). While, 581 samples (160 females and 421 males) with normal ALT level were selected randomly and tested for the presence of total anti-HBc. Ninety seven samples (16.69%) were positive. Comparison between tested samples regarding to Anti-HBc positivity is illustrated in table (II). A significant association between anti-HBc and increasing age was observed ($P=0.0006$). In addition, anti-HBc was strongly associated with the male gender ($P=0.0003$), while there was no significant association between anti-HBc and ALT level.

Table (I): Distribution of ALT intervals among the blood donors

ALT Intervals IU/L	Male (2865)		Female (178)		Total (3043)	
	No.	%	No.	%	No.	%
≤ 10	889	31	87	48.9	976	32
11-20	1182	41.3	62	34.8	1244	40.9
21-30	419	14.6	14	7.9	433	14.2
31-40	189	6.6	9	5.1	198	6.5
41-50	76	2.7	2	1.1	78	2.6
51-60	37	1.3	2	1.1	39	1.3
> 60	73	2.5	2	1.1	75	2.5
≤ 10	889	31	87	48.9	976	32

Table (II): Results of anti-HBc test for 904 selected samples

Variables	Positive anti-HBc	Negative anti-HBc	P Value	
	(No=162)	(No=742)	P1	P2
Age (years)				
≤ 30	76 (14.2%)	459 (85.8%)	0.0006	0.0006
> 30	86 (23.3%)	283		
Gender				
Male	147 (20.1%)	585 (79.9%)	0.0003	0.0007
Female	15 (8.7%)	157 (91.3%)		
ALT level				
Normal	97 (16.7%)	484 (83.3%)	0.2059	0.2311
Elevated	65 (20.1%)	258 (79.9%)		

Fisher's exact test. P2 for Chi-square test.
 $P < 0.05$ is considered statistically significant

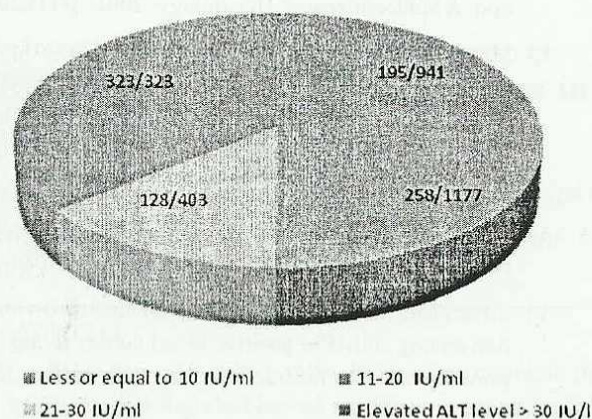


Figure (1): Proportions of selected samples according to ALT level (negative for all routine serological assays) tested for anti-HBc

Discussion

The risk of infection with transfusion-transmitted viruses has been reduced remarkably since the introduction of serological screening. However, a zero-risk blood supply remains a goal⁽¹⁰⁾. The risk of transfusion-transmitted HBV infection has reduced by screening all blood donations for HBsAg since 1970⁽¹¹⁾. However, screening of blood bank donors for HBsAg does not totally eliminate the risk of HBV infection through blood transfusion⁽¹²⁾.

In transfusion, anti-HBc screening has been used initially as a surrogate marker for non-A, non-B hepatitis⁽¹³⁾. However, its use was no longer relevant due to the implementation of anti-HCV screening tests. The importance of anti-HBc assay has resurfaced as a potential tool to prevent occult HBV transmission⁽¹⁴⁾. Testing of blood donors for anti-HBc has been implemented in several countries, including the USA, France, Brazil, Greece, and Japan⁽¹⁵⁾.

The prevalence of anti-HBc in the prospective blood donors is proportional to the incidence of HBsAg in the general population. Anti-HBc prevalence in Europe and North America is quite low; an anti-HBc prevalence of 0.07% in the UK and 1.5% in Germany has been reported⁽²⁾. In areas of higher prevalence of HBsAg; anti-HBc prevalence was higher such as Greece (15.8%), China (70.0%) and Ghana (83.6%)⁽¹⁰⁾.

The frequency of anti-HBc in Egyptian blood donors is not well studied. In order to evaluate the role of anti-HBc in blood screening for HBV infection, 904 HBsAg non-reactive blood samples (either with elevated (323) or normal (581) ALT

level) were tested for the presence of total anti-HBc. One hundred and sixty two samples were reactive (17.92 %). The present study showed 20.12 % and 16.7% anti-HBc positivity for samples with elevated and normal ALT level respectively. This result was higher than previously reported in the few studies recently concerned with the prevalence of Anti-HBc in Egyptian blood donors^(4,10).

In conclusion, anti-HBc antibody should be tested routinely on blood donor-volunteers to avoid the adverse implications of missed occult HBV infection. Rejection of all anti-HBc positive blood donors will be beneficial in decreasing the risk of HBV transmission with its potential consequences particularly in immunocompromised recipients.

References

- Schmidt M et al. Anti-HBc screening of blood donors: a comparison of nine anti-HBc tests. *Vox Sang*; 2006, 91(3): 237-243.
- Dhawan H. K. et al. Anti-HBc screening in Indian blood donors: Still an unresolved issue. *World J Gastroenterol*; 2008, 14(34): 5327-5330.
- Schreiber GB, Busch MB, Kleinman SH, Korelitz JJ. The risk of transfusion-transmitted viral infection. The retrovirus epidemiology donor study. *N Engl J Med*; 1996, 334:1685-1690.
- El-Sherif AM, Abou-Shady MA, Al-Hiatmy MA, Al-Bahrawy AM, Motawea EA. Screening for hepatitis B virus infection in Egyptian blood donors negative for hepatitis B surface antigen. *Hepatol Int*; 2007, 1:469-470.
- Elghannam DM, Aly RM, Goda EF, Eltoraby EE, Farag RE. Clinical significance of antibody to hepatitis B core antigen in multitransfused hemodialysis patients. *Asian J Transfus Sci*; 2009, 3(1): 14-17.

6. Yotsuyanagi H et al. Frequent presence of HBV in the sera of HBsAg-negative, anti-HBc-positive blood donors. *Transfusion*; 2001, 41(9): 1093-1099.
7. Sacher RA, Schreiber GB, Kleinman SH. Prevention of transfusion-transmitted hepatitis. *Lancet*; 2000, 355: 331-332.
8. Zervou EK, Dalekos GN, Boumba DS, Tsianos EV. Value of anti-HBc screening of blood donors for prevention of HBV infection: results of a 3-year prospective study in Northwestern Greece. *Transfusion*; 2001, 41: 652-658.
9. Said ZNA et al. High prevalence of occult hepatitis B in hepatitis C-infected Egyptian children with haematological disorders and malignancies. *Liver International*; 2009, 29 (4): 518-524.
10. El-Zayadi AR et al. Anti-HBc screening in Egyptian blood donors reduces the risk of hepatitis B virus transmission. *Transfusion Medicine*; 2008, 18: 55-61.
11. Hennig H, Puchta I, Luhm J, Schlenke P, Goerg S, Kirchner H. Frequency and load of hepatitis B virus DNA in first-time blood donors with antibodies to hepatitis B core antigen. *Blood*; 2002, 100: 2637-2641.
12. Conjeevaram HS, Lok AS. Occult hepatitis B virus infection: A hidden menace? *Hepatology*; 2001, 34(1):204-206.
13. Martelli CMT, Turchi MD, Souto FJD, Sáez-Alquézar A, Andrade AL, Zicker F Anti-HBc testing for blood donations in areas with intermediate hepatitis B endemicity. *Rev Panam Salud Publica/Pan Am J Public Health*; 1999, 6(1):69-73.
14. Kleinman SH, Busch MP. HBV: amplified and back in the blood safety spotlight. *Transfusion*; 2001, 41:1081-1085.
15. Silva CMD. et al. Low rate of occult hepatitis B virus infection among anti-HBc positive blood donors living in a low prevalence region in Brazil. *Journal of Infection*; 2005, 51: 24-29.

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الكشف عن الأجسام المضادة للفيروس الإلتهاب الكبدى (ب) بين متبرعى الدم المصريين السلبيين للضد السطحى للحد من انتقال العدوى

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على الرغم من أن نسبة الإصابة بالإلتهاب الكبدى الفيروسي (ب) عن طريق نقل الدم قد قلت بصورة واضحة على مدى السنوات القليلة الماضية بعد استخدام الكشف عن الضد السطحى للفيروس إلا أنه قد تم توثيق انتقال العدوى نتيجة لنقل وحدات دم سالبة للضد السطحى. تهدف هذه الدراسة لتعيين معدل تواجد الأجسام المضادة للفيروس الإلتهاب الكبدى (ب) بين متبرعى الدم المصريين السلبيين للضد السطحى. وذلك لتقييم فاعلية الكشف عن الأجسام المضادة للفيروس كطريقة للمسح الوبائى قبل التبرع بالدم للحد من انتقال العدوى. ولقد شملت الدراسة ٣٠٤٣ متبرع تم فحصهم طبقاً للاختبارات الروتينية الخاصة بينك الدم و المتضمنة الكشف عن الضد السطحى لفيروس الإلتهاب الكبدى (ب)، الأجسام المضادة لفيروس الإلتهاب الكبدى الوبائى (سى) وكذلك الأجسام المضادة لفيروس نقص المناعة البشرية. تم تعيين الأجسام المضادة للفيروس الإلتهاب الكبدى (ب) فى ٩٠٤ حالة سالبة للضد السطحى (٥٨١ حالة ذات مستوى طبيعى لإنزيمات الكبد و ٣٢٣ حالة ذات مستوى مرتفع). و قد وجدت الأجسام المضادة للفيروس الإلتهاب الكبدى (ب) فى ١٧,٩٪ من العينات تحت الدراسة. نستخلص من هذا أن استخدام الكشف السيولوجى عن الأجسام المضادة للفيروس الإلتهاب الكبدى (ب) لابد أن يعمم بشكل روتينى على المتطوعين المتبرعين بالدم بجميع مراكز و بنوك الدم بجمهورية مصر العربية و ذلك للتقليل من نسب الإصابة.