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The Role of Hepatitis B Core Antibody Testing in Improving Blood Safety in Resource-Limited Countries Study on Voluntary Blood Donors Fayoum, Egypt

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Abstract

Background: Transmission of hepatitis B virus (HBV) via hepatitis B surface antigen (HBsAg) negative blood donors has been reported. HBsAg is still the only mandatory HBV screening test of blood donors in Egypt due to high cost of DNA testing of all collected blood. Many resource- limited countries have implemented screening antibodies to hepatitis B core antigen (anti-HBc) to further improve transfusion safety. The objective of study was to evaluate the significance of screening anti-HBc to reduce the risk of transfusion transmitted HBV infection in Egypt.

Study Design and Methods: The study was conducted on 800 voluntary blood donors negative for HBsAg, hepatitis C antibody (HCVAb) and human immunodeficiency virus Ab. They were subjected to screening for anti-HBV core antibodies (total). Anti-HBc-positive samples were further tested for the antibodies to HBsAg (anti-HBs), and "anti-HBc alone" sera were tested for HBV DNA.

Results: Among 800 healthy voluntary donors, 99 (12.37%) were anti-HBc-positive including 78 anti-HBs positive. The remaining 21 donors were anti-HBc alone, 2 of which (9.52%) were HBV DNA-positive.

Conclusion: Greater consideration should be given to the implementation of anti-HBc as an additional screening test for blood donors in Egypt as the most cost-effective measure for further improvement of transfusion safety.

Keywords: Anti-HBc; Anti-HBc alone; Blood donors; Occult HBV infection

Introduction

Hepatitis B virus (HBV) remains a major public health problem. It is estimated that approximately 400 million people worldwide are chronically infected with HBV, where Egypt is considered as an area of intermediate endemicity [1]. Hepatitis B virus (HBV) is easily transmitted by blood products as both cellular and plasma-derived components may be infected [2].

Transfusion-transmitted HBV played a major role in the spread of this infection some decades ago all around the world, and is still a threat in developing countries, where the prevalence of this infection is higher and the donor selection and screening procedures are less tight [2,3].

Occult hepatitis B infection (OBI) is defined by the presence of HBV DNA in the liver tissue of individuals who test negative for HBsAg, regardless of the detection of HBV DNA in serum [4]. OBI was reported for the first time almost 30 years ago in a case report of HBV infection through blood transfusion by an antibody to hepatitis B core antigen (anti-HBc) only positive donor [5].

In most developed countries, nucleic acid amplification testing (NAT) has been introduced along with serological testing for HBV, hepatitis C virus and human immunodeficiency virus in order to enhance blood safety [6-8].

In contrast, limited-resources developing countries cannot implement NAT for screening of all donors collected blood and are relying on proper donor selection which is complemented by sensitive cost effective serological screening tests to exclude the transmission of infective agents [9,10].

In Egypt, screening for HBsAg is the only mandatory screening test for the detection of Hepatitis B virus (HBV) infection in blood banks [1], only four qualified blood centres are already implementing NAT in Egypt, and these are National Cancer Institute (NCI) blood bank, blood bank of Nasser Institute, blood bank of EL-Shabrwishy Hospital (Private hospital) and the Egyptian Organization for biological products and vaccines (VACCERA) blood bank [11], given the constrained economy, lack of appropriate infrastructure and inadequate trained personnel that limit its implementation in all blood banks [12,13].

New cost-effective strategies and stringent donor selection implementation are very important measures to ensure blood safety in limited- resources countries.

The aim of this study was to determine the presence of HBcAb and HBV DNA among Fayoum university hospital blood bank HBsAg negative healthy blood donors to evaluate the significance of implementing screening anti-HBc to reduce the risk of transfusion transmitted HBV infection in Egypt blood banks.

Materials and Methods

Blood samples

The present study included 800 samples from blood donors negative for anti- hepatitis C antibody (HCV), anti-human immunodeficiency virus (HIV), and HBsAg collected over a period of 6 months (from April 2014 to September 2014) in Fayoum university hospital blood bank.

Detection of serologic markers

Serum HBV total anti-HBc was performed by ELISA technique, Monoliza Anti-hepatitis B core Plus-Bio-Rad, according to manufacturer's instructions on all donor samples. Positive samples were subjected to quantitative detection of antibodies to hepatitis B surface (anti-HBs) with commercially available kits (ETI-AB-AUK-3, Dia Sorin-Italy). Serum anti-HBs titers >10 IU/L was considered positive.

Detection of hepatitis B viral DNA

HBV DNA level was estimated for blood units with low or undetectable serum anti-HBs levels "anti-HBc alone" using real time polymerase chain reaction (PCR) automated system. HBV fluorescence quantitative diagnostic kit (Hangzhou Bioer Technology, China). The kit combines the Viral DNA extraction and the technologies of nucleic acid amplification and hybridization probe. Real-time PCR was performed on the Chromo4 DNAEngine Peltier thermal Cycler (BIO-RAD, Hercules, CA). Thermal profile was set according to manufacturer's guideline.

Statistical analysis

Data were statistically described in terms of frequencies (number of cases) and percentages when appropriate. All statistical calculations were done using computer programs Microsoft Excel 2003 (Microsoft Corporation, NY, and USA) and SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) version 15 for Microsoft Windows.

Results

Serological results

All participants were negative for HBsAg. 99/800 (12.37%) of blood donors were negative for HBsAg and positive for anti-HBc. Anti-HBs antibody was detected in 78/99 (78.78%) of HBsAg negative and anti-HBc positive samples, with serum levels >10 IU/L.

Molecular findings

Detection of HBV-DNA performed on all samples that were negative for HBsAg and positive for anti-HBc antibody only by use of real time PCR technique. HBV-DNA was detected in 2 out of 21 anti-HBc positive specimens (9.52%).

Results of antibodies to hepatitis B core, antibodies to hepatitis B surface and hepatitis B virus DNA among the studied blood donors are summarized in Figure 1.

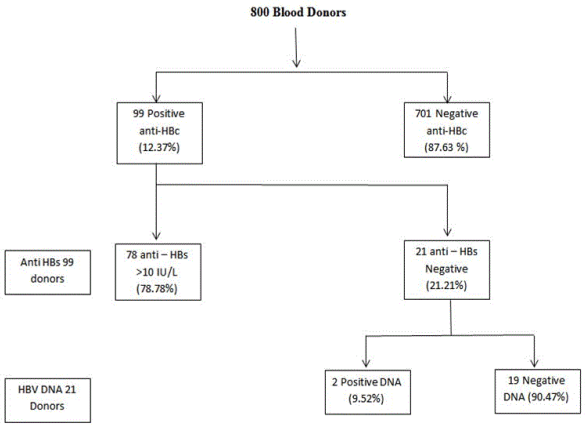

Figure 1: Results of antibodies to hepatitis B core, antibodies to hepatitis B surface and hepatitis B virus DNA among the studied blood donors.

Discussion

OBI is defined as the presence of HBV DNA in the liver (with detectable or undetectable HBV DNA in the serum) of individuals who tested negative for HBsAg [14,15]. Occult HBV is transmissible by blood transfusion, although the transmission rate is considered to be very low. The clinical outcome of OBI transmission mainly depends on the immune status and copies of HBV DNA in blood products of the recipient [16]. At present, HBsAg detection is the only obligatory diagnostic screening test for HBV infection in blood transfusion centers in Egypt [12,13]. We examined 800 HBsAg negative sera obtained from healthy blood donors and found that 12.37% of them were positive for anti-HBc, which is comparable to two previous Egyptian studies with a prevalence of 14.2% and 10.9% of HBsAg negative volunteer blood donors [1,17]. The study is also comparable to the older anti-HBc prevalence rates reported among HBsAg-negative blood donors in India; 10.01% [9] and 11.2% in Syria [10], respectively.

The prevalence of anti-HBc only in Europe and North America is overall quite low. A prevalence of 0.07% in the UK and 1.5% in Germany was reported [18,19]. In areas of higher HBV infection prevalence about 20%-70% of subjects are positive for anti-HBc antibody [20].

In our study the overall prevalence of occult HBV infection in healthy blood donors was 9.52% among anti-HBc positive alone individuals. Different results have been reported in other studies regarding the rate of OBI in blood donors. These differences in the occult HBV prevalence may be attributed to race and ethnicity, geographical area and the HBV subtypes [21,22]. The frequency of HBV-DNA detected in HBsAg negative samples also varies considerably according to the prevalence of the infection. In Northern countries where the prevalence of chronic infection is less than 1%, no more than 5% of HBsAg negative/anti-HBc positive blood donor samples contain HBV-DNA [19,23]. In contrast, higher OBI levels in HBsAg-negative blood were recorded in several published reports. In India, the prevalence was 24% [24] and in a published study from

Korea, 16% of the studied sample was found to be positive for OBI **[25]**. Other reports of the prevalence of HBV-DNA in only anti-HBc positive blood donors revealed 0% in Brazil [26], 0.3% in china [27], 1.1% in Japan [28], 3.2% in Saudi Arabia [29] and 12.7% in Ghana [30]. Some information is available regarding the infectivity of anti-HBc-only blood products or organs. The infectivity of blood donations containing anti-HBc as the only marker of HBV infection has been known for several decades and indicated that no more than 4% of recipients of anti-HBc-only blood developed HBV infection post-transfusion [31]. However, Mosley reported 17% infectivity of antiHBc-only blood products [22,32]. Anti-HBc screening has the potential of excluding the vast majority of occult HBV infection but this exclusion of anti-HBc positive donors is impractical in countries where HBV infection is prevalent and higher than 20% of the populations are anti-HBc positive [33]. The use of HBV anti core testing to eliminate the residual transfusion risk of transmission of HBV has not been evaluated in Egypt.

Conclusion

One of the main mechanisms for OBI transmission is most likely through infected blood and its components and our findings revealed that OBI exists among Egyptian blood donors. Screening for HBsAg in blood banks in Egypt is not sufficient to completely exclude HBV infection in an intermediately endemic area like Egypt. NAT cannot be implemented for screening of all donors collected blood because of the high cost for a limited resources country like Egypt. New screening policy to further increase the safety of blood transfusion is strongly indicated.

Anti-HBc antibody should be tested routinely on blood donor volunteers, and if the sera become positive regardless of anti-HBs titer, the blood should be discarded. Further testing for HBV-DNA is appropriate to follow up the blood donor patient for HBV infection.

Conflict of Interest

There is no conflict of interest with any organization regarding the material discussed in the manuscript.

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