

Prevalence of "anti-HBc alone" among Syrian blood donors

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Abstract

Introduction: We aimed to evaluate the prevalence of "anti-HBc alone" among Syrian blood donors, highlighting the possibility of representing occult HBV infection.

Methodology: Sera of 3,896 healthy blood donors were tested for both HBsAg and anti-HBc. HBsAg-negative, 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: Of 3,830 HBsAg-negative donors, 63 were "anti-HBc alone" donors, five of whom were HBV DNA positive.

Conclusions: Greater consideration should be given to the "anti-HBc alone" serological profile in blood screening, premarital testing, organ transplantation tests, and other HBV transmission-related procedures in Syria.

Key words: anti-HBc; anti-HBc alone; occult HBV infection; blood donors; Syria.

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Introduction

Hepatitis B virus (HBV) infection is a serious public health issue causing more than a million annual deaths worldwide [1]. In Syria, it is intermediately prevalent (5.62%) [2], leading to significant clinical and economic burdens due to chronic infection consequences, such as cirrhosis and hepatocellular carcinoma (HCC) [3].

In general, screening for HBV infection is usually based on the detection of serum hepatitis B surface antigen (HBsAg). The disappearance of this antigen is considered an indication of HBV clearance and infection resolution [4]. Previous reports have shown, however, that HBsAg might not be detected in the serum of infected patients. This can be attributed to chronicity with HBsAg levels below the detection limits [5], HBsAg synthesis downregulation [6], or S gene mutations leading to detection inefficiency [7].

Absence of serum surface antigen and its antibodies (anti-HBs) might be accompanied by the presence of antibodies to hepatitis B core antigen (anti-HBc). This "anti-HBc alone" serological profile is frequently observed in HIV-infected individuals, intravenous drug abusers, pregnant women, and patients co-infected with HBV and hepatitis C virus [7]. Albeit inadequately explained, "anti-HBc alone" might represent occult HBV infection in which HBV

DNA is present in the liver and/or blood while serum HBsAg is undetectable [6]. Still, it is undervalued locally, as HBsAg is almost the only serological test relied on for blood donation screening, premarital testing, organ transplantation operations, and diagnostic investigations.

This study aimed to evaluate the prevalence of "anti-HBc alone" serological profile among blood donors in Syria, highlighting the possibility that it may represent an occult HBV infection, and to alert healthcare providers and decision makers in Syria to this significant serological profile.

Methodology

This prospective cross-sectional cohort study enrolled 3,896 healthy blood donors assigned to different blood transfusion centers in all Syrian geographic areas. Five milliliters of peripheral blood were drawn from all enrolled donors during the second half of 2011. Written informed consent had been obtained at the time of sampling.

All sera were tested for both HBsAg and anti-HBc. HBsAg-negative, anti-HBc-positive sera were further tested for the antibodies to hepatitis B surface antigen (anti-HBs). All serological tests were carried out using chemiluminescent microparticle immunoassay (CMIA) kits on an ARCHITECT System (Abbott,

Lake Forest, Illinois, USA). "Anti-HBc alone" sera were stored at -80°C for HBV DNA testing. Viral DNA was isolated using MagNA Pure Compact Nucleic Acid Isolation Kit (Roche Diagnostics, Mannheim, Germany), and quantitative real-time PCR was performed on the LightCycler instrument using LC-FastStart DNA Master HybProbes kit (Roche Diagnostics, Mannheim, Germany), targeting the HBV surface gene as previously described [8].

Results

HBsAg was detected in 66 of 3,896 donors. In addition, 402 of 3,896 donors (10.32%) were HBsAg-negative, anti-HBc positive, 63 of whom were "anti-HBc alone" donors. Five anti-HBc alone donors (5 of 63; 7.9%) were HBV DNA positive with an average viral load of 2.5E+04 copies mL⁻¹.

Discussion

In the present study, prevalence of anti-HBc-positive, HBsAg-negative serological profile among Syrian blood donors was 10.32%, a comparable rate to those reported in Egyptian (10.3%) and Lebanese (11%) blood donors [9,10], but far different from those found in Saudi Arabia (20.8%) [11] and Western European countries such as Germany (1.4%) and Italy (4.8%) [12,13]. This enormous variation in anti-HBc prevalence reflects the differences in HBV endemicity among these countries [14]. More attention should be paid to the anti-HBc prevalence rate among countries suffering from HBV infection such as Syria (which has an HBsAg prevalence rate of 5.62%) [2], particularly because anti-HBc positivity represents a risk of HBV transmission [8,14].

False positivity of anti-HBc was diminished in our study by the use of a chemiluminescent microparticle immunoassay (CMIA), in which samples are treated with reducing agents [7]. The observation of a relatively high anti-HBc positivity rate, in spite of using highly specific detection methods, supports our concerns about this serological profile in Syria.

This national study suggests that 1.62% of healthy individuals are "anti-HBc alone". Occult HBV infection was proven in five "anti-HBc alone" individuals (7.9%) with relatively low viral loads. However, the actual prevalence of occult HBV infection with the "anti-HBc alone" serological profile might be higher if we performed the real-time PCR assay in triplicate to enhance the detection rate, as previously recommended [15]. Nevertheless, HBV DNA positivity rates reported among "anti-HBc alone" subjects in previous studies were highly variant,

ranging between 2.9% and 22.8%. These discrepancies can be explained by differences in HBV endemicity, the studied population, and the efficiency of HBV DNA detection methods [6].

"Anti-HBc alone" might be attributed to (i) a resolved infection with undetectable anti-HBs or (ii) a formation of HBsAg-anti-HBs immune complexes [7], and hence it is not solely considered to be proof of infectivity. However, as our study showed, "anti-HBc alone" donors cannot be acquitted of potential occult HBV infection demonstrated by HBV DNA positivity with undetectable low-level or mutated HBsAg [5,6].

Conclusion

In conclusion, "anti-HBc alone" is frequently encountered among healthy individuals in Syria. Greater consideration should be given to this serological profile in diagnostic investigations, blood screening, premarital testing, organ transplantation tests, and other HBV infection transmission-related procedures. This should help reduce the risk of HBV transmission and its consequences, particularly among immunocompromised and repeatedly transfused patients.

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