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Isolated Antibody to Hepatitis B Core Antigen in Egyptian Patients with Chronic Hepatitis C Virus Infection

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Abstract

Background: Occult hepatitis B virus (HBV) infection is characterized by the presence of HBV infection with undetectable hepatitis B surface antigen (HBsAg). Such infections have been reported to be common in patients with chronic hepatitis C virus (HCV) infection.

Objective: This study investigates the prevalence of occult HBV infection in patients with chronic liver disease by HCV.

Methods: In a 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). All samples negative for HBsAg and positive for anti-HCV were tested for the presence of anti-hepatitis B core antigen (anti-HBc).

Results: One hundred and forty samples (4.6 %) were positive for anti-HCV. Of these 140 cases, 36 (25.71 %) were anti-HBc positive.

Conclusion: Occult hepatitis B infections occur frequently in patients with chronic hepatitis C liver disease.

Keywords: Occult Hepatitis B; HBV; HCV; Coinfection; Prevalence.

Introduction

Hepatitis B virus (HBV) and hepatitis C virus (HCV) infections account for a substantial proportion of liver diseases, including chronic hepatitis, cirrhosis, and liver cancer worldwide[1,2]. It is estimated that there are 350 million HBV carriers and 170 million HCV carriers worldwide[3]. Both viruses share similar risk factors and modes of transmission and as a consequence, combined HBV and HCV infection is frequent especially in areas where the two viruses are endemic, and among people at high risk of parenteral infections[3,4] HCV infection is diagnosed by the detection of specific antibodies and viral RNA in the serum. HBV infection is usually diagnosed when the circulating hepatitis B surface antigen (HBsAg) is identified[5]. The presence of HBV infection with undetectable HBsAg resulted in the introduction of the concept of occult, silent or latent HBV infection[6]. In most cases, antibody to hepatitis B core antigen (anti-HBc) is detectable, and thus anti-HBc is believed to be a surrogate marker for latent carriers[7].

Occult HBV infection has frequently been identified in patients with HCV-related chronic hepatitis. Clinical interaction of HCV and occult HBV infection is still controversial. Some studies report that cirrhosis is seen more frequently in those patients with HCV and occult HBV co-infection than in those with HCV infection alone[8]. Patients with active HBV and HCV co-infection tend not to respond to interferon treatment. Some studies show that such low interferon response exists in patients with HCV and occult HBV co-infection[8,9].

In view of the high incidence of HBV and HCV infections among the Egyptian population, the aim of this study is to determine the prevalence of anti-HBc in patients with hepatitis C as a screening test for occult HBV infection.

Material and Methods

Study Population: The study was conducted on 3043 random blood samples collected from healthy blood donor volunteer, who were referred

to the blood donation center at the teaching Hospital of Suez Canal University between January and August 2009. Briefly, a 10 ml blood sample was collected from each donor during the donation visit, centrifuged at 2500 rpm and serum sample were stored at – 80oC.

Biochemical tests for liver function: The concentration of alanine aminotransferase (ALT) was determined in all samples.

Routine serological assay: All blood specimens were tested on sequential basis for routine serological tests according to predefined protocol s of blood banking safety requirements by the Ministry of Health and Population (MOHP) issued 1994 comprised HBsAg, anti-HCV, and anti-HIV I / II. Detection of HBsAg and anti-HCV was done using the commercially available ELISA kit (DiaSorin, Italy), while detection of anti-HIV I / II, was done using ELISA kit (TETRA, Biotest, Germany).

Anti-HBc assay: Detection of total anti-Hbc was performed for all blood samples that are positive for anti-HCV using ELISA kit (DiaSorin, Italy).

Results

The studied sample included 3043 randomly selected blood donors with a mean age of 28.3 ± 6.8 years. Donors of ages between 21-30 years constituted the largest proportion (57.5%) with a median age of 25 years (Table I). 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 tested for routine serological viral markers.

HBsAg was detected in donations from 58 males with a mean age of 29.93 ± 7.9 years and a single female aged 25 years. HCV Ab was detected in donations from 135 males with a mean age of 32.74 ± 8.32 years, and 5 females with a mean age of 31.8 ± 10.55 years. HIV I / II Ab was not detected in any blood donation (Table II).

The prevalence of anti-HBc among the one hundred and forty patients infected with hepatitis C was 25.71 %. Comparison between tested samples regarding to Anti-HBc is illustrated in (Table III). There was a significant association between age and anti-HBc in HCV patients. Gender and ALT level showed no significant association.

Table (I): Age and gender distribution of selected blood donors

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Age range (years)	Male		Female		Total	
	No (%)	Age (median)	No (%)	Age (median)	No (%)	Age (median)
< 21	295 (10.29)	19	33(18.86)	19	328 (10.78)	19
21-30	1665 (58.16)	25	82(46.86)	25	1750 (57.50)	25
31-40	720 (25.10)	34	51(29.14)	36	771(25.34)	34
41-50	169 (5.9)	43	9(5.14)	9	178 (5.85)	43
> 50	16 (0.55)	52	------	-----	16 (0.53)	52
All	2865 (94.25)	27	178(5.75)	27	3043 (100)	27

Table (II): Age and gender distribution of the volunteers with rejected * blood donations

Age range (years)	Male: 2865 (94.15%)		Female: 178 (5.85 %)		Total 3043 (100 %)	
	No (%)	Age■	No (%)	Age■	No (%)	Age
HBsAg	58 (2.03)	29.98 ±7.81	1 (0.56)	25	59 (1.94)	29.89 ± 7.77
Anti-HCV	135(4.7)	32.74 ± 8.32	5(2.81)	31.8 ± 10.55	140 (4.6)	32.71 ± 8.36
HIV I / II Ab	0 (0)	-----	0 (0)	------	0 (0)	-----
All	192 (6.7)	31.91 ± 8.25	6 (3.4)	30.67 ± 9.83	198 (6.5)	31.87 ± 8.27

* Rejection according to routine serological assays (HBsAg, anti-HCV, & anti-HIV I / II).

■ Data are expressed as mean ± SD.

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Table (III): Distribution of total anti-HBc among HCV patients

Variables	Positive anti-HBc (No=36)	Negative anti-HBc (No=104)	P Value	
			P1	P2
Age (years)				
≤ 30	10 (15.4%)	55 (84.6 %)	0.0116	0.0160
> 30	26 (34.7 %)	49 (65.3 %)		
Gender				
Male	34 (25.2 %)	101 (74.8 %)	0.6030	0.8233
Female	2 (40 %)	3 (60 %)		
ALT level				
Normal	23 (25.3%)	68 (74.7%)	1.0000	0.8712
Elevated	13 (26.5%)	36 (73.5%)		

P1 for Fisher's exact test. P2 for Chi-square test.
P < 0.05 is considered statistically significant.

Discussion

HBV and HCV infections account for the majority of cases of chronic liver disease worldwide, including chronic hepatitis, cirrhosis, and hepatocellular carcinoma (HCC). In countries where HCV infection is widespread, prevalence of HBV infection is also reported as high, and consequently multiple HBV and HCV infection is frequent and is generally found to be associated with more severe liver damage[10].

HCV-infected patients should be tested for HBV markers to determine those who should receive HBV vaccination and those who need anti-HBV treatment. For patients with chronic HCV infection, prevention of HBV infection is critical, because this viral infection can be particularly severe and may adversely affect disease outcome[4].

Clinical data obtained from chronic HBV carriers superinfected with HCV suggest that HCV may inhibit HBV replication. This hypothesis is supported by the fact that patients with chronic HCV infection frequently have a special form of HBV infection, termed occult HBV infection[5,11,12].

Several recent studies have indicated that this occult HBV infection can be found in patients with chronic HCV infections at various frequencies[5,11,13,14] Meanwhile, accumulating evidence suggests that were found anti-HBc positive patients almost invariably have occult HBV infection[15]. In a previous study 71% of HCV Egyptian patients were fasand to by positive for anti-HBc [16]. While in our study 25.71 % of the patients with HCV infection for whom there is no serological evidence for HBV, when screened with HBsAg, were positive for anti-HBc. There is a significant association between positivity of anti-HBc and age in HCV patients, 34.7 % of them > 30 years (p=0.0116).

The high prevalence of occult HBV infection in HCV patients has been suggested to have clinical implications in the pathogenesis of HCV induced chronic liver disease[3]. Additionally it has been reported that the response of interferon treatment is lower in patients with chronic HCV- infection having occult HBV than those without HBV infection[5,17].

In conclusion, isolated anti-HBc sero-pattern is a common finding in patients with chronic HCV infection, and may represent an occult infection in a substantial Percantage age screening strategy that tests only for HBsAg in HCV infected patients will miss a large number of individuals with isolated anti-HBc, and a considerable number of patients with occult HBV infection. Addition of anti- HBc screening is recommended to avoid the adverse implications of missed HBV occult co-infection.

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الأجسام المضادة لفيروس الإلتهاب الكبدى (ب) المعزولة فى المرضى المصريين الذين يعانون من الإلتهاب الكبدى الوبائى المزمن (سى)

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الإلتهاب الكبدى الفيروسى (ب) المستتر يتميز بوجود الحمض النووى للفيروس فى عدم وجود المستضد السطحى (HBsAg). وهذه الحالات قد أفادت أن تكون شائعة في المرضى الذين يعانون من الالتهاب الكبدي الوبائي المزمن (سي). وتهدف هذه الدراسة إلى تعيين معدل تواجد الإلتهاب الكبدى الفيروسى (ب) المستتر بين هولاء المرضى. وشملت الدراسة ٣٠٤٣ متبرعاً تم فحصهم طبقا للإختبارات الروتينية الخاصة ببنك الدم و المتضمنة الكشف عن المستضد السطحى لفيروس الإلتهاب الكبدى (ب) (HBsAg) ، الأجسام المضادة لفيروس الإلتهاب الكبدى الوبائى (سى) (anti-HCV) وكذلك الأجسام المضادة لفيروس نقص المناعة البشرية (anti-HIV I/II). تم تعيين الأجسام المضادة للب فيروس الإلتهاب الكبدى (ب)(anti-HBc) فى الحالات السالبة للمستضد السطحى والموجبة للأجسام المضادة لفيروس الإلتهاب الكبدى الوبائى (سى) . ستة وثلاثون حالة من الحالات الموجبة للأجسام المضادة لفيروس الإلتهاب الكبدى الوبائى (سى) وجد بها الأجسام المضادة للب فيروس الإلتهاب الكبدى (ب) بمعدل استيطان ٢٥,٧١ ٪. ونخلص من ذلك أن عدوى الإلتهاب الكبدى الفيروسى (ب) المستتر تحدث بشكل متكرر بين المرضى الذين يعانون من الالتهاب الكبدي الوبائي المزمن (سي).