Serological pattern of hepatitis B virus among HBsAg negative blood donors in Alexandria, Egypt

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النموذج المصلي لفيروس التهاب الكبد "بي" بين المتبرعين بالدم السلبيين للمستضَدّ السطحي لفيروس التهاب الكبد في الإسكندرية، مصر إنجي محمد الغيطاني، عزة جلال فرغلي

الخلاصة: أجرّت الباحثتان هذه الدراسة في الإسكندرية، مصر، للتعرُّف على تونُّع مختَلف واسهات فيروس الالتهاب الكبدي "بي" بين المتبرعين بالدم الذين يبدون أصحاء، ويكون لديهم المستضد السطحي لفيروس التهاب الكبد سلبياً، وللتعرُّف على عوامل الاختطار المستقلة الكبرى. وقد اتضح وجود بيِّنات على تعرُّض سابق بفيروس الالتهاب الكبدي "بي" لدى 148 متبرعاً من بين 508 متبرعين تم تحرَّي الفيروس لديهم (29.1). وقد كان أكثر الواسهات شيوعاً هو المضاد اللبي لفيروس الالتهاب الكبد سلبياً، وللتعرُّف على عوامل الاختطار المستقلة الكبرى. وقد اتضح وجود بيِّنات على تعرُّض سابق بفيروس الالتهاب الكبدي "بي" لدى 148 متبرعاً من بين 508 متبرعين تم تحرَّي الفيروس لديهم (29.1). وقد كان أكثر الواسهات شيوعاً هو المضاد اللبي لفيروس الالتهاب الكبدي اليات لدى 20 من بين 508 من بين 508 متبرعين تم تحرَّي الفيروس لديهم (29.1). وقد كان أكثر الواسهات شيوعاً هو المضاد اللبي لفيروس الالتهاب الكبدي الكبري الذي لوحظ لدى 124 من بين 508 من بلترعين بالدم (24.4)، وكان لدى نصفهم (63 متبرعاً من أصل 124 متبرعاً) إيجابية تقتصر على المضاد اللبي لفيروس الالتهاب الكبدي الياتي لديوس الالتهاب الكبدي "بي" في حكر منالته بعروس الالتهاب الكبدي "بي" في الاتهاب الكبدي "بي" في 20.5 من معدًا انتشاره و20.5 من وقد (20.5)، وكان معدراً من أصل 124، معروس الالبي لفيروس الالتهاب الكبدي "بي" في 120. معدراً مع المضاد اللبي لفيروس الالتهاب الكبدي "بي" في 20.5 من معدراً مع المن اللبي لفيروس الالتهاب الكبدي الي" في 20.5 من معدراً مع المن اللبي لفيروس الالتهاب الكبدي "بي" في 20.5 من معدراً مع المن الي المند اللبي لفيروس الالتهاب الكبدي "بي" في 20.5 من معدراً مع المن المن المن مع المضاد اللبي لفيروس الالتهاب الكبدي الي أل وحظ در المعن المادة لفيروس الالتهاب الكبدي الي أل ومعالم الخطار المنتقلة المرتبة الأرجحية 20.5 من معدي مع مع المن المادة المعاد اللبي في مدون أل وحظ در من الواسمات هي ومدون المعاد السبق معدرا مع مع مع مع والم وعن المان من 20.5 من معررا مع المادة المعاد اللبي في معدوي المام من 20.5 من معروس الالتهاب الكبدي الي الارتفاع معن مع معم مع مع مع مع مالمادة المعادة المعادة المادة المادة المعادة المعروس الي معروس الالتهاب الكبدي الي أل واحداً منهم مع مع مع ما المن ووى الغور مع مع مع مي مع مع

ABSTRACT This study in Alexandria, Egypt was conducted to investigate the distribution of different hepatitis B virus (HBV) markers in apparently healthy blood donors who were hepatitis B surface antigen (HBsAg) negative, and to determine the major independent risk factors. Evidence of past exposure to HBV was found in 148/508 screened donors (29.1%). The most prevalent marker was anti-HBc in 124/508 donors (24.4%), half of whom (63/124) showed anti-HBc only. Anti-HBs prevalence was 15.9%, combined anti-HBc and antiHBs was 12.0% and anti-HBe was 5.7%. Independent risk factors associated with the presence of at least 1 marker were: being married (OR 3.82), history of blood transfusion (OR 3.04) and parenteral antibilharzial treatment (OR 2.49). Receiving a full HBV vaccination schedule was reported by 39 donors, but only 1 of them had isolated anti-HBs. The relatively high prevalence of HBV exposure necessitates solid infection control measures and adult vaccination programme awareness.

Sérologie du virus de l'hépatite B chez des donneurs de sang négatifs pour l'antigène de surface du virus de l'hépatite B à Alexandrie (Égypte)

RÉSUMÉ La présente étude, menée à Alexandrie (Égypte), a évalué la répartition des différents marqueurs du virus de l'hépatite B chez des donneurs de sang apparemment en bonne santé qui étaient négatifs pour l'antigène de surface de l'hépatite B, et a identifié les principaux facteurs de risque indépendants. La preuve d'une exposition antérieure au virus de l'hépatite B a été retrouvée chez 148 des 508 donneurs dépistés (29,1%). Le marqueur le plus prévalent était l'anti-HBc, observé chez 124 des 508 donneurs (24,4%), dont la moitié (63/124) ne présentait que ce marqueur. La prévalence de l'anti-HBs était de 15,9%, celle de l'anti-HBc et anti-HBs combinés était de 12,0% et celle de l'anti-HBe de 5,7%. Les facteurs de risque indépendants associés à la présence d'au moins un marqueur étaient les suivants : le fait d'être marié(e) (OR 3,82), d'avoir des antécédents de transfusion sanguine (OR 3,04) et d'être sous traitement parentéral contre la schistosomiase (OR 2,49). Trente-neuf donneurs ont indiqué avoir reçu toutes les injections du vaccin contre le virus de l'hépatite B, mais seul l'un d'entre eux avait des anti-HBs isolés. La prévalence relativement élevée de l'exposition au virus de l'hépatite B requiert des mesures de lutte contre les infections qui soient robustes et une sensibilisation au programme de vaccination des adultes.

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Introduction

Hepatitis B virus (HBV) infection is a serious global health problem, with 2 billion people infected worldwide, and 400 million suffering from chronic HBV infection. Approximately 2 people die each minute from HBV infection; representing the 10th leading cause of death worldwide [1]. Although the prevalence of HBV has declined due to the effectiveness of vaccination programmes, HBV infection is still a significant health concern in the world [2]. The prevalence of HBV infection in Egypt showed a massive decline after the application of the vaccination programme in 1991, from 10.1% in 1985 [3] to 1.3% in a recent study in 2009 on blood donors [4].

The presence of hepatitis B virus surface antigen (HBsAg) is an essential serological marker for diagnosing ongoing HBV infection; however, the presence of IgG antibodies against core antigen (anti-HBc), alone or in combination with antibodies against surface antigen (anti-HBs), indicates previous exposure to the virus [5]. Absence of HBsAg can be interpreted in a number of ways: no current or past HBV infection if no other HBV markers are detected; recovered past infection with detectable anti-HBs and anti-HBc; immunity due to vaccination with only detectable isolated anti-HBs; occult HBV infection in the presence of HBV-DNA in serum or liver with or without other markers; or false occult HBV infection if the serum DNA is comparable to that of overt infection in case of HBsAg mutants [6–8]. The persistent presence of anti-HBc is associated with chronic HBV infection and can be selective for HBVinfected samples even in the absence of HBsAg [9]. These patients who remain HBsAg negative/anti-HBc-positive are at risk of transmitting the disease on rare occasions, such as donation of solid organ tissue, or of reactivation of HBV disease if they are immunosuppressed [10].

Screening for HBV status using these markers provides an overview of the exposure, probability of transmission and immune status of the general population. This is crucial to anticipating the future impact of the disease on the health system and also to ensure adequate allocation of financial resources. We therefore conducted this study to investigate the distribution of anti-HBc and other HBV markers in apparently healthy blood donors who were HBsAg negative and to determine the major independent risk factors beyond HBV exposure with the goal of improving blood donation safety.

Methods

Sample

The study population (n = 508) was randomly selected from among Egyptian donors from blood banks in Alexandria. Assuming a 50% prevalence of anti-HBc among blood donors, the minimum required sample size was estimated by Epi Info, version 6 to be 474 blood donors with a precision = 4.5%, an α -level = 0.05 and a power = 80%. The researchers visited the blood banks at least 4 times weekly for a period of at least 4 hours. All donors attending blood banks during the researchers' visits and who consented to participate were included. Blood bank laboratory results were collected thereafter and only the eligible donors were included. The donors were screened continuously and the results from the blood banks were obtained a week later and those who had positive HBsAg were excluded (n = 13). There were 73 people who refused to participate.

Data collection

The study was conducted from September 2009 to March 2011. An interview using a structured questionnaire was conducted at the time of the participant's blood donation after getting his/her informed consent. The questionnaire included information about demographic, social and behavioural factors. Blood samples were taken from each participant and sera were stored at –20 °C until tested. After obtaining the blood bank results, HBsAg reactive sera were excluded and the final number of participants included in the study was 508 HBsAg non-reactive blood donors.

Serology comprised anti-HBc, anti-HBs, hepatitis B e antigen (HBeAg) antibodies against HBeAg (anti-HBe) and IgM antibody to hepatitis B core antigen (anti-HBc IgM). Every test was performed twice using enzyme-linked immunosorbent assay (Dialab GmbH) in accordance with the manufacturer's instructions.

The study protocol was approved by the research ethics committee of the High Institute of Public Health, University of Alexandria.

Data entry and analyses

Data entry and analyses were performed using SPSS software, version 15.0. The prevalence of each HBV serological marker was calculated as a percentage of the total population included in the study. The confidence intervals (CI) were calculated manually at the 95% level with continuity correlation. The blood donor was considered exposed if at least 1 positive marker was detected. The titres of different markers in serum were categorized according to quarter percentiles. Cut-off values for low titres were < 50th percentile and for high titres were \geq 50th percentile. The association between the demographic and social variables and the prevalence of HBV markers was evaluated using the chi-squared test. Multivariate logistic regression analyses were done to reveal the independent predictors of past exposure with or without immunity. A 2-sided P-value < 0.05 was considered statistically significant.

The assumed rarity of hepatitis trans-

mission by blood transfusion has been

attributed to the screening of blood for

Discussion

Results

The total number of people with evidence of exposure to HBV infection among the study group (i.e. presence of at least 1 serologic marker) was 148/508, a prevalence of 29.1%. They will be referred to as the exposed group. The prevalence of each marker is shown in Table 1. The most frequent marker was anti-HBc (24.4%), followed by anti-HBs (15.9%) and anti-HBe (5.7%). The number of individuals who had combined anti-HBs and anti-HBc was 61 (12.0%), making the anti-HBc alone (without anti-HBs) 50.8% (63/124) of the total positive anti-HBc. The majority of anti-HBs seropositive donors (n= 49; 60.5%) had high titres compared with almost half of the anti-HBc positive sera (n = 61; 49.2%). Anti-HBc IgM and HBeAg were detected in 3 (0.6%) and 2(0.4%) individuals respectively; all of them had borderline cut-off levels.

As shown in Table 2, although most of the exposed group were males (114/148), female sex was significantly associated with exposure (P = 0.006). The mean age of the exposed group was 38.9 (SD 9.9) years, with 44.2% being older than 35 years. The exposed donors were significantly older than the unexposed group (P < 0.001). Marriage and rural residence were significantly associated with exposure (83.1% and 41.9% versus 61.9% and 31.1% in the

exposed and unexposed groups respectively) (P < 0.001, P = 0.02 respectively). Neither education level nor type of work showed any association with the presence of HBV markers. Other factors that showed significance in the univariate analysis (Table 3) were: history of circumcision using traditional practices (P = 0.047), travelling to HBV-endemic area (P = 0.008), a history of frequent blood transfusion, even after 1992 (when screening began in blood banks) (P = 0.01), frequent dental manipulation (P = 0.002), history of jaundice (P =0.009), reporting elevated liver enzymes (P=0.04) and receiving schistosomiasis treatment by injection (P < 0.001). The independent risk factors revealed in the logistic regression analysis are shown in Table 4.

Among all participants, 461 (90.7%) gave no history of receiving HBV vaccine. No significant relation was found between seropositivity with isolated anti-HBs and self-reported history of receiving HBV vaccine (Table 5). Of the 37 who reported history of complete HBV vaccination, none had HBeAg, 1 had anti-HBc IgM, 4 (10.8%) showed anti-HBe and 9 (24.3%) were anti-HBcpositive. Surprisingly, 8/37 (21.6%) of them showed anti-HBs, of whom 1/37showed only anti-HBs. Most of the blood donors showing anti-HBs alone (16 out of 18; 88.9%) did not report any history of vaccination.

blood donors			
HBV marker	No.	% (<i>n</i> = 508	95% CI
Anti-HBc	124	24.4	20.8-28.3
Anti-HBs	81	15.9	12.9–19.5
Anti-HBe	29	5.7	3.9-8.2
Anti-HBc IgM	3	0.6	0.2-1.9
HBeAg	2	0.4	0.3-1.6
Total	148ª	29.1	23.9-34.2

Table 1 Prevalence of hepatitis B virus (HBV serological markers in HBsAg-negative blood donors

^aPresence of more than 1 marker was common.

Anti-HBc = antibody to hepatitis B core antigen; anti-HBs = antibody to hepatitis B surface antigen; anti-HBe = antibody to hepatitis B envelope antigen; anti-HBc IgM = IgM antibody to hepatitis B core antigen; HBeAg = hepatitis B e antigen.

CI = confidence interval.

markers of HBV and HCV, which has been universally applied in blood banks worldwide since 1992. However, the univariate analysis of different risk factors for hepatitis infection in the present study documented that positive history of frequent blood transfusion especially after 1992 was a significant risk factor for evidence of HBV exposure. Meanwhile, the logistic regression analysis showed that history of blood transfusion was one of the independent risk factors for HBV infection. This latter finding matches well with other published data [11]. It has been reported that despite continued improvements in the selection criteria of blood bank donors and of the applied serological tests protocol in sample evaluation, the transmission of HBV infection by blood transfusion

still occurs in a proportion of cases even if the transfused blood tested negative for HBsAg using highly sensitive assays [12].

The most prevalent marker among exposed people in this study was anti-HBc (24.4%). It should be noted that false positivity is unlikely in the present work as the test was double-checked and was considered positive only if both assays clearly indicated that. Anti-HBc is the first antibody to appear following acute HBV infection and persists at high levels following resolution of infection [13]. It is a marker of acute, chronic or resolved infection and remains detectable for life [14]. The reported prevalence of anti-HBc markers among donors at blood banks varies in other published studies depending on the local prevalence of HBV, ranging from 0.4% in low-endemic areas to 70% in high-endemic areas [11,15–17].

As the safety of blood products is one of the major issues in the area of transfusion medicine, the combined strategy of testing for both HBsAg and

Table 2 Demographic characteristics and clinical history in relation to exposure to hepatitis B virus (HBV) infection						
Variable	Exposed (<i>n</i> = 148)		Not exposed (<i>n</i> = 360)		<i>P</i> -value	
	No.	%	No.	%		
Sex						
Male	114	77.0	313	86.9	0.006	
Female	34	23.0	47	13.1		
Age (years) ^a						
< 25	18	12.2	84	23.5		
25-	64	43.5	183	51.3	< 0.001	
35-	26	17.7	52	14.6		
45+	39	26.5	38	10.6		
Mean (SD)	38.	.9 (9.94)	33	.2 (9.25)	< 0.001	
Marital status						
Single	24	16.2	127	35.3		
Married	123	83.1	223	61.9	< 0.001	
Divorced	0	0	3	0.8		
Widowed	1	0.7	7	1.9		
Residence						
Rural	62	41.9	112	31.1	0.020	
Urban	86	58.1	248	68.9		
Education						
Illiterate	39	26.4	72	20.0		
Read & write	12	8.1	21	5.8		
Primary	17	11.5	24	6.7	0.113 ^b	
Preparatory	22	14.9	65	18.1		
High	34	23.0	100	27.8		
University	24	16.2	78	21.7		
Employment status						
Health care	4	2.7	7	2.0		
Armed force	2	1.4	10	2.8		
Emergency service	0	0.0	4	1.1		
Beautician or barber	1	0.7	3	0.8		
Institution work (daycare, nursery)	1	0.7	0	0.0	0.182 ^b	
Employee	23	15.5	79	21.9		
Manual	55	37.2	123	34.2		
Uneployed	35	23.6	59	16.4		
Others	27	18.2	75	20.8		

^a1 in the exposed group and 3 in the unexposed group were missing data giving a total of 147 and 357 respectively. ^bMonte-Carlo test.

anti-HBc is practised worldwide and testing for anti-HBc was adopted in some areas in the world. This strategy has been found to markedly minimize the possibility of HBV transmission via blood transfusion [14]. On the other hand, it may lead to the exclusion of a significant number of donors' blood, as reported in Brazil where high levels of anti-HBc were recorded (up to 57%) [18].

There has recently been concern about "anti-HBc only" or isolated anti-HBc individuals, i.e. those in whom anti-HBc is the only detectable HBV marker with no evidence of HBsAg or anti-HBs [19]. A serological pattern of anti-HBc as a sole marker is not infrequent. It was reported that 3.7% of randomly selected Lebanese blood donors were confirmed as isolated anti-HBc [20]. Similarly, isolated anti-HBc was reported in 125 out of 6035 (2.1%) of Saudi blood donors [21]. Another study performed on 545 Iranian blood donors; 8% of them were positive for isolated anti-HBc [22]. The

Table 3 Behavioral and clinical history in relation to exposure to hepatitis B virus (HBV) infection

Risk factor	Exposed (<i>n</i> = 148)		Not e (<i>n</i> =	xposed 360)	<i>P</i> -value	
	No.	%	No.	%		
Tattooing	8	5.4	10	2.8	0.146	
Body piercing	2	1.4	7	1.9	1.000	
Acupuncture	8	5.4	18	5.0	0.851	
Sharing razor, toothbrush, comb or any potentially						
infecting items	5	3.4	18	5.0	0.424	
Public barber or manicure	106	71.6	263	73.1	0.742	
Circumcision						
No	81	54.7	51	14.2	0.047 ^c	
Doctor	20	13.5	80	22.2	0.047	
Folk	110	74.3	229	63.6		
Traveled abroad ^a	45	30.4	69	19.2	0.008	
Undergone surgery						
No	70	47.3	195	54.2	0.10.40	
Minor	43	29.1	108	30.0	0.104 ^c	
Major	35	23.6	57	15.8		
Time since surgery (years)						
< 20	58	74.4	132	80.0	0.264	
20+	15	19.2	21	12.7		
History of blood or blood products transfusion						
No	133	89.9	346	96.1	0.0166	
Before 1992	3	2.0	4	1.1	0.016 ^c	
After 1992	12	8.1	10	2.8		
Infrequent	7	4.7	10	2.8		
Frequent	8	5.4	4	1.1	0.010 ^c	
Undergone dental manipulation						
No	54	36.5	177	49.2	0.000	
Infrequent	50	33.8	122	33.9	0.002 ^c	
Frequent	44	29.7	61	16.9		
Undergone invasive intervention						
No	139	93.9	342	95.0		
Endoscopy	7	4.7	17	4.7	0.365	
Catheterization	2	1.4	1	0.3		
History of jaundice	17	11.5	18	5.0	0.009	
Reported elevated liver enzymes ^b	17	13.4	24	7.3	0.040	
Been hospitalized						
No	88	59.5	248	68.9		
Once	43	29.1	86	23.9	0.090°	
More	17	11.5	26	7.2		
Vaccination for HBV						
No	133	89.9	328	91.1		
Incomplete	3	2.0	7	1.9	0.917°	
Complete	12	8.1	25	6.9		
Had antibilharzial treatment by injection	50	33.8	45	12.5	< 0.001	
Parenteral injections or infusion	50	33.0	-13	12.0	0.001	
No	106	71.6	260	72.2		
Once	22	14.9	55	15.3	0.951	
More	22		55 45	15.3		
More HIV-Ab positive	20	13.5 0.7	45 2	0.6	1.00	

None had organ transplantation or been on haemodialysis

^aThe total number is less than those traveled as the rest were missing data. ^bNot all participants had previously measured aspartate/alanine aminotransferase, so the totals were 127 and 331 for the exposed and unexposed participants respectively. ^cMonte-Carlo test.

Table 4 Logistic regression analysis of different risk factors of exposure to hepatitis B virus (HBV infection)					
Variable	OR	SE	<i>z</i> -value	<i>P</i> -value	95% CI
Married	3.82	2.13	2.41	0.016	1.28-11.4
History of blood or blood product transfusion	3.04	1.62	2.09	0.037	1.07-8.65
History of schistosomiasis treatment by injection	2.49	0.91	2.49	0.013	1.21-5.12

Logistic regression analysis of different risk factors significantly associated with exposure to HBV shows that marriage and history of blood transfusion had more prominent effect (OR 3.82 and 3.04 respectively that was followed by history of anti-bilharzial treatment by injection OR = odds ratio; SE = standard error; CI = confidence interval.

results of the present study further confirmed the high rate of isolated anti-HBc among tested blood donors 63/508 (12.4%).

Besides false positive results of anti-HBc assays [23], emergence of 's' mutants which could occur during therapy with nucleoside inhibitors was also suggested as a possible explanation for the presence of isolated anti-HBc [24]. It was declared that mutations occur in HBsAg making it undetectable by conventional assays [25]. Alhababi et al. suggested that in communities where the circulation of antigenic determinant mutants are increasing, surveillance of isolated anti-HBc cases may be a valuable tool to identify the mutants [26]. Some authors considered anti-HBc alone as evidence of past infection with HBV when the anti-HBs level has fallen below the detection level [20]. Others concluded that many years after chronic carriage the level of HBsAg in the circulation becomes too low to be detected [16]. Finally, anti-HBc alone has also been attributed to an acute HBV infection during the so-called "window

period" between the disappearance of HBsAg and the appearance of HBsAb. In this case, if the individual is followed up, anti-HBs will appear [13].

In the present study, combined anti-HBc and anti-HBs was present in almost half of those showing anti-HBc (61/124), constituting 12.0% of the total population tested for HBV markers. A similar high frequency was found by Aguiar et al. [18]. These cases were considered to be previously infected and to have become immune to HBV infection, although we need to bear in mind that the degree of protection depends on the level of anti-HBs. Kaminski et al. reported that 22 out of 41 donors with evidence of anti-HBc had anti-HBs level > 100 mIU/mL, a level generally considered protective against HBV infection [11]. Other investigators stressed the fact that blood components positive for anti-HBc and anti-HBs do not appear to transmit HBV and there is clearly an inverse correlation between anti-HBs level and infectivity [27]. The above explanations could be applied to the combined anti-HBc and anti-HBs cases

found in this study, as we also found that a high proportion of anti-HBs subjects (60.5%) had high titres.

Older age was significantly associated with the detection of HBV markers. Similarly, Dettori et al. reported that the prevalence of markers of a previous HBV infection was low in young persons, whereas in those aged > 50 years the prevalence of markers of previous HBV infection was high [28]. Other authors also showed that anti-HBc prevalence increased with age, suggesting that sexual activity may contribute to horizontal transmission of this infection among adults [29]. This latter explanation finds support in the present work, as being married was a significant risk factor for HBV infection [30]. The significant association of HBV markers with older age could also be due to the greater number of years of potential exposure, lack of awareness of HBV infection and lack of awareness and eventually infrequent HBV vaccination in adults. The latter finding was supported in the present study as 90.7% of our total sample did not report any

Table 5 Relation between history of hepatitis B virus (HBV) vaccination and detection of HBV markers							
HBV markers		No HBV vaccination (<i>n</i> = 461)		Incomplete HBV vaccination (<i>n</i> = 10)		Complete HBV vaccination (n = 37)	
	No.	%	No.	%	No.	%	
Anti-HBs	71	15.4	2	20.0	8	21.6	0.573
Isolated Anti-HBs	16	3.5	1	10.0	1	2.7	0.521
HBeAg	2	0.4	0	0.0	0	0.0	1.000
Anti-HBe	24	5.2	1	10.0	4	10.8	0.189
Anti-HBc IgM	2	0.4	0	0.0	1	2.7	0.253
Total anti-HBc	113	24.5	2	20.0	9	24.3	0.947

Anti-HBc = antibody to hepatitis B core antigen; anti-HBs = antibody to hepatitis B surface antigen; anti-HBe = antibody to hepatitis B envelope antigen; anti-HBclgM = lgM antibody to hepatitis B core antigen; HBeAg = hepatitis B e antigen.

history of vaccination. The very poor response to vaccine among those who reported full vaccination suggests the possibility of incorrect reporting by the participants or poor vaccination practices. It could also be attributed to being infected before vaccination (when other markers were detected) as no screening was done before vaccination. Another explanation is if a long time had elapsed since vaccination (although no data were obtained to confirm this), leading to low undetectable levels of anti-HBs in individuals who did not show anti-HBs.

Although several published studies concluded that male sex seemed to play an important role in acquisition of HBV infection [29,31,32], the results of the present study revealed that females were more prevalent among the exposed group compared with the unexposed group (23.0% and 13.1%).

The other risk factors revealed in this study, namely circumcision in traditional facilities, rural residence and receiving parenteral schistosomiasis treatment denote a lack of hygiene and poor infection control practices in circumcisions and injections. Similar conclusions were reported by other authors who documented community delivery with traditional birth attendants as an important route of horizontal spread of HBV. They suggested that this may be attributed to the procedure being practised under poor hygiene conditions with sharing of ancillary supply equipment such as scissors [33]. This was further documented in another study, which revealed that the main risk factors for HBV transmission was syringe exchange, sexual exposure, nosocomial exposure and more rarely blood transfusion [28].

Conclusion

The prevalence of exposure to HBV infection in this study in Egypt was higher than expected. Public health

measures should be adopted for HBV control including proper infection control measures and better awareness and evaluation of adult vaccination programmes. The need for screening of HBsAg negative donated blood for anti-HBc needs to be evaluated.

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References

- 1. *Statistics*. Hepatitis B Foundation [website] (http://www.hepb. org/hepb/statistics.htm, accessed 2 March 2013).
- Kim SM et al. Prevalence of occult HBV infection among subjects with normal serum ALT levels in Korea. *Journal of Infection*, 2007, 54:185–191
- 3. Sherif MM et al. Hepatitis B virus infection in upper and lower Egypt. *Journal of Medical Virology*, 1985, 15:129–135.
- 4. Ismail AM et al. Decline of viral hepatitis prevalence among asymptomatic Egyptian blood donors: a glimmer of hope. *European Journal of Internal Medicine*, 2009, 20:490–493.
- 5. Laperche S et al. Blood donors infected with the hepatitis B virus but persistently lacking antibodies to the hepatitis B core antigen. *Vox Sanguinis*, 2001, 80:90–94.
- 6. 6. Torbenson M, Thomas DL. Occult hepatitis B. *Lancet Infectious Diseases*, 2002, 2:479–486.
- Giarcia -Montalvo BM et al. Hepatitis B Virus DNA in blood donors with anti-HBc as a possible indicator of active hepatitis B virus infection in Yucatan, Mexico. *Transfusion Medicine*, 2005, 15:371–378.
- Raimondo G et al. Statements from the Taormina expert meeting on occult hepatitis B virus infection. *Journal of Hepatology*, 2008, 49:652–657.
- 9. Elghannam DM et al. Clinical significance of antibody to hepatitis B core antigen in multitransfused hemodialysis patients. *Asian Journal of Transfusion Science*, 2009, 3:14–17.
- El Khouri M, dos Santos VA, Hepatitis B. Epidemiological, immunological, and serological considerations emphasizing mutation. *Revista do Hospital das Clinicas*, 2004, 59:216–224

- 11. Kaminski G et al. Evidence of occult hepatitis B virus infection among Omani blood donors: a preliminary study. *Medical Principles and Practice*, 2006, 15:368–372.
- Zervou EK et al. Value of anti-HBc screening of blood donors for prevention of HBV infection: results of a 3-years prospective study in Northwestern Greece. *Transfusion*, 2001, 41:652–658.
- Al-Mekhaizeem KA, Miriello M, Sherker AH. The frequency and significance of isolated hepatitis B core antibody and the suggested management of patients. *Canadian Medical Association Journal*, 2001, 165:1063–1064.
- 14. Behzad-Behbahani A et al. Anti-HBc& HBV-DNA detection in blood donors negative for hepatitis B virus surface antigen in reducing risk of transfusion associated HBV infection. *Indian Journal of Medical Research*, 2006, 123:37–42
- 15. Hennig H et al. 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.
- Jafarzadeh A et al. 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.
- Aguiar JI et al. Prevalence of antibodies to hepatitis B core antigen in blood donors in the middle West region of Brazil. *Memorias do Instituto Oswaldo Cruz*, 2001, 96:185–187.
- 19. Banerjee A et al. Frequency and significance of hepatitis B virus surface gene variant circulating among antiHBc only

individuals in eastern India. *Journal of Clinical Virology*, 2007, 40:312-317.

- 20. El-Zaatari M et al. Hepatitis B virus DNA in serum of "anti-HBc only" positive healthy Lebanese blood donors: Significance and possible implications. *Journal of Hospital Infection*, 2007, 66:278–282.
- 21. Bernvil SS et al. Hepatitis B core antigen antibody as an indicator of a low grade carrier state for hepatitis B virus in a Saudi Arabian blood donor population. *Transfusion Science*, 1997, 18:49–53.
- 22. Pourazar A et al. Detection of HBV DNA in HBsAg negative normal blood donors. *Iranian Journal of Immunology*, 2005, 2:172–176.
- 23. Heijitink RA et al. Anti-HBs levels after hepatitis B immunization depend on test reagents: routinely determined 10 and 100 IU/l seroprotection levels unreliable. *Vaccine*, 2002, 20:2899–2905.
- 24. Hatzakis A, Magiorkinis E, Haida C. HBV virological assessment. *Journal of Hepatology*, 2006, 44(Suppl. 1):S71–S76.
- 25. Weinberger KM et al. High genetic variability of the groupspecific a-determinant or hepatitis B virus surface antigen (HBsAg) and the corresponding fragment of the viral polymerase in chronic virus carriers lacking detectable HBsAg in serum. *Journal of General Virology*, 2000, 81:1165–1174.

- 26. Alhababi F, Sallam TA, Tong CYW. The significance of 'anti-HBc only' in the clinical virology laboratory. *Journal of Clinical Virology*, 2003, 27:162–169.
- 27. Mosley JW et al. Donor screening for antibody to hepatitis B core antigen and hepatitis B virus infection in transfusion recipients. *Transfusion*, 1995, 35:5–12.
- 28. Dettori S et al. Identification of low HBV-DNA levels by nucleic acid amplification test (NAT) in blood donors. *Journal of Infection*, 2009, 59:128–133.
- 29. Matos MA et al. Epidemiological study of hepatitis A, B and C in the largest Afro-Brazilian isolated community. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, 2009, 103:899–905.
- 30. Tahan V et al. Sexual transmission of HCV between spouses. *American Journal of Gastroenterology*, 2005, 100:821–824.
- 31. Habibollahi P et al. Occult hepatitis B infection and its possible impact on chronic hepatitis C virus infection. *Saudi Journal of Gastroenterology*, 2009, 15:220–224.
- 32. Lewis-Ximenez LL et al. Risk factors for hepatitis B virus infection in Rio de Janeiro, Brazil. *BMC Public Health*, 2002, 22:26.
- 33. Matos MA et al. Epidemiological study of hepatitis A, B and C in the largest Afro-Brazilian isolated community. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, 2009, 103:899–905.

Hepatitis B transmission

Hepatitis B virus is transmitted between people by direct blood-to-blood contact or semen and vaginal fluid of an infected person. Modes of transmission are the same as those for the HIV, but the hepatitis B virus is 50 to 100 times more infectious. Unlike HIV, the hepatitis B virus can survive outside the body for at least seven days. During this time, the virus can still cause infection if it enters the body of a person who is not protected by the vaccine. In developing countries, common modes of transmission are:

- perinatal (from mother to baby at birth)
- early childhood infections (inapparent infection through close interpersonal contact with infected household contacts)
- unsafe injection practices
- unsafe blood transfusions
- unprotected sexual contact.

Source: WHO Fact sheet No. 204 July 2012