

The prevalence of hepatitis B core antibody positivity in donors for liver transplantation in Saudi Arabia

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ABSTRACT

Objective: The risk of transmitting hepatitis B virus from donors who are positive for hepatitis B core antibody but negative for hepatitis B surface antigen has been a major concern in liver transplantation. In the Kingdom of Saudi Arabia the overall prevalence of hepatitis B core antibody among the general population was reported to be very high indeed. The purpose of this study is to establish the prevalence of hepatitis B core antibody positivity among liver donors who are negative for hepatitis B surface antigen and offered for liver transplantation in the Kingdom of Saudi Arabia.

Methods: Hepatitis B serological markers were studied in 145 of 209 donors offered for organ transplantation over a 4-year period in King Fahad National Guard Hospital, Riyadh, Kingdom of Saudi Arabia.

Results: Out of 145 donors, 51 donors tested positive for hepatitis B core antibody but negative for hepatitis B surface antigen with an overall prevalence of 35.2%. The

majority of donors were non-Saudi (75.2%), and predominantly from the Indian subcontinent and Far East. The prevalence of hepatitis B core antibody positive donor was significantly higher in non-Saudi (41.3%) compared with Saudi nationals (16.7%).

Conclusion: In the view of this high prevalence, we believe that all donors considered for liver transplantation in the Kingdom of Saudi Arabia should be tested for hepatitis B core antibody. Furthermore, an algorithmic approach should be developed to minimize the risk of transmitting hepatitis B virus from donors to liver recipients, at the same time not to affect the existing small pool of available donor organs in the Kingdom of Saudi Arabia.

Keywords: Liver transplantation, hepatitis B virus, donor, prevalence, hepatitis B virus core antibody.

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Transmission of hepatitis B virus (HBV) infection from donors who are negative for hepatitis B surface antigen (HBsAg) but positive for hepatitis B core antibody (HBcAb) has been reported.¹⁻³ In the Kingdom of Saudi Arabia (KSA), the overall prevalence of HBcAb in the absence of HBsAg was found to be as high as 31.8%.⁴ Therefore, the prevalence of HBcAb among liver donors in KSA is expected to be high as well. In this study we review the prevalence of HBV markers among liver donors

in KSA. We will also discuss the best possible approach to use these donors without compromising the limited donor pool in KSA.

Methods. This study included 209 donors who were offered to the liver transplant program at King Fahad National Guard Hospital, Riyadh, KSA (KFNGH) during the period between February 15, 1994 and November 4, 1998. All donors were brain-

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dead heart-beating donors, documented and consented by the Saudi Center of Organ Transplantation (SCOT) in KSA. All donors were tested negative for both HBsAg and hepatitis C virus (HCV). We retrospectively collected the following data from the donor's work-up sheet provided by SCOT: nationality, age, sex, alanine aminotransferase (ALT), HBsAg, hepatitis B surface antibody (HBsAb), HBcAb, hepatitis B core immunoglobulin (HBcIgM), hepatitis B envelope antigen (HBeAg), and hepatitis C virus antibody (HCVab). Hepatitis B serological markers were available in 145 of 209 donors. Data was loaded on Microsoft Excel sheet and analyzed using the Statistical Package for Social Sciences (SPSS) for Windows statistical program (SPSS Inc). Continuous variables are expressed as mean \pm standard deviation (SD) and compared with Fisher's exact test.

Results. Hepatitis B serological markers were available in 145 of 209 donors. Out of 145 donors, 51 donors tested positive for HBcAb but negative for HBsAg (35.2%). Characteristics of liver donors in KSA according to HBcAb status are listed in **Table 1**. The majority of donors were non-Saudi (75.2%), and they were mostly from the Indian subcontinent and Southeast Asia, **Table 2**. The prevalence of HBcAb positive donors was notably higher in non-Saudi, 41.3% compared with Saudi nationals, 16.7%, **Table 3**. This difference was statistically significant ($P < 0.01$). Hepatitis B surface antibody positivity was considerably higher in HBcAb positive donors (66.7%) compared with HBcAb negative donors (7.4%), **Table 4**. This difference was statistically highly significant ($P < 0.0001$).

Discussion. In KSA, the overall prevalence of HBsAg is as high as 16.7%, while the prevalence of hepatitis B antibodies in the absence of HBsAg was 31.8%. The overall prevalence of HBcAb was proven to be as high as 51.2%.⁴ In the absence of HBsAg, the presence of hepatitis B antibodies both alone or in association with each other are usually an indication of recovery from past HBV infection or active immunization. Hypothetically, the use of HBsAg negative but HBcAb positive donors should be safe for liver transplantation, unfortunately, this is not the case. Studies have shown that the risk of transmission of HBV infection has been as high as 78% when HBcAb positive donors were transplanted to HBV negative recipients.⁵ This has been explained by the existence of HBV in the liver tissues of healthy HBcAb positive donors but not in their serum.⁶⁻⁸ In this study the prevalence of HBsAg negative but HBcAb positive liver donors was as high as 35.2%, which is a major concern especially when considering the scarcity of available donors in KSA. The majority of those donors were non-Saudi

Table 1 - Characteristics of 145 liver donors according to hepatitis B core antibody status in the Kingdom of Saudi Arabia.

Variable	HBcAb negative (N=94 donors)	HBcAb positive (N=51 donors)	P value
Saudi/non-Saudi	30/64	6/45	0.013
Age	27.9 \pm 12.2	34.5 \pm 9.7	NS
Sex (M/F)	79/15	50/1	NS
ALT	74 \pm 70	82 \pm 84	NS
N - number, HBcAb - hepatitis B core antibody, M - male, F - female, ALT - alanine transaminase, NS - not significant			

Table 2 - Distribution of donor's according to nationality in the Kingdom of Saudi Arabia.

Nationality	N	(%) (N=145)
Saudi	36	(24.8)
Non-Saudi (Total)	109	(75.2)
Indian	36	(24.8)
Bangladesh	23	(15.9)
Pakistani	16	(11.0)
Filipino	13	(9.0)
Others	21	(14.5)
N - number		

Table 3 - Prevalence of hepatitis B surface antigen negative/hepatitis B core antibody positive donors according to nationality in the Kingdom of Saudi Arabia.

Nationality	N	HBcAb+	Prevalence (%)
Overall	145	51	(35.2)
Saudi	36	6	(16.7)
Non-Saudi	109	45	(41.3)
Filipino	13	7	(53.8)
Pakistani	16	8	(50.0)
Indian	36	14	(38.9)
Bangladesh	23	8	(34.8)
Others	21	8	(38.1)
N - number HBcAb+ - hepatitis B core antibody positive			

Table 4 - Pattern of hepatitis B viral markers in 145 liver donors according to hepatitis B core antibody status in the Kingdom of Saudi Arabia.

Variable	HBcAb negative (N=94 donors)	HBcAb positive (N=51 donors)	P-value
HBsAg+	none	none	NS
HBsAb+	7 (7.4%)	34 (66.7%)	<0.0001
HBcIgM+	none	none	NS

N - number, HBcAb - hepatitis B core antibody, HBsAg+ - hepatitis B surface antigen positive, HBsAb+ - hepatitis B surface antibody positive, HBcIgM+ - hepatitis B core immunoglobulin M positive, NS - not significant

(75.2%), predominantly from the Indian subcontinent and Far East. The prevalence of HBsAg negative but HBcAb positive donors was significantly higher in non-Saudi compared with Saudi nationals, 41.3% versus 16.7% (P=0.01). This difference is readily explained by the fact that these countries are hyper endemic HBV foci.⁹ However, the low prevalence of HBcAb among Saudi donors (16.7%) contradicts previous local studies indicating a higher prevalence up to 31.8%.⁴ This could be due to selection bias and small sample size. Most of HBcAb positive donors in this study were positive for HBsAb as well (66.7%). Although this may indicate solid immunity, it does not exclude the risk of HBV transmission.¹⁰ Van Thiel¹¹ and his colleagues assessed the presence of polymerase chain reaction HBV-deoxyribose nucleic acid (DNA) in the liver tissue of 133 consecutive patients undergoing liver biopsy for clinical reasons. Hepatitis B virus-DNA was detected in 8.2% of these livers. Interestingly the rate was higher among those who were HBsAb positive (12.5%) as compared to those without detectable HBsAb (5.7%).¹¹ In the view of our results, we believe that donors considered for liver transplantation in KSA must be tested for HBcAb. In addition, donors who are HBcAb positive should be both IgG and IgM determined. Hepatitis B core immunoglobulin positivity reflects recent infection in the donor, and it is advisable not to use such donors for any organ transplantation. Hepatitis B core immunoglobulin negative but HBcIgG positive livers are suitable for HBV negative recipients only in the setting of extremely sick patients when life expectancy is only a few days with no other potential donor availability (for example, acute fulminant failure, primary non-function graft, or early hepatic artery thrombosis).¹² With the existing universal shortage of organs, HBcAb positive livers have been used in HBcAb positive or HBsAb positive recipients accepting disease

transmission risk of 8.2% and 12.1%.¹¹ It is always advisable to use hepatitis B hyperimmune globulin and lamivudine in HBV negative recipients whom received a HBcAb positive liver in order to minimize the risk of disease transmission.¹³

We believe that the results from this study warrant further in-depth study into the different risk factors involved in transmitting HBV from HBcAb positive donors to liver transplant recipients in KSA. We also believe that in the view of the very high prevalence of HBcAb positive donors in KSA, an algorithmic approach should be developed to minimize the risk of transmitting HBV without compromising the already limited pool of available donor organs in KSA.

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