Original
article

Hepatitis B markers in heterosexual patients attending two genitourinary medicine clinics in the West Midlands

A A El-Dalil, D T Jayaweera, M Walzman, K W Radcliffe, R Richmond, A A Wade, M Shahmanesh

Objective: To determine the prevalence of hepatitis B virus (HBV) infection in heterosexual patients attending two genitourinary medicine (GUM) clinics in the West Midlands and to examine whether heterosexual activity is a risk factor for acquiring HBV infection with the view to extend HBV vaccination policies to cover this group.

Design: HBV markers were determined in the GUM study group and compared with that of the control groups. Responses to a questionnaire were used to examine sexual behaviour patterns that may be related to heterosexual acquisition of HBV infection.

Setting: The West Midlands, UK April 1992–January 1993.

Subjects: 788 male patients and 688 female patients attending GUM clinics were compared with 498 male blood donors and 563 females attending antenatal clinics for the seroprevalence of HBV markers. Potential risk factors related to heterosexual activity were assessed in 1436 patients in the study group.

Main outcome measures: Prevalence of HBV markers in the GUM study group and the controls. The possible use of the risk factors examined as predictors for acquiring HBV infection.

Results: The seroprevalence of hepatitis B core antibody (anti-HBc) in GUM patients was 1.9% and 0.5% in the control group. In the study groups the prevalence of anti-HBc from Birmingham was 3.2% while that from Coventry was 0.8%. The low seroprevalence of HBV prevented a multiple logistic analysis. A limited regression analysis showed that being non-white ($p < 0.001$) and duration of sexual activity ($p = 0.013$) were risk factors for HBV infection. However, these two factors were poor predictors of the risk to exposure to HBV infection.

Conclusion: The prevalence of HBV infection in heterosexual patients in the West Midlands is very low and does not provide any indications to broaden HBV vaccination into heterosexual patients attending GUM clinics. Risk factors were poor predictors of the exposure to HBV infection. This is partially due to the low prevalence of HBV infection in this study. Further studies are required before definitive conclusions are made regarding the potential predictive value of risk factors.

(*Genitourin Med* 1997;73:127–130)

Keywords: hepatitis B; markers; heterosexuals

Introduction

Hepatitis B virus (HBV) infection is a major cause of acute and chronic hepatitis, cirrhosis and primary hepatocellular carcinoma world wide.¹ Furthermore, it establishes a reservoir of carriers who are able to transmit the infection.² It is generally acknowledged that HBV can be transmitted by routes other than transfusion of blood products and percutaneous needle exposures.^{3–7} Sexual contact is known to play an important role in the transmission of this disease and has been documented to occur between heterosexuals.^{8–11}

The relative importance of heterosexual transmission of HBV in the UK, and the extent to which it may be prevented by immunisation strategies, has yet to be determined. In this study the prevalence of HBV serological markers was measured in heterosexual patients attending two genitourinary medicine (GUM) clinics in the West Midlands and in a control

group. The seroprevalence of HBV serological markers in the study group was related to sexual behaviour after excluding other risk factors associated with acquiring HBV infection.

Methods

POPULATION STUDIED

Male and female patients attending Coventry and Warwickshire Hospital and Birmingham General Hospital GUM clinics were enrolled in the study if they were between the ages of 18 and 40 years at the time of presentation. (The range being selected such that age matched controls may be identified.) Only new patients and patients with new conditions were included. The study was started in April 1992 and was completed by January 1993.

Patients were excluded from HBV core antibody (anti-HBc) analysis if they were homosexuals or bisexuals, intravenous drug users

Coventry and
Warwickshire
Hospital, Coventry,
UK

A A El-Dalil
D T Jayaweera
M Walzman
A A Wade
R Richmond

General Hospital,
Birmingham
K W Radcliffe
M Shahmanesh

Correspondence to:
Dr A A El-Dalil, Department
of Genitourinary Medicine,
The Guest Hospital, Tipton
Road, Dudley, West
Midlands, DY1 4SE, UK.

Accepted for publication
8 November 1996

(IVDU), known to be HIV seropositive or voluntarily declared that they were sex workers. In some cases exclusion could only be established after the study questionnaire had been completed. An approximate age and geographically matched control group was enrolled to the study. The males were new blood donors and the females were attendees of antenatal clinics in Coventry.

Patient information and consent: Patients were given the option of refusing to participate in the study. Those who agreed to be included in the study gave a written informed consent. A patient questionnaire was used to collect standardised information. Demographic details including sex, date of birth, place of birth, occupation, civil status, ethnicity and history of living outside the UK for longer than three months were recorded for every patient in the study group. The information on sexual activity included age at first sexual intercourse, sexual practice of vaginal and/or anal intercourse, number and sex of sexual partners in the last 12 months and over lifetime, and history of sexual intercourse with foreign nationals. Other risk factors such as history of IVDU, blood transfusion and occupational exposure risk as well as history of HBV infection or vaccination were recorded. Current and past history of syphilis, gonorrhoea, chlamydia, non-specific urethritis, trichomonias, genital herpes and genital warts were documented for each patient.

BLOOD SAMPLING AND LABORATORY ANALYSES

Blood samples (10 ml) for hepatitis serology were drawn at the same time as samples for syphilis analysis. Blood samples were centrifuged and serum stored at -20°C before analysis. Serum samples tested positive for anti-HBc were further tested for surface and e antigen and antibodies. Anti-HBc, surface antigen (HBsAg), surface antibody (anti-HBs), e antigen (HBeAg) and e antibody (anti-HBe) were analysed by SYVA UK, 23–25 Marlow Road, Maidenhead, Berkshire, SL6 7AA.

STATISTICAL ANALYSIS

STAT XACT (Cytel software corporation, 675 Massachusetts Avenue, Cambridge, MA 02139, USA) was used to determine the 95% confidence intervals for the prevalence of HBV infection in the GUM study patients and the controls. It was originally planned to make a detailed investigation of risk factors for HBV infection using a logistic regression analysis. However, because of the low prevalence of HBV infection it was not feasible to make an assessment involving several factors. Instead, univariate analysis using continuity corrected χ^2 test was applied to investigate potential risk factors and a limited logistic regression was carried out based on two factors which appeared to be linked with infection on the basis of the results of the study.

Results

GUM patients entering the study numbered

1549. Seventy three patients were excluded from the assessment of seroprevalence of HBV: 25 patients were outside the age range, 33 were male homosexuals/bisexuals, nine were IVDU, seven were prostitutes and 23 male patients had had anal intercourse with another male but did not consider themselves to be homosexuals or bisexuals. It should be noted that some patients met more than one criterion for exclusion. Another 40 GUM patients were excluded from the assessment of risk factors, having been vaccinated for hepatitis B, but were included in the assessment of HBV seroprevalence since the control group may have included vaccinated individuals. Hence, 1436 GUM patients were evaluable for the assessment of risk factor for HBV infection and 1476 were evaluable for the assessment of the seroprevalence of HBV markers. Five of the excluded GUM patients (four male homosexuals and one drug user) were anti-HBc positive.

Controls numbering 1064 were entered into the study. Three controls were excluded from the study because they were outside the age range. None of these three controls had positive anti-HBc.

The median age of the GUM patients was 25 years and that of the controls was 27 years. Fifty three per cent of the GUM patients were males compared with 47% of the controls. The prevalence of anti-HBc in the study group was 1.9% (28 of 1476, 95% confidence intervals 1.2% to 2.7%) and 0.5% for the control group (five of 1061, 95% confidence intervals 0.2% to 1.1%). Twenty two of the 28 GUM patients positive for anti-HBc were from Birmingham. Hence the prevalence of anti-HBc among GUM patients attending the Birmingham General Hospital was 3.2% while that of the GUM patients attending Coventry and Warwickshire Hospital was 0.8% ($p < 0.001$). Among the control group, five were anti-HBc positive. One was from Birmingham and four were from Coventry.

Twenty seven of the 28 GUM patients with anti-HBc had results for HBsAg and anti-HBs and anti-HBe. Of these 22 had anti-HBs, two had HBsAg and 19 had anti-HBe detected. Twenty six of the 28 patients with anti-HBc had results for HBeAg and all were negative.

Table 1 Demographic analysis of GUM study group, comparing Anti-HBc positive to Anti-HBc negative patients (percentage)

	Anti-HBc positive	Anti-HBc negative
Mean age (year) (SD)	29 (6)	26 (5)
Male	19 (68)	751 (53)
Female	9 (32)	657 (47)
Married	6 (21)	177 (13)
Single	18 (64)	1047 (74)
Living together	1 (4)	101 (7)
Separated	3 (11)	68 (5)
Divorced	0 (0)	15 (1)
Ethnicity		
White	7 (25)	1170 (83)
Non-white	19 (75)	238 (17)
Afro-Caribbean	12 (43)	187 (13)
Asian	5 (18)	45 (3)
Other*	4 (14)	6 (< 1)
Born or lived outside UK		
Born outside UK	15 (54)	124 (9)
Lived outside UK for > 3 months	13 (46)	298 (17)

*Far East, Iranian, South American, African.

Table 2 Analysis of risk factors for GUM study group, comparing anti-HBc positive with anti-HBc negative patients (percentage)

	Anti-HBc positive	Anti-HBc negative
Duration of sexual activity (years) (SD)	12 (7)	9 (6)
Sexual intercourse with foreign national	13 (46)	293 (21)
Number of partners in past 12 months		
1–3	22 (78)	1193 (85)
4–10	5 (18)	199 (14)
> 10	1 (4)	15 (1)
Number of partners during lifetime		
1–5	6 (21)	621 (44)
> 5	22 (79)	787 (56)

Table 3 Univariate analysis of hepatitis B risk factors

Risk factors	Continuity correction	Odds ratio	95% confidence interval
Ethnicity	< 0.0001	14.8	6.2–35
Duration of sexual activity in years*	0.004	—	1–5.2
Number of partners in lifetime	0.03	2.9	1.2–7.2
Born outside UK	< 0.0001	12.3	5.7–26.4
Lived outside UK	0.0001	4.3	2.9–7.2
Sexual intercourse with foreign national	0.002	3.3	1.6–7

*Duration of sexual activity; test of equality of means was employed for statistical analysis.

Table 4 Logistic regression analysis of hepatitis B risk factors

Risk factor	p value	Odds ratio	95% confidence intervals
Ethnicity	< 0.001	14	6–34
Duration of sexual activity in years*	0.013	8%	2–15%

*The odds of having positive anti-HBc increases by 8% per year of sexual activity.

Table 5 Analysis of sexual practice for GUM study group, comparing anti-HBc positive with anti-HBc negative patients (percentage)

	Anti-HBc positive	Anti-HBc negative
Mean age at first intercourse (SD)	17 (2)	17 (2)
Vaginal intercourse		
Never	0 (0)	4 (< 1)
Once	0 (0)	9 (< 1)
Occasionally	5 (18)	304 (22)
Regularly	23 (82)	1091 (77)
Anal intercourse with opposite sex		
Never	28 (100)	1195 (85)
Once	0 (0)	118 (8)
Occasionally	0 (0)	84 (6)
Regularly	0 (0)	11 (1)

*No statistical significance between anti-HBc positive and anti-HBc negative patients.

Table 6 History of STD and presenting STD in the GUM study group, comparing anti-HBc positive with anti-HBc negative patients (percentage)

Diagnosis	History of STD anti-HBc		Presenting STD anti-HBc	
	+ve	– ve	+ve	– ve
Syphilis	1 (4)	1 (0)	0	2 (0)
Gonorrhoea	4 (14)	54 (4)	7 (25)	159 (11)
Chlamydia	3 (11)	177 (13)	3 (11)	193 (14)
NSU	3 (11)	106 (8)	2 (7)	120 (9)
Trichomonias	0	25 (2)	0	67 (5)
Genital herpes	2 (7)	41 (3)	1 (4)	53 (4)
Genital warts	2 (7)	198 (14)	0	169 (12)

Current or past history of STD was not statistically significant when anti-HBc positive patients were compared with anti-HBc negative.

Of the five controls with anti-HBc, two had anti-HBs and one had HBsAg. HBeAg and anti-HBe was measured in only three of the five control patients with anti-HBc. All three had anti-HBe and were negative for HBeAg.

ANALYSIS OF RISK FACTORS

When anti-HBc positive patients were compared with anti-HBc negative patients, there was no difference in age and civil status in the two groups (table 1). Univariate analysis revealed several significant risk factors: ethnicity (white versus non-white; non-white included Afro-Caribbean, Asian, Iranian, for the purpose of the analysis) ($p < 0.0001$); the duration of sexual activity ($p < 0.0001$); patients born outside the UK ($p < 0.0001$) or had lived outside the UK for longer than 3 months ($p < 0.0001$) and patients who had sexual intercourse with foreign nationals ($p < 0.002$) (tables 2 and 3). This may have implications for travellers to countries with high endemicity. A similar proportion of patients in the core antibody positive and the core antibody negative groups had more than 10 sexual partners during their lifetime. Patients who had five or fewer lifetime sexual partners were found to have a smaller risk for being core antibody positive ($p < 0.02$). However, because of the small number of patients with positive anti-HBc logistic regression analysis could not be used for potential risk factors. A limited regression analysis for two factors showed that both ethnicity and the duration of sexual activity were risk factors for HBV infection in this study (ethnicity: $p < 0.001$; duration of sexual activity: $p = 0.013$) (table 4). None of the potential risk factors were good predictors for the risk of exposure to HBV infection. In the two groups, there was no difference in the mean age of the first sexual intercourse and the number of sexual partners in the past 12 months. There was also no difference in the two groups, when sexual practices (table 5) or the history of sexually transmitted diseases were compared (table 6).

Discussion

This prospective, cross sectional study is one of the first studies conducted to determine the prevalence of hepatitis B infection in the United Kingdom. The overall prevalence of anti-HBc in the GUM study group was 1.9% whereas for the control group, it was 0.5%. This is in contrast with parts of Europe and the United States, where the reported prevalence of HBV markers in similar populations, ranged from 8–30%.^{12–14} This may reflect the very low prevalence of HBV infection in the general population in the UK.¹⁵ The control group was drawn from males attending for blood donation. This is a self-selected group as patients with high risk behaviour such as male homosexual and IVDU patients, are requested not to give blood. Risk factors for HBV acquisition would be low in this group. Female controls were drawn from patients attending for antenatal care.

Of the 28 patients positive for anti-HBc in

the study group, 22 had anti-HBs and 19 had anti-HBe. None had HBeAg (two patients not tested) and only two patients had HBsAg, and were, therefore, capable of infecting other individuals. Since chronicity is more likely to develop in patients exposed to HBV infection during infancy or childhood,¹ it is probable that most of the patients positive for anti-HBc in this study were exposed to the infection during adulthood, thus suggesting that the raised prevalence in the study group may be due to heterosexual transmission of HBV, since other risk factors for HBV infection were excluded.

The seroprevalence of HBV markers in Birmingham was (3.2%) and Coventry was (0.8%) suggesting that there is a geographical difference in the prevalence of hepatitis B within the UK. However, during the study period, 25.2% of Birmingham GUM study patients were non-white compared with 11.7% in Coventry. Thus the difference in HBV markers in these two clinics may be partially due to a different racial mix of their populations. No data were available on the ethnic origin or the socioeconomic background of the control population to compare with GUM study group. In a study from Arizona, USA, the prevalence of HBV in heterosexuals attending STD clinics was 8% for the whites and 11% for blacks.¹² Additional similar studies at various geographical locations within the UK would be required in order to determine any geographical or racial variations in the prevalence of HBV markers.

Both ethnicity (white/non-white) and the duration of sexual activity have been shown to be significant risk factors for HBV infection by limited regression analysis. Other potential risk factors, which include number of sexual partners in lifetime; being born outside the UK; lived outside the UK for more than 3 months; and having had sexual intercourse with foreign nationals, were significant by univariate analysis (table 3). These results, however, must be viewed with caution because the overall prevalence of HBV is low, thus the impact of these risk factors on the prevalence of HBV is very small, and their predictive value was poor. Both ethnicity and duration of sexual activity are likely to be related quite closely to other variables. For instance, ethnicity is closely linked to place of birth and history of living outside the UK. Duration of sexual activity probably correlates with the number of sexual partners. With so few patients with positive core antibody it is not feasible to investigate these relationships.

Past history of STD and presenting STD

was not shown to be a significant risk factor for HBV acquisition. However, the STD data were obtained by self reporting which may have diluted the relation between STD and acquisition of HBV.

This study indicated that heterosexuals attending the Birmingham GUM clinic were at a higher risk for HBV than those attending at Coventry, and the latter were at a marginally higher risk for HBV than the control group. The risk was higher among non-whites and with increasing duration of sexual activity. The study showed that the risk factors investigated could not be used as predictors that could identify risk group that should be vaccinated. The low prevalence of HBV markers in this study was a limiting factor that affected the sensitivity of the study.

We thank SmithKline Beecham for their financial support of this study.

- 1 Maynard JE, Kane NA, Alter MJ, Hadler SC. Control of hepatitis B by immunization: global perspective. In: Zuckerman AJ, ed. *Hepatitis and Liver Disease*. New York, NY: Alan R Liss Inc, 1988:967-9.
- 2 Perillo RP, Schiff ER, Davis GL, Bodenheimer HC Jr, Lindsay K, Payne J, et al. A randomised, controlled trial of interferon alfa-2b alone and after prednisone withdrawal for the treatment of chronic hepatitis B. *N Engl J Med* 1990;323:295-301.
- 3 Krugman S, Giles JP, Hammond J. Infectious hepatitis, evidence for two distinctive clinical, epidemiological, and immunological types of infection. *JAMA* 1967;200:365-73.
- 4 Prince AM, Hargrove RL, Szmunn W, Cherubin CE, Fontana VJ, Jeffries GH, et al. Immunologic distinction between infectious and serum hepatitis. *N Engl J Med* 1970;282:987-91.
- 5 Szmunn W, Prince AM. Epidemiologic patterns of viral hepatitis in Eastern Europe in the light of recent findings concerning the serum hepatitis antigen. *J Infect Dis* 1971;123:200-12.
- 6 London WT, Sutnick AI, Blumberg BS. Australia antigen and acute viral hepatitis. *Ann Intern Med* 1969;70:55-9.
- 7 Villarejos VM, Visona KA, Gutierrez A, Rodriguez A. Role of saliva, urine and feces in the transmission of type B hepatitis. *N Engl J Med* 1974;291:1375-8.
- 8 Van Doornum GJ, Van Haastrecht JH, Hooykaas C, Van Den Hoek JA, Van Der Linden MM, Coutinho RA, et al. Hepatitis B virus infection in a group of heterosexuals with multiple partners in Amsterdam, The Netherlands: implications for vaccination? *J Med Virol* 1994;43:20-7.
- 9 Barrett CL, Austin H, Louw WC, Alexander WJ, Hadler SC. Risk factors for hepatitis B virus infection among women attending a clinic for sexually transmitted diseases. *Sex Transm Dis* 1992;19:14-8.
- 10 Hou MC, Wu JC, Kuo BI, Sheng WY, Chen TZ, Lee SD, et al. Heterosexual transmission as the most common route of acute hepatitis B virus infection among adults in Taiwan—the importance of extending vaccination to susceptible adults. *J Infect Dis* 1993;167:938-41.
- 11 Alter MJ, Hadler SC, Margolis HS, Alexander WJ, Hu PY, Judson FN, et al. The changing epidemiology of hepatitis B in the United States: Need for alternative vaccination strategies. *JAMA* 1990;263:1218-22.
- 12 Alter MJ, Ahtone J, Weisfuse I, Starko K, Vacalis TD, Maynard JE. Hepatitis B virus transmission between heterosexuals. *JAMA* 1986;256:1307-10.
- 13 Hentzer B, Skinhoj P, Hoybye G, Neilsen AO, Kvorning SA, Faver V, et al. Viral hepatitis in a venereal clinic population. *Scand J Infect Dis* 1980;12:245-9.
- 14 Siebke JC, Wessel N, Krandal P, Lie T. The prevalence of hepatitis A and B in Norwegian merchant seamen—a serological study. *Infection* 1989;17:77-80.
- 15 Gilson RJC. Sexually transmitted hepatitis: a review. *Genitourin Med* 1992;68:123-9.