Original article

Hepatitis B virus infection in patients attending a genitourinary medicine clinic: risk factors and vaccine coverage

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Background: The hepatitis B virus (HBV) immunisation policy in the United Kingdom includes offering vaccine selectively to those at risk by sexual contact. Among genitourinary medicine (GUM) clinic attenders, homosexual men are offered vaccine, but estimates of the vaccine uptake are required to monitor policy and estimate the possible impact on transmission; heterosexuals are not routinely offered vaccine, but this policy might change if the prevalence was found to be high.
Objective: To determine the prevalence of HBV infection and vaccine uptake among patients attending a GUM clinic.
Methods: HBV seroprevalence determined by unlinked anonymous testing of consecutive blood samples sent for syphilis serology. Demographic and risk factor data and history of HBV immunisation extracted from clinic notes before unlinking. Prevalence data were compared with a population of first time blood donors from the same area.
Setting: Open access GUM clinic in central London.
Results: Samples were obtained and tested from 441 homosexual and 527 heterosexual men and from 821 women over a 4 month period in 1990. After exclusion of injecting drug users and their sexual partners (n=30) and HBV carriers attending for follow up (n=12), the prevalence of antibody to HBV core (anti-HBc) was 38.7% in homosexual men, 5.9% in heterosexual men, and 3.5% in women (50.0%, 6.0%, 3.7% respectively if previous vaccinees were also excluded). The prevalence of HBV surface antigen positivity was 4.2%, 0.60%, and 0.39% respectively after exclusion of vaccinees (χ^2 $p<0.001$ for homosexual men versus others). The prevalence of anti-HBc in first time blood donors was 1.1% (8/749). Among male GUM clinic attenders, the prevalence of anti-HBc was higher in those of non-UK origin or place of birth and/or non-white ethnicity (odds ratios 2.87, 95%CI 1.57–5.24 and 8.06, CI 3.39–19.1, in homosexuals and heterosexuals respectively). In homosexual men anti-HBc prevalence increased with age (OR 1.05, CI 1.02–1.07 for each year) and lifetime number of STDs (OR 6.36, CI 3.77–10.8 for ≥2 versus <2) and in clinic reattenders compared with new patients (OR 5.42, 95% CI 3.32–9.16). Among heterosexuals, age was associated with anti-HBc prevalence in women (OR 1.09, CI 1.04–1.12) but not men (OR 0.99, 95% CI 0.95–1.02). There were no other associations in heterosexuals. A history of HBV immunisation in homosexual men was recorded in 13/131 (9.9%) of new patients and 103/305 (33.8%; OR 4.63, CI 2.49–8.60) clinic reattenders.
Conclusions: Although higher than a sample of blood donors, the prevalence of serological markers of HBV infection among heterosexuals was low, providing little support for extending HBV immunisation to all heterosexuals attending GUM clinics as a targeted strategy for control of HBV infection. Homosexual men remain at high risk of infection, but many are now being immunised. Efforts to improve compliance with existing vaccine policies in GUM clinics should be encouraged.
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Keywords: hepatitis B virus; sexual transmission; prevalence; vaccine

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Introduction

The policy for immunisation against hepatitis B virus (HBV) infection in the United Kingdom, a country with a low prevalence of infection is to offer vaccine selectively to those most at risk.[1] Countries with a higher prevalence are adopting universal immunisation.[2] Most HBV infections in the United Kingdom occur in adults, like other low endemicity countries.[3] Studies in the United States have suggested that up to 26% of acute infections in adults may be acquired by sexual transmission among heterosexuals and a further 7% among homosexual men.[4] The contribution of sexual transmission in the United Kingdom is uncertain. Data are limited to laboratory and case reports, neither of which include detailed information about probable routes of transmission.[3] The number of laboratory reports of HBV infections in the United Kingdom, from all causes, has fallen since 1985 although the number in homosexual men may have increased recently.[5]

In the United Kingdom, the strategy for the control of sexually transmitted HBV infection is to immunise those who change sexual partner frequently although this is not further defined.[1] Its effectiveness is unproved. In the United States, HBV immunisation has had little impact because there has been a failure to

immunise those at risk.[4] One approach is to offer vaccine to genitourinary medicine (GUM) clinic patients, either selectively or universally.[6 7] In GUM clinics, those offered vaccine include sex industry workers, homosexual men, injecting drug users and their sexual partners, and contacts of cases of HBV infection. Most clinics, including our own, do not offer vaccine routinely to heterosexuals unless they fall into one of the other groups above.[8]

We reported previously a high prevalence of HBV markers in heterosexual clinic attenders, suggesting that they could be targeted in a vaccine policy.[9] The study included only limited information about injecting drug use and prior risk of vertical or early horizontal transmission, suggested by origin in a high endemicity region. Furthermore, we reported poor coverage of hepatitis B vaccine among homosexual male clinic attenders,[10] questioning the efficacy of a targeted policy.

The aims of this study were to determine the prevalence and risk factors for HBV infection in clinic attenders by testing anonymised serum samples from those having serological tests for syphilis and to compare the prevalence with that of first time blood donors tested by the North London Blood Transfusion Service. Data on HBV immunisation were collected to assess the immunisation coverage and the factors associated with prior immunisation.

Participants and methods

PARTICIPANTS AND STUDY METHODOLOGY

Sera were collected from consecutive patients attending the GUM clinic at the Middlesex Hospital over 4 months in 1990 and having blood taken for syphilis serology as part of routine investigation or screening for sexually transmitted diseases. Hepatitis B carriers, defined as patients with detectable HBV surface antigen (HBsAg) in serum for more than 6 months, were excluded from the study if they were attending specifically for hepatitis follow up, but not if attending for routine GUM services. Demographic and risk factor data were extracted from the medical notes after each clinic visit including age, sex, sexual orientation, current and previous sexually transmitted diseases. In addition, by attaching a short questionnaire to the syphilis serology request, further information was obtained concerning past history of blood transfusion, injecting drug use, sexual contact in Africa, immunisation against hepatitis B, number of different sexual partners in the past year, ethnic origin, and place of birth. New patients were distinguished from repeat attenders. Before serological tests were carried out, the serum samples and historical data were anonymised.

The prevalence of serological markers of HBV infection was also determined in a comparison group of blood donors. Data were obtained from a study of the prevalence of raised alanine transaminase, anti-HBc, and anti-HCV among blood donors recruited by the blood transfusion centres at Bristol, Manchester, and North London.[11] For this analysis, those selected were first time blood donors from the North London centre, which draws from a similar catchment area to the GUM clinic. Informed consent was obtained from donors and the study was approved by the local research ethics committee. At the time of the transfusion service study, which was undertaken shortly before the GUM clinic study, potential donors were asked to refrain from donation if they were at risk of blood borne infections characterised by any of the following: having had male homosexual contact, injected drugs, or received unheated blood clotting factors since 1977, or been a sexual contact of anyone in these categories; worked as a prostitute; or, for men, had sexual contact with a prostitute in the preceding 18 months. Anonymised data comprising age, sex, and anti-HBc status were provided for analysis.

LABORATORY METHODS

All serum samples from GUM clinic attenders were tested for HBV serological markers. HBsAg was assayed by enzyme immunoassay (EIA, Wellcozyme, Wellcome Diagnostics, Dartford, Kent). Samples reactive in this assay were also tested by a reverse passive haemagglutination assay (RPH, Hepatest, Wellcome Diagnostics) and equivocal or weakly reactive samples by neutralisation. Anti-HBc and antibody to surface antigen (anti-HBs) were assayed by in house radioimmunoassays (RIA).[12] Samples reactive for only one marker were only considered positive if the test was repeatably reactive. Patients with repeatedly equivocal or borderline test results were considered negative for that HBV marker, or excluded if this was the only test reactivity detected.

Serum samples from first time blood donors were only screened for anti-HBc. Samples were tested by Wellcome EIA and repeatedly reactive samples were then tested by the same in house RIA as the GUM clinic samples.

STATISTICAL METHODS

Data were analysed using the SPSS (SPSS, Chicago, IL, USA) and SAS (Statistical Analysis System Institute, Cary, NC, USA) statistical software packages. Prevalences are presented with 95% confidence intervals (CI) calculated using the CIA software package (BMJ Publishing, London). Odds ratios (OR) were calculated for associations between categorical variables, and tested by χ^2 tests; comparisons between continuous variables were by the Mann–Whitney test. Multivariate analysis was performed using the GLIM procedure (SAS).

Results

Serum samples were collected from 1801 patients (repeat samples from 19 patients were excluded). Twelve homosexual/bisexual men were excluded from the analyses because they were known HBV carriers attending for routine follow up. The age, mean number of lifetime episodes of sexually transmitted disease, mean number of sexual partners in the preceding 12 months, history of ever having been an injecting drug user or sexual contact with a known user, and hepatitis B immunisation history are shown

Table 1 Characteristics of 1789 patients attending a genitourinary medicine clinic

	Men		Women
	Homosexual*	Heterosexual	
Number	441	527	821
Age (years): mean (SD)	33.4 (9.9)	31.5 (8.8)	28.2 (7.0)
Lifetime STDs†: mean (SD)	2.9 (3.74)	1.2 (2.04)	0.67 (1.15)
Sexual partners in past year: mean (SD)	7.7 (13.2)	2.8 (3.7)	1.8 (3.7)
History of injecting drug use or contact‡: % (n)	1.5 (6/403)	2.2 (11/498)	1.7 (13/762)
History of HBV immunisation: % (n)	26.6 (116/436)	2.4 (12/498)	4.1 (31/763)
Ethnic origin/place of birth:			
UK			
white (%)	79.1	66.8	70.0
non-white (%)	2.9	6.6	6.2
Europe/Australia/North America (%)	12.5	13.5	16.1
Rest of world (%)	5.4	13.1	7.7

*Excluding 12 patients attending for chronic hepatitis B follow up. Bisexual men are included in the homosexual category.
†Lifetime number of episodes of sexually transmitted disease counting genital herpes and warts once only.
‡Sexual partner of injecting drug user.

in table 1. Ethnic origin and country of birth information were available for 88% of the study population. Where this was not recorded, nationality was used as a proxy for place of birth. The categories were grouped and the resulting distribution is shown in table 1.

The overall prevalence of exposure to infection with HBV, including current and resolved infections, can be estimated from the prevalence of anti-HBc in serum, with or without other markers. The prevalence of anti-HBc in homosexual men was 38.7% (163/421, CI 34.1–43.4), higher than in heterosexual men (5.9%, 30/510, CI 4.0–8.3) or women (3.5%, 28/795, CI 2.4–5.1; p<0.0001), but there was no significant difference between heterosexual men and women. Exclusion of vaccine recipients (n=115) from the homosexual group increased the prevalence in the remaining population to 50.0% (153/306, CI 44.4–55.6) but had little effect on the prevalence in heterosexual men (6.0%) or women (3.7%) as so few had a history of immunisation (n=12 and 31 respectively). Serum anti-HBs may be detectable in the absence of detectable anti-HBc or HBsAg in patients who have not been immunised, but the specificity of the reaction may be in doubt.[12] Fourteen such patients were excluded from the analysis in this study.

The prevalence of current HBV infection (HBsAg positivity), after exclusion of vaccine recipients, was higher in homosexual men at 4.2% (13/306; CI 2.28–7.16) than in either heterosexual men or women; 0.60% (3/499; CI 0.13–1.8) and 0.39% (3/764; CI 0.079–1.14) respectively (χ^2 p<0.0001). Most of those infected are likely to be chronic carriers; none were diagnosed clinically as suffering from acute hepatitis at the time of the study.

In all analyses of the association between the variables recorded and serological markers of HBV infection, patients with a history of injecting drug use or a sexual partnership with an injecting drug user were excluded. Those with a history of immunisation against HBV were also excluded. The prevalence of anti-HBc increased with age in homosexual men (OR 1.05, CI 1.02–1.07, for each 1 year increase) and in women (OR 1.09, CI 1.04–1.12) but not in heterosexual men (OR 0.99, CI 0.95–1.02). Comparison of the prevalence of anti-HBc in different ethnicity/place of birth groups (table 2) showed the prevalence to be lower in white men, whether homosexual or heterosexual, of United Kingdom origin (the United Kingdom white group) than in the others; a similar but non-significant trend was observed in women.

Univariate odds ratios for lifetime number of episodes of STDs, number of sexual partners in the past 12 months and history of previous GUM clinic attendance are shown in table 2. Among homosexual men, anti-HBc prevalence increased with lifetime number of STDs, and there was a trend towards an increase with number of partners in the past year. The prevalence was higher in clinic reattenders compared with first time attenders. Among heterosexuals, there was no significant association with lifetime number of STDs in either heterosexual men or women either when the number of STDs was dichotomised (table 2) or when considered as a continuous variable (data not shown). Number of partners in the past 12 months was not related to anti-HBc prevalence in women. In heterosexual men there was an inverse relation between number of partners and HBV prevalence (OR 0.44, CI 0.20–0.99); this was of borderline significance and the number of infections in either group was very small. Restriction of the above analyses to the United Kingdom white groups produced

Table 2 Association between prevalence of serological markers of HBV infection (anti-HBc) and ethnicity/place of birth, lifetime number ofSTDs, number of partners, and GUM clinic attendance

	Homosexual men			Heterosexual men			Women		
	% HBV positive	OR	95% CI	% HBV positive	OR	95% CI	% HBV positive	OR	95% CI
Place of birth/ethnicity:									
UK white	46.0	1		2.1	1		3.7	1	
UK non-white	50.0	1.17	0.29–4.8	0	—		4.3	1.16	0.26–5.14
Europe/N America/Australasia (all ethnic groups)	71.8	5.53	2.66–11.5	11.3	5.98	2.02–17.7	4.2	1.15	0.42–3.13
Rest of world (all ethnic groups)	80.0	4.70	1.29–17.0	25.0	15.7	6.19–39.6	13.1	3.95	1.66–9.41
All except UK white	71.0	2.87	1.57–5.24	14.6	8.06	3.39–19.1	6.6	1.85	0.93–3.69
Lifetime number of STDs:									
⩾2	72.2	6.36	3.77–10.8	6.0	0.94	0.38–2.29	4.5	1.0	0.30–2.68
<2	28.9	1		6.3	1		4.6	1	
Number of partners in past 12 months:									
⩾2	51.9	1.53	0.85–2.74	4.5	0.44	0.20–0.99	4.7	1.15	0.54–2.47
<2	40.5	1		9.6	1		4.1	1	
GUM clinic attendance:									
Repeat attenders	65.8	5.42	3.32–9.16	7.2	1.29	0.62–2.69	5.7	1.49	0.75–2.97
First time attenders	25.9	1		5.7	1		3.9	1	

Table 3 Association between HBV immunisation and clinic attendance, past STDs, and partner number in homosexual men

	Proportion (%) immunised	*OR*	*95% CI*
GUM clinic attendance:			
Repeat attenders	103/305 (33.8)	4.63	2.49–8.60
First time attenders	13/131 (9.9)	1	
Lifetime number of STDs:			
⩾2	68/232 (29.3)	1.33	0.87–2.04
<2	48/202 (23.8)	1	
Number of partners in past 12 months:			
⩾2	79/292 (27.1)	2.26	1.16–4.38
<2	12/85 (14.1)	1	

similar results, except that the inverse relation with number of partners in heterosexual men was no longer statistically significant (data not shown). Modelling of HBV prevalence in homosexual males including all the variables listed above revealed no significant interaction effects. In heterosexuals no multivariate analysis of risks factors was possible in the absence of any significant associations between sexual behaviour variables and HBV prevalence in the univariate analyses.

A history of previous immunisation against HBV was reported by 26.6% (95% CI 22.5–30.8) of homosexual men (table 3). As expected, more of the homosexual men who had attended the clinic before (33.8%, CI 28.5–39.1) than patients new to the clinic (9.9%, CI 5.4–16.4) had a history of HBV immunisation, although they had not necessarily completed a vaccine course. Previous HBV immunisation was associated with partner number, but not number of STDs. The proportion of heterosexual men and women immunised was only 2.4% and 4.1% respectively (table 1). Most heterosexuals immunised were healthcare workers or others recommended to be immunised on occupational health grounds (data not shown).

Comparison of the prevalence of anti-HBc was made with a sample of first time blood donors from the same region (North Thames). The prevalence of anti-HBc in blood donors was 0.78% (3/387, CI 0.17–2.25) in men and 1.4% (5/362, CI 0.45–3.2) in women; combined prevalence 1.1% (CI 0.46–2.09). The prevalence in a selected group of the GUM clinic attenders (heterosexual, United Kingdom born, white, excluding injecting drug users and vaccinees) was 2.6% (21/805, CI 1.62–3.96). Although the number of positives was small, the difference was significant (OR 2.48, CI 1.04–46.1, p=0.04). The blood donors were older than the GUM clinic patients; adjustment for age increases the difference slightly (OR 2.72, CI 1.19–46.2).

This study was prompted in part by the finding of a high prevalence of HBV markers among heterosexuals in a similar study at the clinic in 1987, from which injecting drug users were not excluded. The prevalence of anti-HBc in heterosexual men in 1990 was 6.3% (CI 4.39–8.76) without exclusion of injecting drug users and was similar to that in 1987, 7.2% (CI 4.83–10.4). In women the 1990 prevalence was significantly lower at 3.9% (CI 2.70–5.50) than in 1987, 10.0% (CI 7.21–13.3, p<0.001). Comparison of the prevalence in homosexual men was also complicated by the lack of information about immunisation in the 1987 study; however, an audit of hepatitis B immunisation had suggested that few were immunised at that time.[10] The prevalence in 1990 of 38.6% was lower than the 47.9% found in 1987 (p<0.02), but when vaccinees were excluded from the 1990 sample the difference was not significant (prevalence 49.8%).

Discussion

The prevalence of serological markers of HBV infection in homosexual men in 1990 remained much higher than in heterosexuals, although it had decreased since 1987 (from 47.9% to 38.6%). Changes in sexual behaviour and protection by HBV vaccine may have contributed to the decline, but a change in the population of clinic attenders having syphilis serology (on which the prevalence study was based) may also be a factor. Increasing adoption of safer sex practices may have led to fewer patients having full screening for STDs as well as fewer patients presenting with symptoms. Although syphilis screening of new patients presenting to the clinic or those with a new problem remains clinic policy, clinic practice may have changed. Tests may have been omitted if patients or doctors considered them not to have been at risk, or in those known to be HIV infected (A Nardone, personal communication).

The proportion of homosexual men attending the clinic who have been immunised is increasing. An audit of hepatitis B immunisation in our clinic in 1988 showed that of all new patients only 1.3% (10/758) had been given vaccine before their attendance at the clinic.[10] This had increased to 9.9% in the present study, with 33.8% of clinic reattenders having been given vaccine. Because of the study methodology of anonymous testing it was not possible to collect follow up information to estimate the proportion of patients who were subsequently given vaccine, but it was estimated that at least half of those not already immunised or known to be immune were screened for HBV markers, the first step in the process leading to immunisation. There was evidence that those who had received vaccine in the past were those at greater risk as they had had more partners in the last year, and a trend towards more STDs. The results suggest that the policy of offering HBV vaccine selectively to those GUM clinic attenders at high risk may result in a substantial proportion being immunised. Since 1990, the clinic policy has been changed so that the first dose of vaccine is given at the same time as screening to reduce the number of clinic visits, with the aim of further increasing compliance.

We also determined the prevalence of HBV infection in heterosexual GUM clinic attenders and compared this with a population of first time blood donors, and with clinic attenders in the previous study in 1987. The fall in prevalence in women in 1990 compared with 1987 (anti-HBc prevalence 3.9% *v* 10.0%) cannot be explained with certainty. In 1987, history of drug use was not recorded systematically but the prevalence of 3.9% for 1990

includes those with a history of drug use or contact with a drug user. A higher prevalence of drug use among patients in 1987 could explain the difference but there is no evidence that such a change in the population of clinic attenders has occurred; in 1990 only 1.7% of women had a history of injecting drug use or contact with a user.

In comparing the heterosexual clinic attenders with blood donors, those GUM clinic patients who were of non-white ethnicity or were born outside the United Kingdom and those with other recorded risk factors for HBV infection were excluded. In restricting the GUM clinic population in this way, the aim was to focus on those clinic attenders who were least likely to have been exposed to HBV infection early in life and who would be those to be offered HBV vaccine if the policy changed to include all heterosexual GUM clinic attenders. The prevalence in both groups was low, 2.6% in GUM clinic attenders and 1.1% in blood donors; the absolute difference was small but statistically significant. Blood donors have lower rates of past STD and lifetime number of partners than GUM clinic patients.[13] Blood donors are not a representative sample of the general population. They were subject to the self exclusion criteria detailed above, which aim to reduce the risk of including those who may transmit blood borne virus infections. Blood donors have low rates of many common diseases. However, they are also ethnically heterogeneous and those of non-United Kingdom origin were not excluded from the blood donor group analysed as individual ethnicity data were not available. In this respect, the difference in prevalence may consequently be an underestimate. The donors were also older; adjusting for age increases the difference marginally. Among GUM clinic patients, it is likely that not all patients with other risks, notably injecting drug use, were identified. The true prevalence in heterosexual attenders without other risks may therefore be lower than the estimate here. The difference in prevalence reported here is consistent with sexual transmission among heterosexuals contributing to the risk for HBV infection, with GUM clinic patients being a group at increased risk, but the excess risk of HBV infection is small. The only variable consistently associated with infection in heterosexuals was increasing age among women. There was no consistent association detected between any of the sexual behaviour variables and HBV prevalence. This may be because these variables are not sufficiently sensitive measures of sexual behaviour. The inverse relation with partner number in heterosexual men may have been a chance finding; the number of those infected was very small.

The results of this study are consistent with a report from Amsterdam. In a prospective study of heterosexual, non-drug using STD clinic attenders with at least five partners in the past 6 months no HBV infections occurred during an observation period of 504 person years (95% CI 0–5.9 per 1000 person years).[14] The authors decided not to recommend routine immunisation of clinic attenders. Another study from the United Kingdom, from two centres in the West Midlands, found a prevalence of anti-HBc of only 1.9% (28/1478) among heterosexual GUM clinic attenders.[15] The study excluded homosexual and bisexual men, injecting drug users, known HIV infected patients, and sex workers. Non-white ethnicity, time spent abroad, and duration of sexual activity were related to prevalence. Given the very low prevalence of infection a multivariate analysis of risks was not possible.

Relevant to this issue are the results of a national population survey of sexual attitudes and lifestyles, which included data on the pattern of clinic attendance[16]; 27% of men who had had a male sexual partner in the past 5 years had attended an STD clinic during that period and clinic attendance was more likely in those with more partners. These findings support the rationale for giving HBV vaccine to homosexual male clinic attenders. Among heterosexuals, there was evidence that clinic attenders have a higher prevalence of risk behaviours than non-attenders; however, of all those surveyed only 3.4% of men and 2.6% of women had attended an STD clinic in the past 5 years. Those with risk markers for STDs who have not attended a clinic outnumber those who have by 8 to 1, and 12 to 1 for men and women respectively. Based on these data, a vaccine policy targeting heterosexuals attending GUM clinics cannot be expected to have a rapid effect on the incidence of HBV infection acquired sexually by heterosexuals.

The relative efficiencies of universal childhood or adolescent immunisation versus a targeted immunisation strategy in the United Kingdom remains controversial.[17–19] Williams *et al* have argued, on the basis of complex mathematical models of the impact of different immunisation strategies, that targeted vaccination may be more effective than universal immunisation for a period of at least several decades after the start of the programme.[20 21] The difference is greatest for homosexual men.

Even if a policy of universal immunisation were to be recommended, targeted immunisation of high risk groups would continue to be required until the cohorts of immunised children or adolescents have overtaken those older groups still at risk. Efforts to immunise groups such as homosexual men and injecting drug users should be further encouraged.

This study provides little support for the proposition that offering hepatitis B vaccine to all heterosexuals attending GUM clinics represents an efficient targeting of those substantially at risk of sexual transmission. Individuals may wish to be immunised but this is distinct from routine immunisation as part of a strategy for public health. More needs to be known about the prevalence of hepatitis B in the general population, the attributable risk for sexual transmission, and the relation between risk of hepatitis B and GUM clinic attendance. Importantly, and despite its large size, there was no attribute identified in this study that could define a subgroup of heterosexuals at higher risk, and thereby enable an HBV immunisation strategy to be focused more precisely.

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