

ORIGINAL ARTICLE

Seroprevalence of hepatitis A immunity in male genitourinary medicine clinic attenders: a case control study of heterosexual and homosexual men

J D C Ross, M Ghanem, A Tariq, G Gilleran, A J Winter

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See end of article for authors' affiliations

Correspondence to: Dr J D C Ross, Whittall Street Clinic, Whittall Street, Birmingham B4 6DH, UK; jonathan.ross@bscht.wmids.nhs.uk

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Objectives: To compare the seroprevalence of hepatitis A in homosexual and heterosexual men to determine their susceptibility to infection and provide guidance for a policy on vaccination.

Methods: A case-control study design was utilised to compare the risk factors associated with hepatitis A in homosexual and heterosexual men attending a city centre genitourinary medicine clinic. Demographic and sexual behavioural characteristics were included in univariate and multivariate models.

Results: The overall seropositivity rate was 29% with no significant difference between homosexual and heterosexual men. Ethnicity and age were strongly associated with hepatitis A seropositivity in both homosexuals and heterosexuals. A history of sex in a sauna in homosexual men, and being born outside the United Kingdom for heterosexual men, was associated with hepatitis A seropositivity.

Conclusions: Targeted hepatitis A screening and vaccination of homosexual men attending UK genitourinary medicine clinics is not supported by the results of this study.

Hepatitis A virus (HAV) is a robust RNA virus transmitted by the faecal-oral route and is responsible for most cases of infectious or "epidemic" hepatitis. Around 7000 cases of hepatitis A are notified each year in the United Kingdom, mostly among schoolchildren and young adults.¹ In children infection is usually asymptomatic, but infection later in life can be more severe, causing prolonged illness and even fulminant hepatic failure. As societies become more affluent so the incidence of childhood disease due to overcrowding and poor sanitation falls and adult susceptibility rises. Traditional

methods of transmission are then replaced in importance by other mechanisms, such as food poisoning epidemics² and faecal-oral contamination in sexual contact.³

In the late 1970s several enteric diseases such as shigellosis, amoebiasis, and *Giardia* were recognised as being sexually transmissible among homosexual men.⁴ The advent of specific antibody testing for hepatitis A IgM and the subsequent detection of a number of outbreaks among homosexual men^{5–12} convinced many that sexual transmission was important. A recent community based study in San Francisco found

Table 1 Demographics of study population

Characteristic	Controls* (n=136)	Cases* (n=74)	p Value
Age group (years)			
16–20	8 (6%)	4 (5%)	
21–25	29 (21%)	17 (23%)	
26–30	34 (25%)	19 (26%)	
31–35	26 (19%)	12 (16%)	
Over 35	39 (29%)	22 (30%)	0.99
History of travel outside UK, W Europe, N America, Australia			
No	74 (56%)	47 (64%)	
Yes	59 (44%)	27 (36%)	0.2
Born in the UK			
No	20 (15%)	8 (11%)	
Yes	116 (85%)	66 (89%)	0.3
Raised in the UK			
No	24 (18%)	8 (11%)	
Yes	112 (82%)	66 (89%)	0.13
Ever injected drugs			
No	135 (99%)	73 (99%)	
Yes	1 (0.7%)	1 (1%)	0.6
Ethnicity†			
Black African	3 (2%)	2 (3%)	
Black Caribbean	36 (26%)	1 (1%)	
Black other	3 (2%)	0	
Indian	6 (4%)	3 (4%)	
White	82 (60%)	64 (88%)	
Other	6 (4%)	3 (4%)	<0.001

*Column percentages.

†Data for one patient unavailable.

Cases: men who have ever had sex with men.

Controls: men who have never had sex with other men.

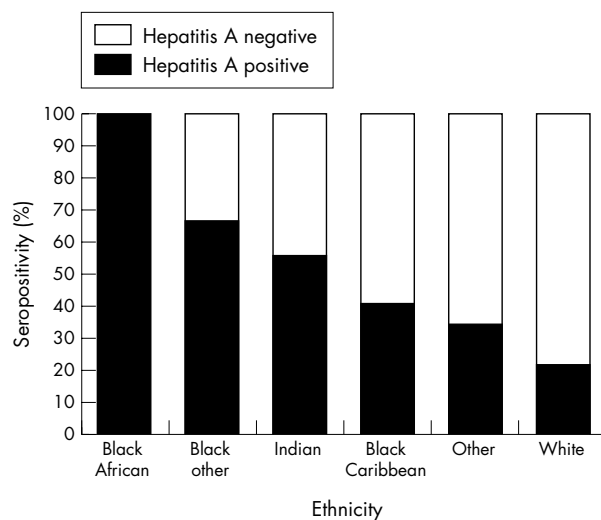


Figure 1 Association of ethnicity with seropositivity to hepatitis A.

that 3.3% of a sample of 411 self identified homosexual men had acute hepatitis A (as shown by anti-HAV IgM).¹³ Some cross sectional seroprevalence studies have also shown higher

rates of hepatitis A exposure in homosexual men than in heterosexuals attending clinics for sexually transmitted diseases (STDs).^{3 14 15} In these studies, oral-anal or digital-anal contact,^{3 15} duration of homosexual activity,^{3 15} number of lifetime sexual partners,¹⁶ sex in saunas,¹¹ and group sex¹⁰ have all been associated with hepatitis A exposure.

Other similar seroprevalence studies set in both the community^{17 18} and STD clinics^{16 18-25} have failed to find evidence that homosexual men have higher rates of hepatitis A than heterosexual men, although in general STD clinic attenders have higher rates than local blood donors.^{16 18 26}

In order to determine the susceptibility of homosexual men to HAV in a non-London UK setting we conducted a seroprevalence survey of homosexual male attenders, comparing them to age matched heterosexual male attenders. We investigated the influence of putative risk factors for HAV acquisition (such as sexual behaviour) on seroprevalence to inform the optimum strategy for pre-immunisation testing.

METHODS

The study was performed at a large city centre genitourinary medicine clinic in Birmingham, United Kingdom. Consecutive new or rebooked male attenders aged 16 and over who needed venepuncture for routine syphilis serology or for HIV testing were invited to participate. Subjects giving informed consent

Table 2 Univariate analysis of associations with hepatitis A IgG seropositivity

Characteristic	Hep A -ve*	Hep A +ve*	p Value
Sexual orientation			
Heterosexual	92 (68%)	44 (32%)	0.1
Homosexual	57 (77%)	17 (23%)	
Age group			
16-20	10 (83%)	2 (17%)	<0.001
21-25	43 (94%)	3 (6%)	
26-30	39 (74%)	14 (26%)	
31-35	26 (68%)	12 (32%)	
Over 35	31 (51%)	30 (49%)	
Past history of gonorrhoea			
No	136 (73%)	50 (27%)	0.049
Yes	13 (54%)	11 (46%)	
Past history of chlamydia			
No	122 (71%)	51 (30%)	0.5
Yes	27 (23%)	10 (27%)	
Past history of genital warts			
No	124 (69%)	55 (31%)	0.14
Yes	25 (81%)	6 (19%)	
Past history of herpes			
No	144 (71%)	59 (29%)	0.7
Yes	5 (71%)	2 (28%)	
Past history of other STI			
No	141 (71%)	58 (29%)	0.6
Yes	8 (73%)	3 (27%)	
History of travel outside UK, W Europe, N America, Australia			
No	91 (75%)	30 (25%)	0.056
Yes	55 (64%)	31 (36%)	
Born in the UK			
No	13 (46%)	15 (54%)	0.003
Yes	136 (74%)	46 (25%)	
Raised in the UK			
No	16 (50%)	16 (50%)	0.005
Yes	133 (75%)	45 (25%)	
Ever injected drugs			
No	148 (71%)	60 (29%)	0.5
Yes	1 (50%)	1 (50%)	
Ethnicity			
Black African	0	5 (100%)	<0.001
Black Caribbean	22 (60%)	15 (40%)	
Black other	1 (33%)	2 (67%)	
Indian	4 (44%)	5 (56%)	
White	115 (79%)	31 (21%)	
Other	6 (75%)	3 (25%)	

*Row percentages. Missing data may result in some characteristic totals not equalling the total group number.

Table 3 Univariate analysis of associations between sexual behaviour and hepatitis A IgG seropositivity for homosexual men

Characteristic	Hep A -ve*	Hep A +ve*	Significance
No of passive anal sex partners in the past year			
0	11 (69%)	5 (31%)	
1	13 (100%)	0	
2-5	20 (80%)	5 (20%)	
Over 5	10 (77%)	3 (23%)	p=0.2
No of passive anal sex partners ever			
0	6 (67%)	3 (33%)	
1	4 (100%)	0	
2-5	18 (95%)	1 (5%)	
Over 5	21 (78%)	6 (22%)	p=0.18
No of active anal sex partners in the past year			
0	10 (77%)	3 (23%)	
1	13 (81%)	3 (19%)	
2-5	22 (76%)	7 (24%)	
Over 5	9 (75%)	3 (25%)	p=0.98
No of active anal sex partners ever			
0	8 (89%)	1 (11%)	
1	6 (75%)	2 (25%)	
2-5	12 (86%)	2 (14%)	
6-10	14 (93%)	1 (7%)	
Over 10	11 (58%)	8 (42%)	p=0.1
No. of oral-anal sexual partners in past year			
0	19 (79%)	5 (21%)	
1	11 (92%)	1 (8%)	
2-5	16 (76%)	5 (24%)	
Over 5	9 (75%)	3 (25%)	p=0.8
No. of oral-anal sexual partners ever			
0	15 (79%)	4 (21%)	
1	5 (100%)	0	
2-5	16 (80%)	4 (20%)	
Over 5	15 (75%)	5 (25%)	p=0.7
No of digital-anal sexual partners in past year			
0	17 (71%)	7 (29%)	
1	7 (88%)	1 (12%)	
2-5	19 (86%)	3 (14%)	
Over 5	12 (80%)	3 (20%)	p=0.6
No of digital-anal sexual partners ever			
0	14 (70%)	6 (30%)	
1	5 (83%)	1 (17%)	
2-5	13 (76%)	4 (24%)	
Over 5	19 (90%)	2 (10%)	p=0.4
History of cottaging†			
No	40 (78%)	11 (22%)	
Yes	17 (74%)	6 (26%)	p=0.4
History of sex in sauna			
No	40 (85%)	7 (15%)	
Yes	17 (63%)	10 (37%)	p=0.03

*Row percentages.

†Visiting public places for sex.

completed a questionnaire in private, which yielded the following data:

- demographic data (date of birth, country of birth, self assigned ethnic status, whether raised in United Kingdom (defined as whether all of childhood was spent in United Kingdom))
- travel history (ever travelled outside United Kingdom, western Europe, North America, or Australia)
- clinical history (history of jaundice (and if this was known to be due to hepatitis A), history of vaccination against hepatitis A or B or both, history of HIV infection)
- sexual behaviour (including number and sex of sexual partners in previous year, history of peno-vaginal, peno-anal, receptive anal, oro-genital, oro-anal, and digital-anal sex ever and in previous year).

We excluded subjects who had received normal immune globulin in the preceding 12 months, who had been immunised against hepatitis A or who were known to be infected with HIV. We categorised the remaining subjects as “homosexual” (men who reported ever having sex with other men) or “hetero-

sexual” (men who reported never having a same sex partner), these terms being used for ease of reference. We assigned every eligible homosexual man as a case, and matched each case with two heterosexual controls from the same 5 year age band who attended on the same day. Hepatitis A total IgG was determined by ELISA (with confirmation if equivocal by radiometric assay). Subjects were informed of their hepatitis A immune status along with their other results, and those who were non-immune given an information leaflet.

Assuming a seroprevalence of 30% in the general (heterosexual) population aged 20–24¹ (typical of our clinic attenders) and 2:1 recruitment of heterosexual controls to homosexual cases, a total sample size of 207 (69 cases and 138 controls) was required to detect a relative risk of 1.7 with a power of 80% and alpha of 5% (EPI-INFO version 6). A univariate comparison of demographic and behavioural factors with seropositivity for hepatitis A was performed using the χ^2 test (SPSS v 10). Variables with a significance level less than 0.1 on univariate analysis and not exhibiting interactions with other variables were entered into a multivariate logistic regression model using a forward conditional (likelihood ratio) method (SPSS v 10).

Table 4 Univariate analysis of associations between sexual behaviour and hepatitis A IgG seropositivity for heterosexual men

Characteristic	Hep A -ve*	Hep A +ve*	Significance
No of female partners in the past year			
0	2 (67%)	1 (33%)	p=0.12
1	36 (80%)	9 (20%)	
2-5	39 (58%)	28 (42%)	
Over 5	14 (70%)	6 (30%)	
No of female partners ever			
1	6 (100%)	0	p=0.23
2-5	10 (67%)	5 (33%)	
Over 5	71 (66%)	36 (34%)	
Ever performed oral-genital sex with female partner			
Never	18 (62%)	11 (38%)	p=0.5
Yes, over 1 year ago	11 (79%)	3 (21%)	
Yes, within past year	63 (68%)	30 (32%)	
Ever performed oral-anal sex with female partner			
Never	73 (66%)	37 (34%)	p=0.7
Yes, over 1 year ago	4 (80%)	1 (20%)	
Yes, within past year	15 (71%)	6 (29%)	
Ever performed digital-anal sex with female partner			
Never	52 (65%)	28 (35%)	p=0.16
Yes, over 1 year ago	1 (33%)	2 (67%)	
Yes, within past year	31 (78%)	9 (22%)	

*Row percentages.

RESULTS

A total of 213 clinic attenders participated in the study. Three patients (1.4%) with equivocal hepatitis A serology were excluded, and the analysis is based on 74 homosexual men (cases) and 136 male heterosexual controls recruited between

February and September 2000. Table 1 shows the demographics of the study population. Homosexual men were more likely to be of white ethnicity.

Overall, 61 (29% (95% CI 23% to 35%)) individuals were hepatitis A seropositive. Homosexual men were less likely to be hepatitis A seropositive than age matched heterosexual controls, although this difference was not significant (23% v 32%, p=0.1). There was a striking difference in hepatitis A seropositivity according to self assigned ethnic status (fig 1).

In a univariate analysis of all subjects, increasing age, being born outside the United Kingdom, spending childhood outside the United Kingdom, and non-white ethnicity were strongly associated with hepatitis A seropositivity, and a weaker association was found for those with a history of gonorrhoea (table 2). In homosexual men, the only significant association between sexual practices and hepatitis A seropositivity was in those ever having had sex in saunas, who were over twice as likely to be HAV seropositive with a prevalence of 37% (table 3). Hepatitis A seropositivity in homosexual men was not associated with other reported sexual behaviours, including oro-anal sex or digital-anal sex (table 3). In heterosexual men there were no associations between a variety of sexual practices and hepatitis A seropositivity (table 4). There was a trend towards heterosexual men acquiring infection at an earlier age (fig 2).

We then constructed three regression models to explore these associations, entering variables with a significance level less than 0.1 on univariate analysis into a forward conditional logistic regression model separately for each of three groups (all subjects, heterosexual men, and homosexual men). Sexual behaviour variables were only included in the models for heterosexual and homosexual subgroups. Ethnicity and age were strongly associated with hepatitis A seropositivity in all three analyses, with weaker associations found for a history of travel outside the United Kingdom or Western Europe (for all patients), history of sex in a sauna (for homosexual men) and being born outside the United Kingdom (for heterosexual men) (table 5).

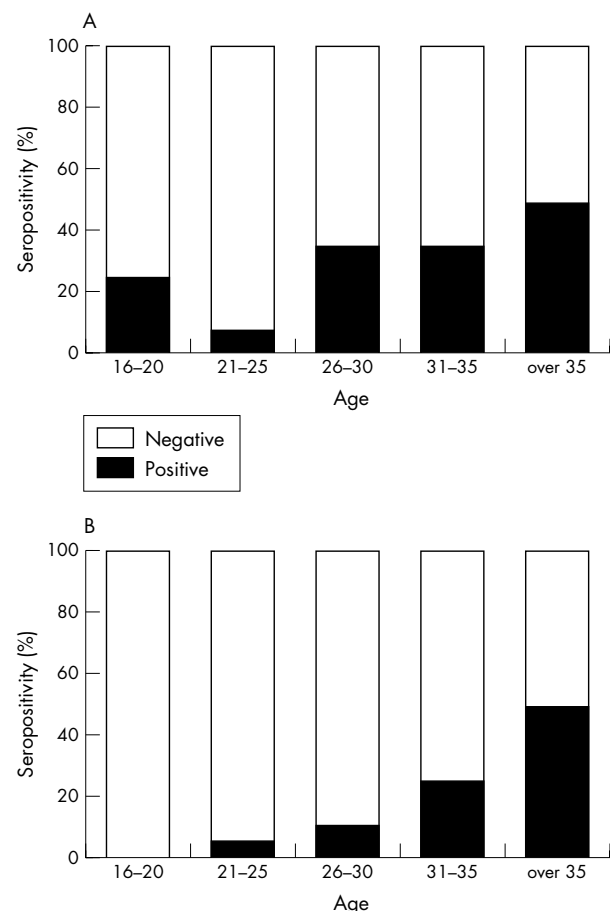


Figure 2 Age related increase in hepatitis A seroprevalence for (A) heterosexual and (B) homosexual men.

DISCUSSION

Our study population had an overall HAV seropositivity prevalence of 29%, although the prevalence of 23% for homosexual men is slightly lower than reported from studies in other

Table 5 Independent risk factors predicting HAV seropositivity

	p Value
All subjects*	
Ethnicity	<0.001
Age	<0.001
History of travel outside UK, W Europe, N America, Australia	0.046
Homosexual men†	
Ethnicity	0.007
Age	0.002
History of sex in sauna	0.025
Heterosexual men‡	
Ethnicity	0.017
Age	0.001
Born outside the UK	0.03

Variables entered in a forward conditional logistic regression analysis with separate modeling for each group.

*Variables also included in the model but not significant: sexual orientation, past history of gonorrhoea, born in the UK.

†Variables also included in the model but not significant: past history of gonorrhoea, history of travel outside UK or western Europe, born in the UK, no of active anal sex partners ever.

‡Variables also included in the model but not significant: past history of gonorrhoea, history of travel outside UK or western Europe.

areas.^{3 13 15 19} The only sexual practice associated with HAV was for men having had homosexual sex in a sauna, an activity reported by 37% of homosexual subjects. Anonymous sex, such as occurs in dark rooms or saunas, is a consistent predictor of risk for hepatitis A infection in homosexual men in several outbreak studies.^{10 11 27} Many other potential behavioural risk factors, including those found to be significant in other studies,^{3 10 11 15 16} were not found to be relevant. This lack of association may be the result of genuine differences in the populations studied or reflect methodological differences.

Identifying risk factors associated with hepatitis A infection may be useful in targeting high risk groups for health promotion, providing advice to patients about high risk behaviours, and to inform policy for providing vaccination against infection. The UK PHLS Communicable Disease Surveillance Centre has suggested in the light of recent HAV outbreaks in London that "HAV vaccine may be considered for homosexual men whose lifestyle puts them at risk" but fails then to define what particular lifestyle this means.²⁸ The 1996 UK DoH "Green Book" on immunisation suggests that homosexual men are at risk of HAV but stops short of recommending blanket coverage, preferring to leave the decision to the discretion of the doctor. Neither document gives guidance on preimmunisation testing, where immunisation is avoided in those testing positive for anti-HAV total IgG.

Our cross sectional study design has some inherent limitations. In particular, it is not possible to establish a causal relation between any sexual behaviour variable found to be associated with HAV infection because it is not known when the infection was acquired and whether the potential risk predated the exposure. It is also not possible to exclude recall bias, and other potentially relevant variables may not have been included. Two seroincidence studies constitute the most convincing evidence that HAV can be sexually transmitted. In the best designed, Corey *et al* followed 102 homosexual and 57 heterosexual non-HAV immune men for 6 and 8 months respectively. The annual incidence of HAV was 22% for homosexuals, but no cases were seen in heterosexuals.³ Coutinho *et al* found that 14% of 399 homosexual men seroconverted over a 690 day follow up, compared to none of 50 heterosexual men over 6 months.¹⁵ Although there is unequivocal evidence that hepatitis A can be transmitted sexually, our study in common with several others suggests that factors other than sexual practices are usually more important.

Our data show that in our cohort hepatitis A had been acquired in many men by the third and fourth decade

whatever their sexual orientation, and by 35 years of age almost half had been exposed to HAV and were immune. Belonging to a non-white ethnic group was also a risk factor for HAV independent of country of birth and sexual orientation. This may be the result of higher rates of infection within subgroups of the population resulting in an increased risk of transmission, or non-white ethnicity may be a surrogate for alternative risk factors such as socioeconomic status. Being born outside the United Kingdom was associated with increased risk of hepatitis A for heterosexual men only, and travel outside the United Kingdom/western Europe slightly increased the chances of having had HAV for all subjects.

The results of this study do not provide any evidence to support the routine testing and vaccination of homosexual men for hepatitis A in UK genitourinary medicine clinics. Patients who report engaging in group or anonymous sex should be apprised of the increased risk of hepatitis A among other sexually transmitted infections. Hepatitis A does, however, remain a common infection with a rapid increase in seropositivity observed between men in the third and fourth decades of life, and is easily preventable with a durable vaccine. Further studies are needed to assess the pattern of infection in women and whether it is cost effective to offer vaccination based on age and/or ethnicity.

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Conflict of interest: none.

CONTRIBUTORS

JR, concept, study design, grant application, supervision, manuscript ; MG, data collection, manuscript review; AT, data collection, manuscript review; GG, data collection, supervision; AW, study design, grant application, manuscript preparation.

Authors' affiliations

J D C Ross, M Ghanem, A Tariq, G Gilleran, A J Winter, Whittall Street Clinic, Birmingham, UK

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ELECTRONIC PAGES.....

Global views



Sexually Transmitted Infections receives an increasing number of articles relating to prevalence of STIs or the performance of various syndromic management protocols in different populations. While these are very important for policymakers and clinicians locally, they tend to have limited applicability to other populations. For this reason we will publish these articles, after peer review, in full through eSTI. The paper edition of the journal will feature full abstracts in the “global view” section.

Prevalence of and risk indicators for STIs among women seeking induced abortions in two urban family planning clinics in Shandong province, People’s Republic of China

SM Chen, A van den Hoek, CG Shao, L Wang, DC Liu, SJ Zhou, YC Peng, CL Li, XF Yin

Objectives: To determine the prevalence and to assess factors associated with STIs in order to set up simple diagnostic procedures and/or prophylactic therapy among women seeking induced abortions.

Methods: Women seeking induced abortions were recruited in two urban family planning clinics in Jinan, Shandong in a cross sectional study. A standardised questionnaire was used to collect demographic characteristics, obstetric and abortion history, condom use, and sexual risk behaviours. Vaginal and cervical samples were taken for the diagnosis of STIs and blood samples were collected for the testing of syphilis and HIV. Univariate and multivariate ORs and 95% CIs of risk factors for several STIs were determined using logistic regression.

Results: Out of 2020 women seeking induced abortions in two family planning clinics, the prevalence of STIs was 4.8% for *Chlamydia trachomatis*, 0.4% *Neisseria gonorrhoeae*, 2.5% trichomoniasis. Bacterial vaginosis was found in 3.4%. Five (1%) out of 503 women tested for syphilis had a positive TPPA and one of 787 women tested for HIV was seropositive. Although some risk factors were associated with the infections in logistic regression models, the positive predictive value was poor in this “low risk” population of women.

Conclusions: Women attending for induced abortions could be a targeted group for STIs, especially for chlamydial infection. Since most infections are asymptomatic and no criteria for screening can be used in practice, other strategies to detect these genital infections need to be developed.

▲ (*Sex Transm Infect* 2002; **78**:e3) www.sextransinf.com/cgi/content/full/78/3/e3