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Hepatitis C virus among high and low risk pregnant women in Dundee: unlinked anonymous testing

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Objective To determine the prevalence of the hepatitis C virus among pregnant women, to gauge the non-injecting, particularly sexual, risk of them being hepatitis C virus infected and to assess the potential impact of selective antenatal screening.

Population Antenatal clinic attenders and women undergoing termination of pregnancy in 1997.

Setting Ninewells Hospital, Dundee.

Design Unlinked anonymous hepatitis C virus antibody testing of residual sera from specimens sent to the virus laboratory for routine serological testing. The results were linked to non-identifying risk information.

Results Overall anti-hepatitis C virus prevalence was 0.6% (23/3548). Prevalences among injecting drug users, non-injectors who had a sexual partner who injected, and those with neither risk respectively were 41% (7/17), 15% (5/33) and 0.3% (11/3498). Relative risks for being an injector and a sexual partner of an injector respectively were 131 (95% CI 58-297) and 48 (95% CI 5-32). It is estimated that one of the 18 antenatal clinic attenders gave birth to an infected child.

Conclusion Findings suggest that non-injecting partners of injectors may be at considerable risk of acquiring hepatitis C virus sexually. Efforts to promote the use of condoms among injectors and their sexual partners should be increased. Selective anti-hepatitis C virus screening of women who reported high risk behaviour would have failed to detect half the cases. Research to gauge the views of women of childbearing age on anti-hepatitis C virus testing is required.

INTRODUCTION

There has been much debate about the role of unprotected sexual intercourse in the transmission of the hepatitis C virus[1]. The prospective follow up of sexual partners, discordant for hepatitis C virus, is considered the most robust approach to investigating the virus's sexual transmission[2]; however, such investigations are extremely difficult to conduct and few have been performed[3]. Hepatitis C virus prevalence studies of, for example, genitourinary clinic attenders and pregnant women have been conducted but rarely have they been designed to differentiate injecting drug users from the rest[4,5]. Since injecting drug use is the principal risk behaviour for the spread of hepatitis C virus in western countries[6], not much can be learnt about non-injecting related, particularly sexual, transmission from prevalence surveys which do not involve the collection of data on injecting drug use. Furthermore, without these data it is not possible to assess what impact selective hepatitis C virus antibody screening of pregnant women with an injecting-related risk would have in detecting infection in this group if such an initiative was introduced.

In 1992 the UK's Medical Research Council funded a study to determine the prevalence of HIV among pregnant women in Dundee[7]. Its design allowed the collection of injecting drug use information and, because women's specimens could undergo either attributable or unlinked anonymous testing, participation bias was minimised. Reflecting the growing concern of the Departments of Health and public health organisations in the UK about Hepatitis C infection, government approval was given for residual sera from routine clinical specimens – taken from patients after March 1996 – to be anonymously tested for hepatitis C virus, in addition to HIV, antibodies[8,9]. Elsewhere in the UK, other than in Edinburgh where a companion study to the Dundee one was being conducted, there was no opportunity to perform such a study on hepatitis C virus. Furthermore, Dundee was known to have a large HIV[10] and hepatitis C virus – infected[11] injecting drug user population and had witnessed many instances of HIV being transmitted sexually, from male injectors to their non-injecting female partners, in the late 1980s and 1990s[12,13]; thus, the city appeared to have acquired many of the necessary condi-

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tions for the sexual transmission of hepatitis C virus. Testing Dundee pregnant women for hepatitis C virus antibodies would 1) gauge the extent to which hepatitis C virus might be spreading sexually in this population, 2) determine what proportion of infected pregnant women would be detected if a selective screening strategy – targeted at women who declared having injected drugs or having had a sexual partner who injected drugs – was implemented, and 3) provide data to estimate the number of babies being born with hepatitis C virus infection.

METHODS

The study population comprised (i) all women who were seen at the antenatal clinic in Ninewells Hospital which served the entire antenatal population of Dundee and (ii) all women who were admitted for termination of pregnancy to the gynaecology wards of the above hospital which, for this population group, served the rural areas of Angus and North Fife as well as the city. The great majority of these pregnant women were caucasian and indigenous to the area.

During January–December 1997, the period of study for hepatitis C virus, all pregnant women who attended Ninewells Hospital were offered a named HIV antibody test; it has been policy to offer such testing since 1992. In the context of the pre-test discussion, each woman was asked the following two questions: 'Have you ever injected drugs?' and 'To your knowledge, has a sexual partner of yours ever injected drugs?', by one of three midwives who were specially trained in HIV counselling. Approximately 90% of women chose to undergo attributable HIV testing. For the remaining 10%, anonymous HIV testing was performed on residual sera from specimens which had been taken for rubella antibody testing. Information, on posters and leaflets, which indicated that anonymous testing for HIV and 'other infectious diseases' might be performed on leftover blood samples, was made available to the women.

For antenatal clinic attenders and women undergoing therapeutic abortion who had blood taken in 1997, their named or anonymous HIV tests were performed soon after their samples were taken; the majority, who underwent named testing, were informed of their results. While full identifiers were removed from those residual specimens eligible for unlinked anonymous HIV testing, certain non-identifying details – age band, history of drug injecting by patient or sexual partner, and pregnancy status, (antenatal or termination) – were retained and linked to each specimen, in the form of a code, prior to testing. These limited data were then united with their corresponding HIV test results and sent to the Scottish Centre for Infection and Environmental Health (SCIEH) for analysis. For those specimens undergoing named HIV testing, residual sera, similarly, were unlinked from their full identifiers; HIV test results, attached to the same limited details which applied to the anonymously tested specimens, were also sent to SCIEH. The resulting uniform dataset, held at SCIEH, was unable to differentiate named from anonymous HIV test results.

Remaining in the virology laboratory at Ninewells Hospital, were residual sera from all pregnant women who underwent named or anonymous HIV testing during 1997; all these sera were linked only to the non-identifying epidemiological information which had been collected for the original study of HIV prevalence.

In 1998 the sera which applied to samples taken from women during January–December 1997 were identified for Hepatitis C antibody testing. Because the overall anti-hepatitis C virus prevalence was expected to be less than 1%, initial screening was performed using the Ortho Diagnostics hepatitis C virus 3.0 ELISA Assay (Chiron Corporation, Emeryville, California) on pooled sera from sets of five different individuals. In the great majority of instances, no antibodies were detected. In instances where antibodies to hepatitis C virus were identified, additional leftover sera, corresponding to those which constituted the antibody positive pool, were retested individually to ascertain the affected one(s). All reactive individual serum samples were subjected to Monolisa hepatitis C virus (Sanofi Pasteur Diagnostics, Marnes-la-Coquette, France) confirmatory testing; only serum samples which were reactive on both tests were considered to be hepatitis C virus antibody positive[14]. Results, together with their corresponding epidemiological codes, were then sent to SCIEH for analysis. The study design was approved by the Ninewells Hospital ethical committee.

RESULTS

Fifteen women (0.4%) objected to their blood being tested anonymously for HIV or any other infectious disease; all were non-injectors who, to their knowledge, had never had a sexual partner who injected. The prevalence of anti-hepatitis C virus was 0.6% (23/3548) overall, 41% (7/17) among those who declared that they had ever injected drugs, 15% (5/33) among those who indicated they had never injected drugs but had had a sexual partner who had done so, and 0.3% (11/3498) among those who indicated neither risk. Compared with the prevalence of this latter (reference) group, relative risks were 131 and 48, respectively, for the injector and the sexual partner of injector populations. The prevalence among antenatal clinic attenders (0.7%–18/2584) was not significantly greater ($P > 0.05$) than that for women who had undergone therapeutic abortion (0.5%–5/964). Of the hepatitis C virus antibody positive injectors ($n = 7$), sexual partners of injectors ($n = 5$) and women who had neither risk ($n = 11$), respectively, 2, 2, and 6 were

Table 1. Prevalence of HCV Antibodies among Pregnant Women by Risk Group. TOP = termination of pregnancy; IDU = Injecting Drug User.

	Antenatal clinic attender				Planned TOP				All pregnant women				
Risk Group[a]	No. tested	No. positive	(%)	95%CI	No. tested	No. positive	%	95%CI	No. tested	No. positive	%	95% CI	RR [95% CI]
Neither IDU nor sexual partner of an IDU	2550	9	(0.4)	0.2–0.7	948	2	(0.2)	0.03–0.8	3498	11	(0.3)	0.2–0.6	1 [Reference]
Sexual partner of IDU	21	3	(14)	3.0–36.3	12	2	(16.7)	2.1–48.4	33	5	(15)	5.1–31.9	48.18 [17.7–131.0]
IDU	13	6	(46)	19.2–74.9	4	1	(25)	0.6–80.6	17	7	(41)	18.4–67.1	130.90 [57.7–297.0]
Total	2584	18	(0.7)	0.4–1.1	964	5	(0.5)	0.2–1.2	3548	23	(0.6)	0.4–1.0	

[a] Includes 80 women whose risk status was unknown but who were all HCV antibody negative.

Note: Confidence intervals were calculated using exact binominal method.

aged less than 25 years, 1, 1, and 2 were aged 25–29 and 4, 2, and 3 were aged 30–39. All results are shown in Table 1.

DISCUSSION

Few hepatitis C virus antibody prevalence studies of 'lower' risk population groups have been designed to allow the differentiation of results between (i) those who have ever and those who have never injected drugs, and between (ii) non-injectors who knew they had a sexual partner who had injected drugs and non-injectors who indicated that, to their knowledge, they had never had such a partner. Accordingly, it has been difficult to gauge the importance of sexual intercourse in the transmission of hepatitis C virus. The prevailing view is that hepatitis C virus can be spread sexually, but that the efficacy of its transmission is lower than that for HIV[15]; this is supported by the findings of a discordant partner study which was conducted in Edinburgh[16]. Of 30 non-injecting sexual partners of persons known to be both HIV and hepatitis C virus antibody positive, 12 and none were found to have antibodies to HIV and hepatitis C virus respectively after a median follow up of 44 months. The results of the reported study, however, suggest that hepatitis C virus could be more of a sexual threat than hitherto thought. The principal findings are the high prevalence of hepatitis C virus antibody among the non-injecting sexual partners of injectors and the excess risk (relative risk 35, 95% CI 12–101) which having sex with a known injector conveyed. How robust are these observations?

The study method has its limitations in that questions about other risk factors such as blood/blood product transfusion and tattooing were not asked, details of current and past injecting and sexual behaviours were not obtained; and the responses to the two key questions were dependent on recall and honesty. Also, women who reported no injecting history and whose specimens were found to be hepatitis C virus antibody positive could not be contacted to probe them further about risk factors, including the possibility of previously undeclared instances of injecting drug use. The very high prevalence of hepatitis C virus antibodies seen in those who indicated that they had injected, and the very low prevalence among those who declared neither of the injecting-related risk activities, is in keeping with our current understanding of hepatitis C virus transmission and suggests that the questions, generally, were answered honestly. It is possible, however, that injectors who either had had, or had never had, an injecting sexual partner could have answered 'no' to the injecting but 'yes' to the sexual partner question. A high level of interviewer performance was achieved by allowing only three well-trained midwives to ask the questions. Additionally, the named/anonymous testing approach ensured that participation bias was negligible.

The 11 antibody–positive cases who indicated 'no' to both injecting-related questions, could have acquired their infection sexually either from someone they did not know was an injector or through a non-sexual, non-injecting, route such as tattooing[17]. It is also possible that some of these women were non-Caucasians who acquired their infections in high prevalence countries through, for example, blood transfusion. The excess risk of anti-hepatitis C virus among the 33 non-injectors who had had an injecting sexual partner, relative to that of the great majority of 'low risk' women, however, is associated entirely with this sexual behaviour. It is possible that the non-injecting sexual partners of injectors were more likely than women with neither risk to acquire hepatitis C virus through, for example accidental needlestick injury or a tattoo; data on other risks, however, were not obtained in this study.

Among the 17 injectors, the 33 sexual partners of injectors, and the remainder who declared neither behaviour, the HIV prevalences were 0%, 0% and 0.06%, respectively[7]. In a city which had a 39% HIV prevalence among its injecting population in 1985[10] and experienced considerable HIV transmission between its injectors and their non-injecting sexual partners in the late 1980s and early 1990s, hepatitis C virus infection has become the greater public health problem. It is estimated that 20–30% of persons develop cirrhosis of the liver within 20–30 years of infection[15]; accordingly, the prevention of hepatitis C virus transmission is extremely important. The findings of this study do not undermine the widely held view that the principal way to prevent the spread of hepatitis C virus in western countries is to stop injectors from sharing injecting paraphernalia. In contrast, the risk among those who have neither injected nor, to their knowledge, had a sexual partner who had injected, is low. This study however indicates that the sexual partners of injectors could be at considerable risk of infection. If so, it is likely that some hepatitis C virus -infected injectors will have acquired their infection through sexual intercourse rather than injecting. The reduction in the incidence of HIV among injectors in Scotland during the 1990s – a consequence of harm reduction measures – led to a decline in the prevalence of infection among this group and thus a decrease in the potential for HIV being spread sexually. Reducing the potential for hepatitis C virus being transmitted through sexual intercourse, however, is likely to prove more difficult: its prevalence among injectors usually exceeds 50%[6] and current harm reduction measures (e.g. needle/syringe exchange) are only partly effective in preventing its transmission through injecting practices[18].

More investigative work on the sexual transmission of hepatitis C virus is required. In the meantime, however, it would be prudent to spread the message that hepatitis C

virus can be spread sexually and to increase our efforts to promote the use of condoms among both injectors and their sexual partners.

Eighteen of 2584 (0.7%) women who planned to continue their pregnancy had antibodies to hepatitis C virus. This compares with an anti-hepatitis C virus prevalence of 0.1% among 3,500 Caucasian and non-Caucasian antenatal clinic attenders from Birmingham in 1990–1991[19]. It is estimated that on average 5–6% of anti-hepatitis C virus positive childbearing women transmit infection to their children in utero or at the time of delivery[14]. It is likely, therefore, that one of the babies who were born to the 18 women was infected with hepatitis C virus. Is there a case for hepatitis C virus antibody screening of antenatal clinic attenders? A selective hepatitis C virus screening approach whereby only those who had injected or had had a sexual partner who had injected were offered a test, would have identified, at best, only half of the eighteen anti-hepatitis C virus positive mothers. This observation is in keeping with the UK's experience of screening pregnant women selectively for HIV and hepatitis B virus antibodies; for both infections the Departments of Health recommended selective screening for many years before changing their recommendation to that of a universal approach.

A universal offer or recommendation of an hepatitis C virus test might have led to more cases being identified, but currently there would appear to be of little benefit to a pregnant woman to know she had anti-hepatitis C virus: there is no therapy to prevent maternofetal transmission of hepatitis C virus, infection leads to infrequent morbidity during childhood and early adult life, and the long term prognosis of persons who are infected at birth is uncertain[20]. Thus, the case for either selective or universal screening of antenatal clinic attenders for hepatitis C virus is not strong. It is possible, however, that antenatal clinic attenders wish to be told about their risk of being infected with hepatitis C virus, the risk of mother to child transmission of the virus, and the availability of an anti-hepatitis C virus test. It is also possible that hepatitis C virus-infected pregnant women might find the knowledge of their infection detrimental to their mental health. The case for offering an hepatitis C virus antibody test to women, particularly those at high risk of being infected, who are planning to become pregnant, is far more compelling than doing so once they have conceived. If an antibody positive woman was viraemic–approximately 75% of infected persons become carriers[15]– she would have, on average, a 40% chance of achieving a sustained clearance of virus from her circulation if she had interferon/ribavirin combination therapy[21]. Since pregnant women, who infect their children, invariably, are PCR RNA positive for hepatitis C virus [22], this intervention would have positive benefits for both mother and child. The acceptability and feasibility of pre-pregnancy testing is unknown, although the family planning clinic setting might be an appropriate place for it to be offered.

We recommend that research be conducted to gauge the views of women of childbearing age on pre-pregnancy and antenatal hepatitis C virus antibody testing.

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