

HCV prevalence in pregnant women in the UK

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(Accepted 5 April 2000)

SUMMARY

The objective of the study was to assess the prevalence and epidemiology of hepatitis C virus (HCV) infection in pregnant women in the North Thames region, and in the UK in general. Demographic data were linked to neonatal samples prior to anonymization and testing by anti-HCV EIA, and with RIBA 3 confirmation. Risk factors for maternal infection were explored. Area-specific seroprevalence rates were multiplied into population sizes to estimate HCV prevalence in pregnant women in the UK. A total of 241/126009 samples were confirmed anti-HCV positive, and a further 40 were indeterminate, representing a seroprevalence of 0·19–0·22%; 51% of maternal HCV infections were in UK-born women (71% of the population), and 22% in women from continental Europe (5% of the population). Among European-born women, HCV prevalence was associated with birth in continental Europe, partner not being notified at birth registration, partner born in a different region to the mother, and inner city residence. Four of the 241 anti-HCV positive samples (1·7%) were also anti-HIV-1 positive. It was estimated that each year an estimated 1150 out of 730000 pregnancies in the UK would involve a woman infected with HCV (uncertainty range 660–1850), a prevalence of 0·16% (0·09–0·25%). On the basis of reported rates of mother-to-child transmission of HCV, this would represent approximately 70 paediatric HCV infections per year.

INTRODUCTION

Hepatitis C is a major cause of chronic liver disease and hepatocellular carcinoma (HCC) [1]. In the USA it is the most common reason for liver transplantation [2]. Infected patients with established chronic liver disease have high rates of cirrhosis, HCC, and mortality. However, chronic infection is predominantly asymptomatic, and prospective follow-up

from infection over a period of 8–14 years has revealed low rates of morbidity and mortality [1].

Hepatitis C infection is associated with transfusion of blood or blood products, and organ transplantation [3]. However, in developed countries these routes of transmission have been virtually eliminated by donor screening, which began about 1991. Prevalence remains high in injecting drug users, among those with sexually transmitted infection, multiple sexual partners, or in lower socio-economic groups [3]. In spite of the association between serological markers of HCV and demographic variables correlated with

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sexual activity, HCV incidence in monogamous, stable, heterosexual partners of infected individuals is extremely low [4, 5]. HCV transmission is also associated with cosmetic or ritual practices that involve percutaneous exposure, and with non-essential injections and surgical procedures with contaminated equipment, particularly in resource-poor settings [5].

Mother-to-child transmission rates of 6% have been reported, or 15% in women co-infected with HIV [6, 7]. Antenatal screening for HCV is routinely carried out in some centres in Europe, particularly in Italy and Spain, but there is no consensus on how pregnancy, delivery and neonatal care should be managed in an HCV-infected mother [8].

The world-wide prevalence of HCV is estimated to be 3%, with marked difference between countries [9, 10]. Published information on HCV prevalence in pregnant women in the UK has been limited to small studies from single maternity units [11]. We report here on a large survey based on neonatal dried blood spot samples collected in the North Thames region, an area including inner city, suburban and rural districts. The findings are tentatively projected to assess the potential prevalence of maternal HCV prevalence in the UK as a whole.

METHODS

Origin of samples and data

A total of 126009 non-repeat dried blood spot samples were tested. These originated from Guthrie card samples arriving between April 1997 and June 1998 at the Neonatal Screening Laboratory serving 29 districts in North Thames and Bedfordshire. Linkage with Child Health Computer (CHC) data (mother's age and ethnic status) was achieved for 62789 samples, about 96% of samples from NE Thames. Linkage with Birth Registration (ONS) records (parent's country of birth) was attempted for 99591 samples. The data linkage methods and success rate, the anonymization methodology, ethical consent, and safeguards against deductive disclosure, have been reported elsewhere [12].

Laboratory methods

Dried blood spot samples were eluted as previously described [13] and screened for anti-HCV IgG by an in-house EIA based on recombinant proteins c22 c200, and NS5, supplied by Ortho Diagnostics.

Reactive eluates ($OD \geq 0.20$) were retested in the same assay, and repeat reactives were confirmed by Ortho RIBA 3 immunoblot. Samples were classified as confirmed, indeterminate or negative according to the manufacturer's guidelines.

Data analysis

Logistic regression models were fitted to the data. Tests for the effects of region, and mother's and father's country of birth and confidence intervals were based on likelihood ratios. Region-specific rates observed in North Thames and elsewhere were applied to area populations of the UK. A range of estimates for antenatal HCV prevalence was constructed, both within each area and nationally, taking account of statistical uncertainty, uncertainty due to indeterminate sero-status, and uncertainty about which rates applied in areas where direct data were unavailable.

RESULTS

Out of 126009 samples, 360 were reactive in the EIA of which 281 were repeat reactive. A total of 241 (85.8%) of these were confirmed as anti-HCV positive in the RIBA 3 assay. The majority (38/40) of the indeterminates were reactive to the c22 recombinant band of the immunoblot. In the analyses that follow, except where minimum and maximum (including indeterminates) estimates are cited, seroprevalence is based on the number of samples confirmed by RIBA.

We found a distinct seroprevalence gradient, increasing from non-metropolitan areas (0.08–0.11%), to outer London (0.19–0.22%) and then to inner London (0.36–0.40%) (Table 1). There was a higher seroprevalence in the small number of samples from outside the surveys area, but these are considered to be a highly unrepresentative group.

HCV prevalence in mothers born in the UK was 0.13–0.15%, and 0.81% in mothers born elsewhere in Europe (Table 2). There was a particularly high prevalence among women from Southern Europe (1.6%). Prevalence in mothers from Africa, and Asia-Pacific was slightly higher than in UK-born mothers; 51% of HCV infection was found in women who were born in the UK and 22% in women born in the rest of Europe (who account for only 5% of the antenatal population); 17% of infected women were born in Asia and 7% in African countries. Outside Europe, a higher maternal prevalence was observed in women

Table 1. Neonatal anti-HCV prevalence by type of local authority area

	Total samples	Anti-HCV positive	Indeterminate	Seroprevalence (%)	
				Min	Max
Inner London	29491	105	14	0.36	0.40
Outer London	46182	90	13	0.19	0.22
Non metropolitan	49807	42	13	0.08	0.11
Outside survey area	529	4	0	0.76	0.76
	126009	241	40	0.191	0.223

Table 2. Neonatal anti-HCV prevalence by mother's country of birth

Mother's country of birth	Total samples (%)*	Anti-HCV positive (%)*	Indeterminate	Seroprevalence (%)	
				Min	Max
Africa	7134 (7.4)	13 (7.5)	2	0.17	0.20
Eastern	3354	7	0	0.21	0.21
Central	559	4	0	0.72	0.72
Northern	629	2	1	0.32	0.48
Southern	267	0	0	0	0
Western	2325	0	1	0	0.04
United Kingdom	69013 (71.5)	89 (51.1)	12	0.13	0.15
Rest of Europe	4789 (5.0)	39 (22.4)	2	0.81	0.86
Other Northern	1948	11	1	0.56	0.62
Eastern	494	2	0	0.40	0.40
Southern	1143	18	1	1.58	1.66
Western	1204	8	0	0.66	0.66
Americas	2205 (2.3)	3 (1.7)	0	0.14	0.14
Central and Caribbean	956	1	0	0.10	0.10
North	759	1	0	0.13	0.13
South	490	1	0	0.20	0.20
Asia-Pacific	13352 (13.8)	30 (17.2)	12	0.22	0.31
Central	300	2	0	0.67	0.67
Eastern	637	1	0	0.16	0.16
South Eastern	976	0	0	0	0
Southern	8942	24	12	0.27	0.40
Western	1968	2	0	0.10	0.10
Oceania	529	1	0	0.19	0.19
ONS unlinked	2827	15	2	0.53	0.60
Not registered	271	0	0	0	0
Total	99591	189	30	0.19	0.22

* Percentage of samples in which mother's country of birth is known.

born in Central Africa and South Asia than elsewhere. The relationship between seroprevalence and father's country of birth was similar (not shown). Maternal ethnic status did not appear to be related to HCV status, except in so far as it reflected country of birth (not shown).

Within Southern Asia, 23 of the 24 confirmed anti-HCV positive samples and 10 of the 12 indeterminates originated from the 2002 mothers born in Pakistan

(prevalence 1.15–1.65%). However, there was only one confirmed and two indeterminate samples among the 6940 samples from mothers born elsewhere in South Asia. This country of birth distribution of confirmed positive, indeterminate and negative samples strongly suggests that indeterminates from South Asia were in fact anti-HCV positive.

Multivariate logistic regression showed that mother's region of birth, father's region of birth and

Table 3. *Anti-HCV prevalence in infants of European-born parents. Logistic regression*

	Estimated risk or relative risk	Significance tests
Base-line risk		
Parents UK-born, non-metropolitan district (%)	0.047 (0.030–0.072)	
Mother's place of birth		$\chi^2_1 = 16.2, P < 0.0001$
Rest of Europe	3.33 (1.79–5.01)	
UK (reference)	1	
Father's place of birth (UK <i>vs.</i> Non-UK)		$\chi^2_2 = 18.6, P < 0.0001$
Different from mother	2.38 (1.33–4.04)	
Not registered	2.66 (1.61–4.25)	
Same as mother (reference)	1	
Type of Local Authority		$\chi^2_2 = 47.6, P < 0.0001$
Inner London	5.48 (3.31–9.37)	
Outer London	2.51 (1.48–4.38)	
Non-metropolitan (reference)	1	

Table 4. *Prevalence of anti-HCV by maternal age. Records with complete age data only*

Age group	Mother born in UK			Mother born in rest of Europe			Mother born outside Europe		
	Total	anti-HCV positive	% prevalence	Total	anti-HCV positive	% prevalence	Total	anti-HCV positive	% prevalence
Under 21	4272	1	0.02	182	0	0	1115	0	0
21 to 25	8699	8	0.09	543	3	0.55	3665	3	0.08
26 to 30	14824	15	0.10	822	5	0.60	4496	9	0.20
31 to 35	12176	22	0.18	777	13	1.67	3479	5	0.14
Over 35	4738	9	0.19	332	6	1.81	1987	4	0.20
Total	44709	55	0.12	2656	27	1.02	14742	21	0.14

type of district (inner London outer London and non-Metropolitan districts) interacted strongly ($P < 0.006$ for all two-way interactions). Two separate analyses were therefore undertaken.

The first focussed on infants of European-born parents. The model shown in Table 3 fitted the data well ($\chi^2_{12} = 11.7, P = 0.97$), and there were no significant interactions. The baseline risk of HCV infection, defined as the rate in UK-born women in non-metropolitan boroughs with partners known to have been born in the UK, was 0.047% or 1:2100 (95%CI 0.30–0.72%). Women born in the rest of Europe were at over three-fold higher risk of being HCV infected. A partner from the rest of Europe was associated with higher risk if the mother was UK-born, but a lower risk if the mother was herself born elsewhere in Europe. Maternal seroprevalence was 2.7 times higher, if the father's details were not recorded at birth registration. The inner city–suburban–rural gradient was pronounced, with inner London women

at a 5.5-fold increased risk compared to those from non-Metropolitan districts.

Among women born outside Europe, however, there was no effect either of type of borough ($\chi^2_2 = 4.54, P = 0.1$), or of father's country of birth ($\chi^2_2 = 1.4, P = 0.5$). Indeed, in contrast to results with European women, there was a non-significant trend towards a lower risk in women whose partners were not registered at birth, and lower risk in inner City districts.

HCV prevalence increases with maternal age, irrespective of country of birth (Table 4). The low prevalence in women under 26 years of age suggests that the majority of HCV infection was acquired in adult life.

Four of the 241 confirmed anti-HCV positive samples (1.7%) were also anti-HIV-1 positive. Two co-infected women were from continental Europe, one was UK-born. The country of birth of the fourth was unknown.

Table 5. *Estimates of HCV prevalence in the UK antenatal population*

	% anti-HCV positive range	Annual number of births	Expected births to infected women¶ and uncertainty range††	
Inner London	0.36–0.40*	45 000	171	130–212
Outer London	0.19–0.22*	60 000	125	93–158
Principle cities	0.19–0.40†	45 000	126	70–210
Other metropolitan	0.08–0.22‡	100 000	137	59–251
Non-metropolitan, SE	0.08–0.11*	90 000	90	53–130
Non-metropolitan, other	0.06–0.17‡	310 000	310	110–615
Scotland, cities	0.50–1.01**	15 000	104	30–196
Scotland other	0.08–0.22‡	40 000	55	24–100
Northern Ireland	0.08–0.22‡	25 000	34	15–63
Total		730 000	1152	664–1845§§

* Table 1.

† Range given by inner London and outer London rates.

‡ Range given by outer London and non-Metropolitan rates.

§ Range as for non-Metropolitan South East, multiplied up or down by a factor of 1.5.

¶ Geometric mean.

** Based on a study in Dundee (SCIEH, unpublished observations), multiplied up or down by a factor of 1.5.

†† The uncertainty range takes account of; uncertainty concerning the status of indeterminates, uncertainty due to statistical sampling (95% confidence), and the uncertainty above which rate to apply.

§§ Overall uncertainty interval takes account of sampling uncertainty and assumes all rates are either 60% of their range below their mean, or all are 60% above their mean.

Estimates of the prevalence of maternal HCV within different population groups are derived in Table 5, using prevalence results from the present surveys, and from a study in Dundee (Scottish Centre for Infection and Environmental Health (SCIEH), unpublished observations). In order to reflect the uncertainties inherent in applying rates observed in North Thames and Scotland to different parts of the country, a wide range of estimates are used (see Table 5 for details). Out of a total 730 000 births each year in the UK, we estimated that the number of mothers infected with HCV is 1152, with an uncertainty range of 664–1845. These estimates would represent a UK overall antenatal anti-HCV prevalence of 0.16% with range 0.09–0.25%. Although metropolitan areas are expected to have a higher prevalence, over 40% of HCV is predicted to be in non-metropolitan areas.

DISCUSSION

Forty (14.2%) of the 281 samples reactive in the anti-HCV EIA were indeterminate in RIBA-3. There was strong evidence that indeterminates from South Asia were true positives, but this does not necessarily mean that indeterminates from other countries are true positives.

The prevalence results (0.38% in inner London, 0.20% in outer London and 0.08% in non-metropolitan districts) are broadly consistent with previous population-based studies of HCV in antenatal samples in England: 0.14% in Birmingham [11], 0.33% in 15 London (mostly inner London) hospitals, and 0.22% in 11 hospitals in mostly metropolitan boroughs in Northern and Yorkshire region (Public Health Laboratory Service (PHLS), unpublished observations). All these estimates are somewhat lower than the 0.7% (95%CI 0.41–1.1%) reported recently from Dundee (SCIEH, unpublished observations). There was little co-infection with HIV. Only 4/241 (1.7%) anti-HCV positive samples were also anti-HIV-1 positive, and all were from inner London (4/105 = 3.8%).

Studies on other populations in the UK have shown HCV infection prevalence of 40–90% in injecting drug users [15]. Routine laboratory reports of HCV infection where likely transmission route is identified give injecting drug use as the probable exposure in 80% [16]. In anonymous surveys of those attending sexually transmitted disease clinics, prevalence of 0.6–1.0% has been reported, excluding intravenous drug users (PHLS, unpublished observations).

The worldwide literature on HCV prevalence is considerable, but national or even regional estimates of prevalence within representative population groups

are few. Our survey suggests two or possibly three separate epidemics in the UK. Applying maternal country of birth-specific seroprevalence rates observed in North Thames to UK birth registration data [14], it would be expected that 76% of maternal HCV infection would be in UK-born women, 13% in women born elsewhere in Europe and 11% in non-European women. The European epidemic has a profile that is correlated with markers of social disadvantage, as has been observed in the USA [3]. This was evidenced both by the concentration of infection in the inner city, and by the higher seroprevalence in neonates whose fathers were not registered at birth. This is considered to be a marker of a single unsupported mother, as the father's details can be registered either if the couple are married, or if the father is present at registration.

The non-European epidemic does not have a demographic profile associated with disadvantage, which is more consistent with HCV being acquired through therapeutic injection, or surgical or cosmetic procedures using contaminated equipment, rather than through injecting drug use. We found that prevalence appeared to be especially high in women from Pakistan (1.15–1.65%). Studies from Pakistan suggest that frequent therapeutic injection with unsterilized equipment may be responsible for this relatively high prevalence [17].

HCV prevalence in the lowest risk group (UK-born mothers with UK-born partners in non-metropolitan areas) was estimated to be 0.047%. Applied to the annual population of 730 000 pregnant women, this would represent 343 HCV infected pregnant women, almost 30% of the estimated 1150 total. This group must comprise HCV attributable to blood or tissue transfer, as well as an unknown proportion attributable to injecting drug use and other body piercing practices. This 'baseline' prevalence is close to the 0.044% reported in first-time blood donors in England and Wales in 1999 [18], and is consistent with earlier studies of blood donors in the UK [19–23]. These studies have found that 40–50% of diagnosed infection could be attributed to intravenous drug use, and 15–20% to previous transfusion. They have also confirmed that tattooing and ear-piercing are also significant causes of HCV transmission in the donor population.

Based on a vertical transmission rate of 6% [6, 7], the expected 1152 (range 664–1845) pregnancies per year in the UK where the mother is infected with HCV, would result in 69 paediatric infections per year

(range 40–110). Until recently there has been no clinical rationale for antenatal screening. Interferon alfa-2b in combination with ribavirin has been shown to reduce HCV viral load [24, 25], an established risk factor for transmission [6]. However, ribavirin is teratogenic and neither drug is recommended for use in pregnancy [26]. Evidence that elective caesarean delivery may reduce the risk of transmission, is now beginning to emerge [27]. Although the sequelae of paediatric disease appear to be mild over the first 20 years of life [28], a full economic analysis taking account of longer term prognosis would be valuable if these reports are confirmed. Such an analysis would have to take account of the additional downstream costs occasioned by earlier diagnosis of the mother, the costs of paediatric care averted, and the life-years gained in both mother and child. The implications of indeterminate serology results, which could cause anxiety and lead to further diagnostic tests, should also be born in mind.

Our results show that, unlike HIV, HCV is diffused throughout the population probably as a result of blood or tissue transfer, intravenous drug use or cosmetic or other body-piercing procedures undertaken with contaminated equipment. The estimated overall annual 1150 antenatal HCV infections per year is nearly four times higher than the 330 recently estimated for antenatal HIV [29]. In addition, the 0.047% neonatal seroprevalence among the low-risk (infants in non-metropolitan districts with UK-born parents) far exceeds the 0/43 000 neonatal HIV seroprevalence observed in this group [12]. Screening only in high prevalence areas would therefore not be an effective strategy, nor would offering HCV tests to women found to be HIV-infected. If, as appears, sexual transmission is not an important route of infection [4, 5], a selective screening programme could be highly effective. This would target intravenous drug users, pre-1992 transfusion recipients, women who have undergone body piercing cosmetic procedures, or who have received injections or surgical treatments in developing countries. The cost of reliably eliciting this information from all women may, however, exceed the cost of universal testing. On the other hand, costs could be drastically reduced by serum pooling. The technical feasibility of pooling has been established for HIV [30], HBV [31] and HCV (PHLS, unpublished observations). In low prevalence areas, serum pooling could make a combined antenatal screening programme for these infections a highly cost-effective option.

ACKNOWLEDGEMENTS

This study was funded by the Department of Health. We thank Ortho Diagnostics for supplying reagents for the in-house EIA assay with the permission of Chiron Corporation. We are grateful to Drs Mary Ramsay and Koye Balogun of the Public Health Laboratory Service Communicable Disease Surveillance Centre, and to Dr David Goldberg (Scottish Centre for Infection and Environmental Health) for kindly allowing us to access and refer to their unpublished findings.

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