Prevalence of hepatitis C among pregnant women attending an inner London obstetric department: uptake and acceptability of named antenatal testing

C Ward, G Tudor-Williams, T Cotzias, S Hargreaves, L Regan, G R Foster

Abstract

***Objective*—To examine the value of universal antenatal screening for hepatitis C virus (HCV) infection among an inner London population, with regard to prevalence, uptake, and acceptability of testing, and identification of new cases.**

***Design*—Serum analysis for antibodies against HCV in pregnant women following informed consent ("opt out" policy). Samples positive for HCV antibodies were tested for the presence of HCV RNA by polymerase chain reaction. Information on hepatitis C was provided for all women. Acceptability of antenatal HCV testing and identification of risk factors for infection were assessed through the use of questionnaires randomly distributed among a cohort of 300 pregnant women.**

***Setting*—Antenatal clinics at St Mary's Hospital, London, serving a multiethnic population.**

***Subjects*—A total of 4825 pregnant women booking for antenatal care between November 1997 and April 1999.**

***Results*—The overall prevalence of anti-HCV was 0.8% and HCV viraemia was 0.6%. Ninety eight per cent of samples (n=4729) were tested; 0.2% of women had a false positive result. In 207 women who completed a questionnaire regarding our testing policy, 84% made a positive decision to be tested for anti-HCV and 92% said that HCV testing should be offered to all pregnant women. The majority (22/32—69%) of HCV infected women were newly diagnosed and although HCV positive women were significantly more likely to have a history of drug abuse, most (16/22—73%) new cases had no identified risk factors for HCV infection at booking.**

***Conclusion*—The prevalence of anti-HCV in an inner London multiethnic antenatal population is high (0.8%). Routine screening for HCV is acceptable to pregnant women. The majority of women diagnosed during their current pregnancy would not have been identified as HCV infected by epidemiological risk factors at the time of booking.**

(*Gut* 2000;**47**:277–280)

Keywords: hepatitis C; pregnancy; transmission; screening

Department of Obstetrics and Gynaecology, Imperial College School of Medicine at St Mary's Hospital, London, UK
C Ward
T Cotzias
L Regan

Department of Paediatrics, Imperial College School of Medicine at St Mary's Hospital, London, UK
G Tudor-Williams

Department of Medicine, Imperial College School of Medicine at St Mary's Hospital, London, UK
G R Foster

Department of Public Health, Kensington Chelsea and Westminster, London, UK
S Hargreaves

Correspondence to:
Dr G R Foster, The Liver Unit, St Mary's Hospital, Praed Street, London W2 1PG, UK. Email: g.foster@ic.ac.uk

Accepted for publication 8 February 2000

Following the identification of the hepatitis C virus (HCV) in 1989[1] and the development of specific diagnostic assays,[2] hepatitis C infection is now recognised as a worldwide public health concern.[3] This single stranded RNA blood borne virus accounts for 15–20% of all cases of viral hepatitis.[4] Hepatitis C is a slowly progressive disease with long term sequelae, including cirrhosis and hepatocellular carcinoma (HCC).[5] Risk factors for infection are well described, with direct percutaneous exposure the most efficient mode of transmission.[5] Current evidence suggests that vertical transmission may occur, particularly in highly viraemic and anti-human immunodeficiency (HIV) positive mothers, but details of the mechanisms of vertical transmission are limited.[6 7] The outcome of perinatal HCV infection is unknown but in babies who are infected at birth the life time risk of severe liver disease is likely to be high.

The seroprevalence of chronic HCV infection among pregnant women in the UK is unknown and estimated to be 1% or less.[8 9] Prevalence rates in Europe of between 1.7% and 2.5%[10–12] have been reported. While screening of blood and blood products is now an accepted and important component in any national programme for the control of hepatitis C, the value of introducing antenatal HCV screening in the UK is the subject of debate.[13] A survey of 128 obstetric units in the UK reported that only 4.9% of units (n=5) had a policy of universal screening for HCV, 53% had a selective policy, and the remaining 43% had no testing policy.[14]

To inform the debate on the value of antenatal screening, we analysed the seroprevalence of anti-HCV within our antenatal population and examined uptake and acceptability of universal HCV testing. To determine if selective testing of "high risk" women would identify infected mothers, we compared identified risk factors between a cohort of HCV negative women and HCV infected women.

Methods

Between November 1997 and April 1999, 4825 pregnant women attending the antenatal clinics at St Mary's Hospital for their first (booking) visit were offered an anti-HCV test. A specific information leaflet on hepatitis C

Abbreviations used in this paper: HCV, hepatitis C virus; HCC, hepatocellular carcinoma; PCR, polymerase chain reaction.

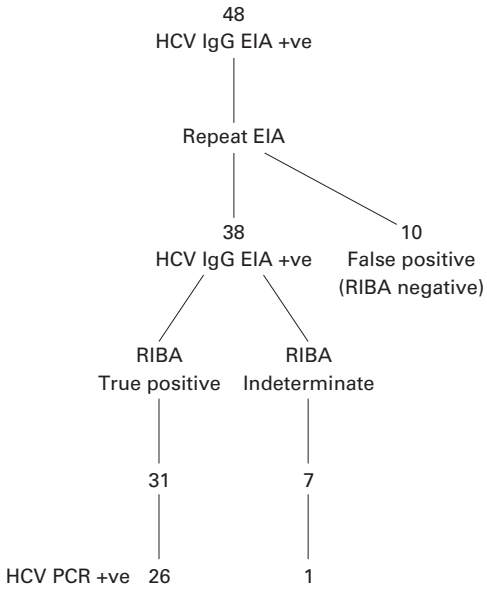

Figure 1 Outcome of testing for hepatitis C virus (HCV) in women with positive antibodies at screening.

was given to women prior to their booking interview. Anti-HCV testing was discussed and offered to all women by the booking midwife. Any woman requesting information beyond the confidence of the booking midwife was offered an appointment with a dedicated specialist midwife.

Prior to the study all booking midwives attended a teaching session on hepatitis C and received information on HCV infection, transmission of the virus, implications for the mother and baby, treatment options, counselling resources, and medical follow-up. Throughout the study a consultant hepatologist was available to discuss issues regarding HCV with infected mothers and all infected mothers and their babies were seen following delivery in a dedicated clinic staffed by the specialist midwife, a hepatologist, and a paediatrician.

SERUM ANALYSIS

Serum taken for hepatitis B testing was used for anti-HCV testing following informed verbal consent. IgG antibodies to HCV (anti-HCV) were detected by EIA (Abbott). All anti-HCV seropositive subjects were recalled for retesting and sera were tested by RIBA-3 (Chiron), detecting antibodies to recombinant HCV antigens (c100p, c33c, c22p, NS5). Reactivity to two or more antigens was considered a positive result, reactivity to one antigen an indeterminate result, and no reactivity was interpreted as a negative (HCV IgG false positive) result. All RIBA positive/indeterminate samples were tested for the presence of HCV RNA by reverse transcription polymerase chain reaction (PCR) using the Amplicor assay (Hoffman-La Roche; sensitivity 2000 copies/ml).

UPTAKE AND ACCEPTABILITY OF ANTENATAL HCV TESTING

Three hundred pregnant women were randomly selected and invited to complete two anonymous questionnaires. The first assessed the acceptability of antenatal HCV testing and the second identified risk factors for HCV infection. The questionnaires were given to women following their booking interview and they were asked to complete them prior to leaving the antenatal clinic. All HCV infected women were asked to complete the questionnaire regarding risk factors for HCV infection. The study was approved by the local ethics committee.

Table 1 Response to questionnaire regarding the acceptability of antenatal screening

	n (%)
Received HCV information	
Yes	213 (90)
No	21 (9)
No response	3 (1)
Read information leaflet	
Yes	225 (95)
No	10 (4)
No response	2 (1)
Information given	
Too much	6 (3)
About right	206 (87)
Too little	8 (3)
No response	17 (7)
Opted for testing	
Yes	199 (84)
No	30 (13)
No response	8 (3)
Testing available to all pregnant women	
Yes	218 (92)
No	12 (5)
No response	7 (3)

Information was given to women both orally, by the attending midwife, and by a leaflet. It is interesting that 12 women read the information leaflet but did not regard the leaflet as providing information—the majority of these women did not complete the section on "Information provided by the leaflet" in the questionnaire.

Results

ANTI-HCV SEROPREVALENCE

A total of 4729 samples (98%) were tested for anti-HCV; 96 women declined the offer of testing. Forty eight samples (1.0%; 95% confidence interval (CI) 0.723–1.27%) were HCV IgG seropositive by EIA (fig 1). All women were informed of their result and retested. Ten samples (0.2%) tested negative with the RIBA-3 assay and were considered false positive results. The true prevalence of HCV exposure (antibody positive) was therefore 0.8% (95% CI 0.55–0.1%). Twenty seven patients (0.6%; 95% CI 0.386–0.814%) were viraemic—that is, HCV RNA PCR positive.

Twenty two women (69% of the infected women) were newly identified as HCV infected during their current pregnancy and they were all viraemic.

ACCEPTABILITY OF HCV ANTENATAL TESTING

Three hundred randomly selected women were asked to complete a questionnaire to assess patient satisfaction with the antenatal screening programme. Two hundred and thirty seven women (79%) completed the questionnaire and 218 (92% of those who responded) believed that all pregnant women should be offered screening for HCV during pregnancy (table 1).

Table 2 Risk factors for hepatitis C virus (HCV) in infected (n=32) and non-infected (n=207) women (No (%))

Risk factor	*HCV infected women*	*Women who refused testing or tested negative*
Any exposure to illicit drugs (chiefly intravenous use)	13 (41)**	3 (1.5)
Partner used iv drugs	8 (25)**	6 (3)
HCV infected partner	4 (13)**	1 (0.7)
Transfusion	1 (3)	17 (8)
Previous surgery	17 (53)	83 (40)
Tattoo/body piercing (chiefly pierced ears)	31 (97)**	114 (55)

**p<0.01.

Table 3 Ethnic origins of hepatitis C virus (HCV) positive (n=32) women and control group (n=206) (No (%))

Ethnic origin	*HCV positive women*	*Control group*
White Caucasian	14 (44)	105 (51)
Mediterranean	8 (25)	23 (11)
Indo	0 (0)	10 (5)
Afro-Caribbean	0 (0)	14 (7)
African	7 (22)	33 (16)
Oriental	0 (0)	6 (3)
Middle East	0 (0)	14 (7)
Other	3 (10)	10 (5)

RISK FACTORS FOR HCV INFECTION

The 300 women who were asked to complete the acceptability questionnaire were also asked to complete a questionnaire regarding known risk factors for HCV infection. By chance, during this six week period no HCV positive samples were found thus ensuring that all women who completed the anonymous questionnaire were either HCV negative or declined testing. Two hundred and seven women (69%) who were not infected with HCV returned the second questionnaire and their replies are shown in table 2 together with the replies to the same questionnaire from women who were identified as HCV infected. The ethnic origin of these patients is shown in table 3. A significantly higher proportion of the HCV positive women had used illicit drugs and a higher proportion of infected women had undergone body piercing (chiefly for ear rings). However, it is clear from table 2 that testing women with a history of illicit drug use would only identify 40% of infected mothers. Of the 13 mothers who eventually admitted to previous drug use only eight gave this information to the booking midwife. Five of these women were known to have chronic HCV infection and 16/22 women (73%), newly diagnosed as HCV infected, had no obvious risk factors for infection recorded at the time of booking.

FOLLOW UP OF INFECTED MOTHERS

To date, 23 infected women have been offered follow up appointments after delivery; 19 (83%) have attended for further investigations.

Discussion

The prevalence of anti-HCV among our multiethnic antenatal population was 0.8%. Our population was derived from an inner city area and it is possible that lower rates of infection may be found in other areas. HCV infection was more common in women of white Caucasian origin, and a history of intravenous drug use was the most predictive risk factor for anti-HCV. However, in 50% of our antenatal patients the history taken by the booking midwife did not identify risk factors for infection. Thus any policy of selective testing of high risk women will fail to identify over half of infected patients. We believe that targeted screening is not appropriate in this setting. The universal offer of HCV testing was acceptable to the local population and the majority of infected women attended for further follow up after delivery. This is in marked contrast with findings in patients referred from sexual health clinics where the majority of patients do not attend for further investigation and treatment.[15]

Antenatal HCV testing provides an opportunity to identify asymptomatic women with a chronic disease who are likely to benefit from modern therapy with interferon and ribavirin which cures nearly 40% of patients with chronic HCV.[16] It is noteworthy that a high proportion of our infected mothers attended for further follow up and treatment, whereas patients with HCV identified in other settings have a high prevalence of subsequent non-attendance. Antenatal screening may therefore identify infected women at a time when they are most receptive to medical intervention. The National Screening Committee Handbook of Population Screening Programmes (National Screening Committee at http://www.open.gov.uk/doh/nsc/nsch.htm) contains detailed criteria that should be met before screening for a condition is initiated. In essence they recommend that a disease should be well characterised and an important health problem for which there is a robust diagnostic assay. Hepatitis C clearly fulfils these criteria. The committee further recommends that there should be an effective therapy for the disease that is more effective in early rather than advanced disease. For infected mothers interferon and ribavirin therapy appears to satisfy these conditions in that there is evidence of reduced efficacy in patients with advanced liver disease (cirrhosis).[16] The national committee also recommend that the screening programme should be rigorously assessed in randomised controlled trials to show that screening is effective in reducing mortality and the benefits outweigh the psychological harm caused by the screening procedure. Our study does not address these important issues but data from our questionnaires indicate that the psychological harm from screening is likely to be very small and we believe that large scale randomised controlled trials of screening for HCV in pregnancy should now be considered.

The relatively high false positive rate in our patients (10/48 EIA positive samples were not confirmed on subsequent assays) is a source of some concern and may indicate that pregnant women are more likely to give rise to a false positive test than those who are not pregnant. In general, patients who are RIBA indeterminate are not infected with HCV and are PCR negative. It was therefore surprising to find that one of our patients whose RIBA test was indeterminate was RNA positive by PCR testing. Again, this may indicate that the antibody response in pregnant women may be qualita-

tively and quantitatively different from those who are not pregnant. Further work is required to clarify this issue but it is important to ensure that all those involved in the screening service are aware of the local false positive rate so that appropriate information can be given to patients.

It is not yet clear if our policy will lead to a reduction in vertical transmission of HCV. Transmission of HCV from mothers to infants is estimated to be 5–10% in mothers who are not coinfected with HIV, and transmission may be enhanced by high viral loads prior to delivery, invasive fetal monitoring, and prolonged labour.[17] We speculate that identification of infected mothers will allow their obstetric care to be performed in a way that reduces transmission. Further studies involving large numbers of infected women are required before this is formally proved.

The optimum monitoring and assessment of infants born to HCV infected mothers is not yet clear. Our current policy is to test the children, by PCR, six weeks and three months after delivery. We perform a further PCR test when the child is 14–15 months old and on this occasion we also perform an EIA assay to detect antibodies against HCV. We believe that this "active monitoring" will allow us to identify infected infants at an early age and by establishing links with the hospital will facilitate compliance. This testing policy is under regular audit and review. As infants born to mothers who have one blood borne virus may be at higher risk of contracting hepatitis B, we discuss vaccination against hepatitis B with the parents and we recommend vaccinating the child against this preventable infection. To date, we have identified three infants with perinatal infection and these children are currently undergoing assessment prior to therapy. We do not yet know if early treatment of infected infants will prevent the complications of chronic HCV (chiefly cirrhosis and HCC) but as these complications develop after 25–30 years of infection we believe that early identification and management of infected children will reduce the risk of death in the second and third decades.

Our study shows that pregnant women are willing to be screened for chronic HCV infection and that infected women want to comply with treatment. We believe that our current policy will benefit infected women and we speculate that early diagnosis and intervention for infected children will reduce long term complications although we accept that this has not yet been formally proved.

1 Choo Q-L, Kuo G, Weiner AJ, Overby LR, Badley DW, Houghton M. Isolation of a cDNA clone derived from a blood-borne non-A, non-B viral hepatitis genome. *Science* 1989;**244**:359–62.
2 Kuo G, Choo QL, Alter HJ, *et al.* An assay for circulating antibodies to a major etiologic virus of human non-A, non-B hepatitis. *Science* 1989;**244**:362–4.
3 WHO Consultation group. Global surveillance and control of hepatitis C. *J Viral Hepat* 1999;**6**:1–15.
4 Alter MJ, Sampliner RE. Hepatitis C. *N Engl J Med* 1989;**321**:1538–40.
5 Hoofnagle JH. Hepatitis C: The clinical spectrum of disease. *Hepatology* 1997;(suppl 1)15–20S.
6 Manzini P, Saracco G, Cerchier A, *et al.* Human immunodeficiency virus infection as risk factor for mother-to-child hepatitis C virus transmission; Persistence of anti-hepatitis C virus in children is associated with the mother's anti-hepatitis C virus immunobloting pattern. *Hepatology* 1995;**21**:328–32.
7 Zanetti AR, Tanzi E, Paccagnini S, *et al.* Mother-to-infant transmission of hepatitis C virus. *Lancet* 1995;**345**:289–91.
8 Thomas S, Newell ML, Peckham C. *Vertical transmission of hepatitis C virus and the potential role of antenatal screening. A review and systematic analysis*. London: Institute of Child Health. Prepared for the Department of Health hepatitis C research initiative, 1997.
9 Boxall E, Skidmore S, Evans C, Nightingale S. The prevalence of hepatitis B and C in an antenatal population of various ethnic origins. *Epidemiol Infect* 1994;**113**:523–8.
10 Floreani A, Paternoster D, Zappala F, *et al.* Hepatitis C virus infection in pregnancy. *Br J Obstet Gynaecol* 1997;**103**:325–9.
11 Pipan C, Amici S, Aston G, Ceci GP, Botta GA. Vertical transmission of hepatitis C virus in low risk pregnant women. *Eur J Clin Microbiol Infect Dis* 1996;**15**:116–20.
12 Roudot-Thoraval F, Pawlotsky JM, Deforges L, Girollet PP, Dhumeaux D. Anti-HCV seroprevalence in pregnant women in France. *Gut* 1993;(Suppl):S55–6.
13 Kane M, Alter M, Esteban R, Rizzetto M. Role of screening in prevention and treatment. *Gut* 1993(Suppl):S45–7.
14 Newell M-L, Thorne C, Pembrey, Nicoll A, Goldberg D, Peckham C. Antenatal screening for hepatitis B infection and syphilis in the UK. *Br J Obstet Gynaecol* 1999;**106**:66–71.
15 Foster GR, Goldin R, Main J, Murray-Lyon I, Hargreaves S, Thomas HC. The management of chronic hepatitis C: clinical audit of a biopsy based management algorithm. *BMJ* 1997;**315**:453–8.
16 McHutchison JG, Gordon, Schiff MR, *et al.* Interferon alpha 2b alone or in combination with ribavirin as initial treatment for chronic hepatitis C. *N Engl J Med* 1999;**339**:1485–92.
17 Spencer J, Latt N, Beeby P, Saunders J, McCaughan G, Cossart Y. Transmission of hepatitis C to mothers of infants of human immunodeficiency virus-negative intravenous drug-using mothers: rate of infection and assessment of risk factors for transmission. *J Viral Hepat* 1997;**4**:395–409.