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The seroprevalence of hepatitis C virus infection among children and their mothers attending for dental care in Glasgow, Scotland, United Kingdom

M O'Leary¹, J Bagg², R Welbury², SJ Hutchinson^{3,5}, R Hague⁴, I Geary², KM Roy⁵

1. Department of Infectious Disease Epidemiology, London School of Hygiene and Tropical Medicine, London, United Kingdom

2. University of Glasgow Dental School, College of Medical, Veterinary & Life Sciences, Glasgow, United Kingdom

3. Glasgow Caledonian University, Glasgow, United Kingdom

4. Royal Hospital for Sick Children, Yorkhill, Glasgow, United Kingdom

5. NHS National Services Scotland, Health Protection Scotland, Glasgow, United Kingdom

Corresponding author:

Jeremy Bagg,

Glasgow Dental Hospital & School,

378 Sauchiehall Street,

Glasgow G2 3JZ, UK

Tel: +44 (0)141 211 9741

Fax: +44 (0)141 331 2798

E-mail: jeremy.bagg@glasgow.ac.uk

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Abstract

This paper describes a voluntary anonymous survey to investigate the seroprevalence of Hepatitis C (HCV) in children in Glasgow, UK attending a Dental Hospital and the proportion of HCV positive mothers who have a child who is HCV seropositive. The study was undertaken among children and accompanying parents and household contacts attending a general anaesthetic assessment clinic at Glasgow Dental Hospital and School.

Children were asked to provide an oral fluid specimen for HCV testing. Accompanying adults were asked to provide demographic data on the child and information on familial risk factors for HCV infection using a standardised questionnaire. Birth mothers were also asked to provide an oral fluid specimen. Specimens and questionnaires were linked by a unique anonymous study number.

Between June 2009 and December 2011, samples were collected from 2141 children and 1698 mothers. None of the samples from the children were HCV seropositive but 16 (0.9%, 95% CI 0.6% to 1.5%) of the specimens from mothers were HCV antibody positive.

In summary, the prevalence of HCV seropositivity in the birth mothers of the children was similar to that estimated in the general population served by the hospital and showed no evidence of mother-to-child transmission of HCV.

Introduction

HCV is a major public health problem in Scotland, with an estimated 38,000 individuals chronically infected with the virus (1). It is believed that around half of those infected are undiagnosed (approximately 18,000) and the majority have a history of injecting drug use (2).

A significant number of studies of the prevalence of HCV infection have been completed in a variety of international locations, including both endemic and non-endemic areas (3-20). There are few data on the prevalence of HCV in children and, with the exception of a pilot study in Glasgow (21), no prevalence surveys have been conducted exclusively among children in the UK. Many of the data on childhood prevalence globally have been derived from sub-analyses of larger cross-sectional surveys of the general population (3-5, 7-9, 12), though some have focused on children (6, 10, 13-20). There is worldwide geographic variation in the prevalence of HCV infection in children. With the exception of surveys of children from African countries (8, 9, 17, 18) the reported prevalence of HCV in children is usually very low and frequently less than 1% (6, 10, 13-16, 19, 20).

Perinatal (vertical) transmission is widely believed to be the most common source of HCV infection in children (22). The risk of transmission from an HCV RNA positive mother at birth is estimated at 5%, increasing with increasing viral load, and almost entirely confined to those with viral loads of $\geq 10^6$ /ml (23-25). Transmission has also been shown to be associated with maternal history of injecting drug use (26).

Although paternal HCV infection has been reported as a risk factor for perinatal HCV infection, it is not an independent risk factor, but is dependent on maternal intravenous drug use (26).

There are an estimated 5000 people who inject drugs (PWID) currently in the NHSGG&C health board area aged between 15 and 54 years (27) and the prevalence of HCV in this population has been reported as 68% (28). While it is anticipated that children of current and former PWIDs will be at increased risk of HCV infection, little is known about the prevalence of HCV in children in this geographical area. A previous pilot study in Glasgow (21), which assessed the feasibility and acceptability of recruiting children for an anonymous cross-sectional survey of HCV infection using an oral fluid collection device, reported a prevalence of

2.9% (2/70, 95%CI: 0.35 – 9.9), which was higher than in the general Scottish population, where the prevalence is approximately 1% (1). Although the sample size for the study was small, the surprisingly high prevalence rate reported in this study underscored the need to investigate HCV prevalence in the paediatric population in Scotland. The high prevalence rate was thought likely to reflect the large population of current and former injecting drug users who reside in Glasgow and the high level of social deprivation of the population who attend the Dental Hospital and School.

The primary objective of this study was, therefore, to determine the seroprevalence of HCV among children in Glasgow. Secondary objectives were to determine the association between markers of HCV infection in mothers and children, and to identify risk-factors for HCV infection in children. This information is important in order to inform whether case finding of children living in households with guardians who inject is required, and the treatment, care and support needs for this population, which in the USA have been identified as substantial (29).

Methods

Study design

A cross-sectional survey of children, and when possible their birth mothers, resident in Glasgow and the West of Scotland, recruited from the child patient population attending the General Anaesthetic (GA) Assessment Clinic at the Glasgow Dental Hospital and School, for assessment prior to dental extraction.

Ethical approval

Approval for the study was granted by the West Glasgow 2 Research Ethics Committee.

Recruitment of participants

Prior to each child's attendance at the clinic, an invitation letter and information leaflet was sent to parents / guardians along with the child's appointment card, in order to inform them of the study. Upon attendance, a research nurse approached parents / guardians, explained the study and procedure in detail and invited them to provide informed written consent for the child to participate in the survey. Children aged over seven years were also asked to provide written consent and children aged less than seven years were asked to assent verbally to participate. The investigator employed a variety of communication strategies, including play, to communicate with the children, in particular pre-school children.

Children were excluded from the study if they were accompanied by a guardian who did not have parental rights to consent for them to participate; were not attending the clinic for assessment; or were aged less than 3 years and more than 14 years.

Data collection and handling

The Research Nurse interviewed the parents / guardians to collect anonymous demographic and risk factor data for HCV infection for the child and mothers using a

standardised questionnaire. Age, gender and ethnic background of participants were recorded, together with post-code data to allow a deprivation category to be assigned to each participant. In addition, for each child, data were recorded on recognised risk factors for HCV infection (blood transfusion, organ transplant, surgery, tattoos and piercings and overseas medical treatment); co-habitation with a parent or other household member who was a current or former injecting drug user; co-habitation with a parent or other household member who was HCV positive; risk factors for intra-familial horizontal transmission (including sharing toothbrushes); risk factors for vertical transmission (maternal HCV infection, maternal HCV / HIV co-infection, mode of delivery at birth) and maternal country of birth. The maternal risk factors for infection collected were intravenous drug use, history of blood transfusion or organ transplant and overseas medical treatment. Household contacts were identified using the definition used in the 2001 Scottish census, as *“a group of people (not necessarily related) living at the same address with common housekeeping, sharing either a living room or sitting room, or at least one meal a day”*.

Data collected on those who declined to participate were the age and gender of the child, the relationship of the accompanying adult to the child and the reason for non-consent, to allow assessment of any response bias.

Data were entered on a daily basis into a password protected Microsoft Access database on a secure password protected computer. Post-code data were automatically converted to a social deprivation category using the Scottish Index of Multiple Deprivation (SIMD), then redacted on the questionnaire and rendered unreadable, in order to protect patient confidentiality. All data were held in accordance with the Caldicott guidelines (<http://www.connectingforhealth.nhs.uk/systemsandservices/infogov/caldicott>) and the Data Protection Act 1998 (<http://www.legislation.gov.uk/ukpga/1998/29/contents>).

Saliva specimen collection

Saliva specimens were collected from both children and birth mothers using the OraSure collection device (Epitope Inc, Oregon, USA). Participants were asked to insert the device into their mouth between the lower cheek and gum and retain it for two minutes. Specimens were placed into a labelled vial and stored at -40°C before transport to the West of Scotland Specialist Virology Centre (WSSVC) for testing. Specimens from a child and adult were linked to the questionnaire data using a unique anonymous number.

Laboratory testing

Oral fluid specimens were tested for HCV antibodies using a modified protocol for the Ortho HCV 3.0 SAvE ELISA (Product number 940982, Ortho Diagnostics Amersham). The sensitivity and specificity of this assay are 92% and 99% respectively (30). All reactive samples were repeated using the same assay and weakly reactive samples were further tested using modified protocols of the recombinant immunoblot assay (RIBA). The virology laboratory held a secure Microsoft Access database containing the unique anonymous study number, date of HCV test, sample viability and HCV antibody test result, which was merged on a quarterly basis with the main study database.

Data analysis

All statistical analyses were carried out using SPSS version 17 and STATA version 9.2. Results were presented as numbers and percentages. Representativeness of the study population was assessed using chi-square test comparing the gender, age, ethnicity and relationship with accompanying adult of the participants and non-participants. HCV prevalence is presented with the 95% confidence limits (CI) calculated using the Wilson method for small n . Factors associated with maternal HCV infection were determined using univariable logistic regression analysis. Associations were expressed as odds ratio (OR) together with their 95% CI.

Multivariable logistic regression analysis was not performed due to the collinearity of the predictor variables

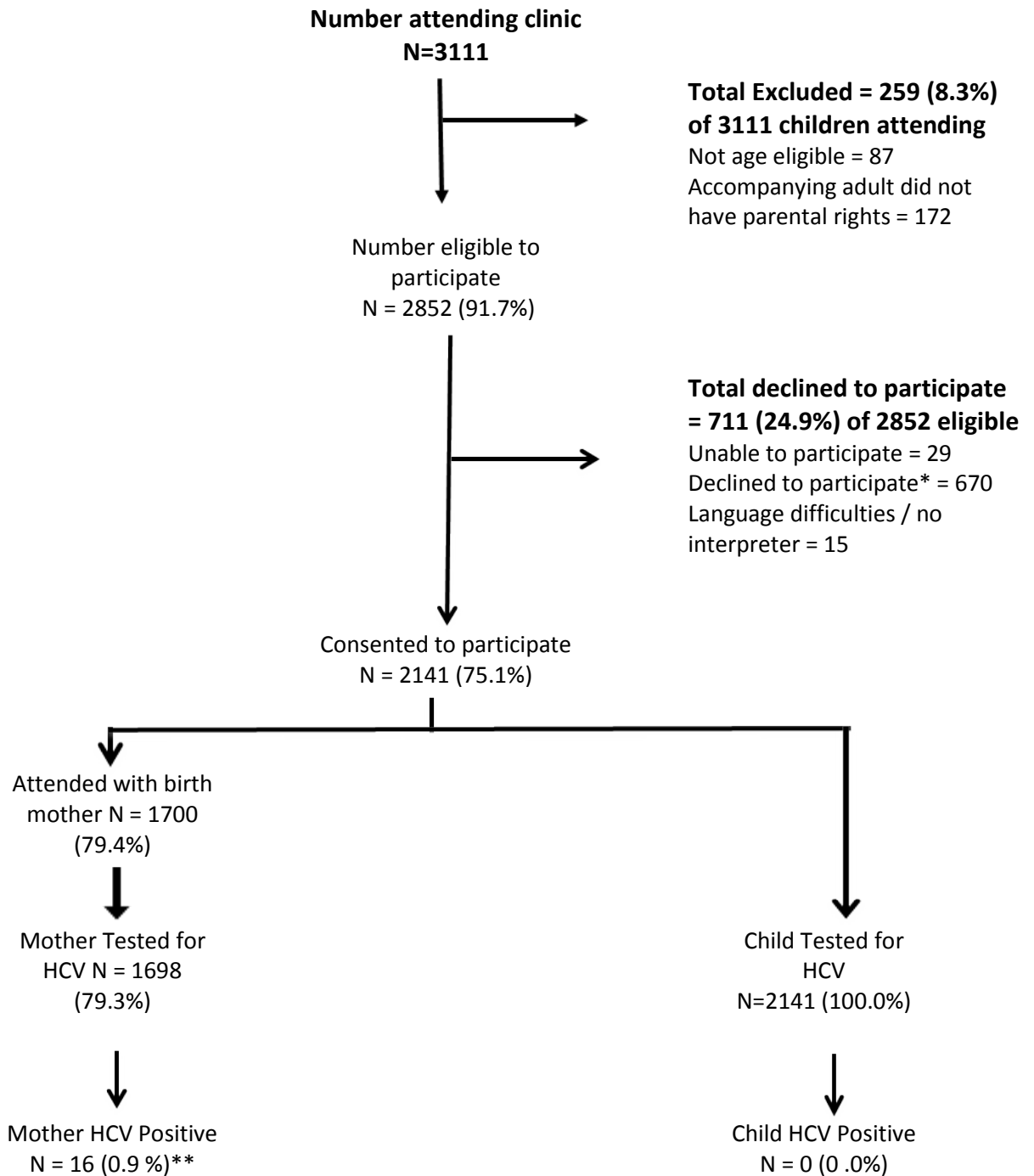
Results

Of the 3,111 children attending the General Anaesthetic (GA) Assessment Clinic at Glasgow Dental Hospital and School during the recruitment period, 259 did not meet the inclusion criteria and were excluded. Of those eligible to participate (n=2852), 2141 consented to participate in the survey giving an overall participation rate of 75% (Figure 1). Compared to participants, non-participants tended to be younger ($P < 0.001$) and non-Caucasian ($P < 0.001$) (Table 1).

Of the 2141 children participating, 1141 (53%) were female and 1333 (62%) aged between 3-6 years. Fifty nine percent of children participating were resident in areas of Glasgow considered to be the most deprived (SIMD quintile 4 and 5). Sixty seven children (3.1%) reportedly lived with someone who had a history of drug use; of these 31 (46.3%) also lived with someone who was HCV positive. One hundred and three (4.8%) children were of South Asian ethnicity. Ten (9.7%) lived with, and 12 (11.6%) had contact with, someone who was HCV positive. Twenty four children (1.15%) were living with someone who was HCV positive but did not live with someone who had a history of drug use or were of South Asian ethnicity. All children provided an oral fluid specimen for HCV antibody testing, and zero (0%, 95% CI 0% to 0.2%) were antibody positive

Oral fluid specimens were obtained from the majority of birth mothers accompanying their children (n= 1698, 99.3%). Sixteen birth mothers (0.9%, 95% CI 0.6% to 1.5%) were HCV antibody positive. Half of the HCV antibody positive mothers were aware of their HCV positive status at the time of interview. Factors associated with maternal HCV antibody were South Asia place of birth ($P = 0.03$) and history of injecting drug use ($P < 0.001$). In addition to South Asia place of birth ($P = 0.001$), receipt of medical treatment overseas ($P = 0.007$) was also associated with maternal HCV antibody when mothers with a history of injecting drug use were excluded from the analysis (Table 2).

Figure 1: Recruitment and hepatitis C testing of participants in the hepatitis C prevalence survey of children at Glasgow Dental Hospital and School, August 2009 to December 2011.



* Reasons for not being able to take part include physical and learning disabilities.

** 10 of 12 mothers (83.3%) who had confirmatory RIBA tests tested RIBA positive

Table 1: Comparison of characteristics of participants and non-participants in the eligible study population (n= 2855)

Characteristic	Non participants n = 711 % (n)	Participants n = 2141 % (n)	p- value¹
Sex			
<i>Female</i>	49.6 (353)	46.7 (1000)	NS
<i>Male</i>	50.4 (358)	53.3 (1141)	
Age-group (years)			
<i>3-6</i>	72.7 (517)	62.3 (1333)	<0.001
<i>7-10</i>	23.6 (168)	29.8 (638)	
<i>11-14</i>	3.6 (26)	7.9 (170)	
Ethnicity			
<i>Caucasian</i>	79.7 (567)	92.0 (1970)	<0.001
<i>South Asian</i>	11.0 (78)	4.8 (103)	
<i>Other</i>	9.2 (66)	3.2 (68)	
Relationship of accompanying adult			
<i>Mother</i>	83.1 (591)	79.4 (1700)	0.004
<i>Father</i>	16.5 (117)	18.4 (395)	
<i>Guardian lives with child</i>	0.4 (3)	2.12 (46)	

¹chi-square test. NS is not significant at 5% level

Table 2 Factors associated with HCV Ab prevalence among mothers of children attending Glasgow Dental Hospital, 2009 to 2011

	Prevalence of HCV Antibodies (All)					Univariate Analysis All					Prevalence of HCV Antibodies (excluding PWID)					Univariate Analysis ² Excluding PWID		
	Total N	n	% of N	95% CI		OR	95% CI	P		Total N	n	% of N	95% CI		OR	95% CI	P	
All	1698	16	0.9	0.6	1.5					1684	10	0.6	0.3	1.0				
Deprivation ¹ (NR=1)																		
<i>Most deprived</i>	1026	13	1.3	0.7	2.2	1.0*				1017	10	0.9	0.5	1.8	1.0*			
<i>Less deprived</i>	671	3	0.4	0.2	1.3	0.4	0.1	1.2	0.1	666	0	0.0	0.0	0.5	0.2	0.0	1.3	NS
Maternal place of birth																		
<i>UK</i>	1608	13	0.8	0.5	1.4	1.0*				1595	7	0.4	0.2	0.9	1.0*			
<i>South Asia</i>	28	2	7.1	2.0	22.6	9.5	2.0	44.0	0.004	28	2	7.1	2.0	22.6	17.5	3.5	88.1	0.001
<i>Other</i>	62	1	1.6	0.3	8.6	4.7	0.3	15.6	NS	61	1	1.6	0.3	8.7	3.8	0.5	31.2	0.221
Previous blood transfusion (NR=13)																		
<i>No</i>	1515	14	0.9	0.6	1.6	1.0*				1504	10	0.7	0.4	1.2	1.0*			
<i>Yes</i>	170	2	1.2	0.3	4.2	1.3	0.3	5.7	NS	167	0	0	0	2.2	1.0	0.1	7.9	NS
Overseas medical treatment (NR=3)																		
<i>No</i>	1589	13	0.8	0.5	1.4	1.0*				1577	7	0.4	0.2	0.9	1.0*			
<i>Yes</i>	106	3	2.8	1.0	8.2	3.5	1.0	12.6	0.05	104	3	2.9	1.0	8.1	6.7	1.7	26.1	0.007
History of injecting drug use (NR=16)																		
<i>No</i>	1684	10	0.6	0.3	1.1	1.0*												
<i>Yes</i>	14	6	42.9	21.4	67.8	125	36.8	428.	<.001									

¹ most deprived = simdqintile 1-3; less deprived = simdqintile 4 & 5; ² Sampling zeros were managed by adding one to each zero cell.

NR= non response

*Baseline

Discussion

There are no data on HCV infection in the child population of the UK, although the prevalence is expected to be much lower than in the adult population. In Scotland, approximately 0.8% of the population aged 15-59 years had been diagnosed HCV antibody positive by the end of 2014. The largest proportion of the diagnosed individuals resides in the NHS Greater Glasgow and Clyde Board area. Those at greatest risk of infection include past and current people who inject drug and individuals of South Asian origin (1, 31). It is therefore possible that children of infected women with a history of injecting drugs will be at the greatest risk. Children born to migrants from HCV endemic areas may also be at increased risk.

A high proportion of children attending the general anaesthetic assessment clinic at Glasgow Dental Hospital and School come from areas of high social deprivation. They are more likely to be from families with a history of injecting drug use and therefore more likely to have a family member who is infected with HCV. While the prevalence of HCV antibodies in participants from medium to low deprivation areas (SIMD deciles 4-6) was as expected (0.4%), the prevalence among those recruited from high deprivation areas (SIMD 1-3) was lower than expected (1.3% compared to an anticipated 4%).

The overall HCV antibody prevalence in the mothers recruited to this study is consistent with the epidemiology of HCV infection among the general population of Scotland (1). As expected, mothers with a history of injecting drug use or those of South Asian origin were significantly more likely to be HCV antibody positive. These groups were, however, under-represented, with only 1.5% and 0.5% of the final sample reporting to be of South Asian origin or providing a history of injecting drug use respectively. The prevalence in both groups was higher than that reported previously, but the figures are based on small numbers (28, 31). Given the small number of HCV positive mothers in the sample, it is perhaps not surprising that no HCV positive children were identified. The prevalence of HCV antibodies in this study was lower than that previously reported in a small pilot study undertaken in the same clinic setting (21). The pilot study did not collect any demographic or risk information on the participants or their mothers, and the reasons for the observed difference are unknown.

There are a number of possible explanations for the small proportion of mothers in the final sample with a recognised risk for HCV infection. First, self-exclusion of mothers who had a history of injecting drug use is likely, as 32% of adults accompanying the child to the clinic

indicated that the reason for non-participation was their unwillingness to disclose risk factors; it is not known whether these individuals were more likely to be infected. Self-exclusion of mothers who knew that they or their children were already infected with HCV is also possible. Second, non-disclosure of a previous risk for HCV is also plausible. Indeed, only half of the HCV antibody positive mothers disclosed a recognised risk factor(s) at the point of recruitment. Third, the under-representation of those from S. Asia in the final sample may have been a result of fewer children being accompanied by their birth mother when compared with the Caucasian children (60% versus 86%) or as a consequence of a language barrier, though fewer than 2% of those eligible to participate specifically mentioned this as a reason for non-participation. Finally, the study protocol excluded any child who attended with an adult who did not have parental rights to consent to the child's participation. Certain adults who are '*in loco parentis*' such as foster parents or social workers may accompany children who are more likely to come from areas of deprivation or to have parents with a history of drug use. Under-recruitment of such children may have led to an underestimation of HCV prevalence in our child population. However, our data indicate that only 17 children were accompanied by a social worker or a foster carer.

As the mothers at greatest risk of HCV infection are under-represented, there is the possibility that HCV antibody positive children may have been missed. If we assume that the participants are similar in all other respects, we might estimate (by applying the prevalences found) that we missed four HCV antibody positive mothers who were born outwith the UK; four HCV antibody positive mothers who had received treatment outwith the UK (most likely these being the same individuals) and 22 HCV antibody positive mothers who had a history of injecting drug use. Therefore, overall there may have been 42 HCV infected mothers in the population eligible to participate. If we assume 75% chronicity and 5% HCV transmission rate we might have expected one HCV antibody positive child to be identified.

The strengths of this study were our large sample size of healthy children with paired maternal and child specimens for HCV antibody testing linked to risk information for HCV infection from both mother and child. In addition, our study was conducted in a clinic that treats a large number of children from areas of high level social deprivation that include a large population of current and former injecting drug users.

There were three key limitations to the study. First, there was the risk that mothers who believed they were at risk of HCV infection chose not to take part. We know this was an issue in this voluntary study and it is a pertinent reminder of the challenges of voluntary surveys of children where the maternal risk can be stigmatising and fear of social care interventions can prevent participation and/or disclosure. Secondly, while the decision to collect a non invasive saliva specimen was taken to encourage participation of children, the sensitivity of the assay we used was only 92% and we were unable to establish chronic infection. Finally, we have assumed that the HCV-seropositive women were positive at the time of birth of the child, but this may not have been the case, since infection may have occurred after the pregnancy.

In conclusion, despite the limitations alluded to above, this study showed that the prevalence of HCV infection in the birth mothers of children attending a General Anaesthetic pre-assessment clinic prior to dental extractions was similar to the estimate of infection in the general population served, and showed no evidence of mother to child transmission in this small group of infected individuals. However, given the introduction of highly effective antiviral treatment for hepatitis C, resources should be concentrated on identifying and testing infants born to HCV infected women.

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Conflicts of interests

The authors have no conflicts of interest to declare.

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