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ABSTRACT

Objectives: An unlinked anonymous seroprevalence study was conducted to estimate the prevalence of hepatitis C virus (HCV) infection in samples derived from antenatal clinic attendees at 2 East London Hospitals. An unexpectedly high HCV seroprevalence of 2.6% (1.2% viraemic) had been revealed during an unlinked study of the emergency department at 1 of these hospitals.

Design: 1000 stored residual samples were tested for HCV antibody (anti-HCV) and reactive samples were further tested for HCV RNA. The study was reviewed by the East Midland NRES ethics committee project ID 181154, approval number 15/WS/0125.

Results: The anti-HCV reactivity rate was 0.5% (5/1000) with 0.1% (1/1000) confirmed viraemic. Prevalence for the other blood-borne viruses was higher: 1% (10/1000) were hepatitis B surface antigen positive and 0.3% were HIV antigen/antibody positive (3/1000). There were no co-infections.

Conclusions: More data to establish the prevalence of HCV in the antenatal population is needed. The addition of anti-HCV testing to the well-established antenatal screening programme provides a unique opportunity to impact on the health of pregnant women, their children, partners and future pregnancies in this new era of treatment for hepatitis C.

Strengths and limitations of this study

- The retrospective unlinked design does not allow clinical correlations to be made.
- The study is not powered for comparisons between age and ethnic groups.
- The inclusion criteria may have resulted in the introduction of bias as patients from ethnic minorities may be less likely to have accurate ethnicity data completed.
- The findings in our population may not be applicable to antenatal clinics in other geographical locations; local data need to be established for local hepatitis C virus screening recommendations.

BACKGROUND

With around 130–170 million people living with hepatitis C virus (HCV) worldwide, HCV is clearly a significant global public health concern.[1] In the UK, about 160 000 people are chronically infected with HCV and the prevalence is estimated to be 0.4%.[2] One-quarter of those infected in the UK live in London.[3] Hospitalisations associated with HCV-related end-stage liver disease, hepatocellular carcinoma, liver transplant and death are rising year on year.[2] Directly acting antiviral (DAA) therapies for HCV now offer close to 100% cure rates, are tolerable, of short duration and currently accessible on the British National Health Service (NHS) for those with HCV and cirrhosis.[4 5]

In the UK, half of those infected with HCV are undiagnosed.[3] While universal screening for other blood-borne viruses (BBVs) such as HIV is recommended in the UK and the USA, no such universal recommendations exist for HCV.[6 7] In the USA, the Centre for Disease Control and Prevention (CDC) recommends one-time HCV 'birth cohort' screening for those born between 1945 and 1965.[8] In the UK, risk-based HCV testing is recommended by the National Institute for Health and Care Excellence (NICE), a strategy acknowledged to underestimate the size of the problem due to varying interpretation by clinicians and patients as to what constitutes risk.[9] Accurate data are important in shaping appropriate screening strategies; however, in England, the estimation of HCV prevalence varies widely and is informed by relatively few representative population-based serosurveys.[10]

In 2013, there were over 700 000 attendances to antenatal clinics in England with 97.54% having bloods taken for HIV and 97.68% for hepatitis B virus (HBV).[11] In the antenatal setting, HIV and HBV opt-out screening is recommended and has been instituted since 1999 to reduce HIV and HBV transmissions through intervention.[12 13] Vertical transmission occurs in 4–8% of HCV viraemic patients. Studies to determine

whether antenatal HCV screening is justified were last conducted in the late 1990s, at a time when there was no possibility of intervention for mother or child and limited options following delivery.

Following recent advances in hepatitis C treatment, antenatal clinic screening for HCV needs to be re-evaluated as it provides a unique opportunity to identify asymptomatic women of child bearing age with hepatitis C.

Antenatal derived data from across the UK have revealed a seroprevalence ranging from 0.21% to 0.8% in different regions.[14 15] More recent London data have suggested a prevalence of 0.3–0.4%, with the latter figure from another area in East London.[16 17] In a retrospective review of HCV screening in pregnancies between 2003 and 2013 at St Mary's Hospital London, there were three vertical transmissions.[16] In the era of directly acting agents against hepatitis C, at least some of these transmissions could be preventable.

We sought to determine the retrospective prevalence of active HCV infection in samples derived from antenatal attendees in two of the hospitals within our NHS Trust to inform us on the potential benefits of screening in this population. Both are busy ethnically diverse East London hospitals. In 2014, an unlinked seroprevalence survey of the emergency department (ED) at one of these hospitals revealed a high HCV antibody (anti-HCV) prevalence of 2.6% (1.2% viraemic).[18]

METHODS

One thousand residual virology samples derived from women over the age of 18 years who had attended antenatal clinics during 2013 at two London hospitals were retrospectively tested for anti-HCV in June 2015. Samples required data regarding age, ethnicity and post code to be present for inclusion. HIV antibody/antigen (HIV Ag/Ab) and hepatitis B surface antigen (HBsAg) results from the original antenatal screen were also collected to allow comparison with the prevalence of these other BBVs. Sequential samples with these data present from January 2013 were selected for testing. Previous anti-HCV results for these patients were available. Five hundred samples were from the Royal London Hospital (the same hospital as the ED survey showing a high HCV prevalence) and 500 were from Newham General Hospital. Both hospitals serve boroughs falling within the highest deprivation index quintiles in the country. Following the acquisition of the list of patient samples fulfilling these criteria, samples were anonymised and given a unique study number. Those performing the tests and analysing the data were blinded to any patient details.

Samples were tested for anti-HCV using an automated EIA (Architect, Abbott) assay. The previous testing of HIV Ag/Ab and HBsAg was also performed on this platform. Reactive samples were further tested for HCV RNA (COBAS Amplicor V.2). Data were statistically analysed using the SPSS Statistics V.20 software (IBM). The study was reviewed by the East Midland NRES ethics committee and approved.

RESULTS

One thousand samples were tested during the study period. Age range was 15–49 years (median 29; table 1). The main ethnicity groups were Asian (478/1000), white European (148/1000), white British and Irish (121/1000) and African 110/1000). Overall, 5/1000 (0.5%; 95% CI 0.06% to 0.94%) samples were reactive for anti-HCV and 1/1000 (0.1%; 95% CI 0% to 0.3%) was HCV RNA positive. Two of the five anti-HCV positive samples had previous positive tests on our system, including the HCV RNA-positive individual. Four of the five reactive samples were in the 25–34-year age group.

The prevalence of HBV and HIV was higher: 1% (10/1000; 95% CI 0.38% to 1.62%) were HBsAg positive; 0.3% were HIV Ag/Ab positive (3/1000; 95% CI 0% to 0.64%). The HBV cases were aged 25–43 years and mainly of African (40%), Asian (30%) and Chinese (20%) ethnicities. The HIV cases were aged 33–39 years and of African ethnicity. There were no co-infections (tables 1 and 2). It is not possible to establish from these data if any of these infections were newly identified.

Data from the seroprevalence survey in the ED showed an age-specific and gender-specific prevalence for HCV and a predominant white British ethnicity. This antenatal cohort was significantly younger than the ED cohort (median of 29 vs 48 years, p<0.001, Mann-Whitney U test). However, owing to the very small numbers, it is difficult to comment meaningfully on ethnicity.

CONCLUSIONS

The prevalence of HCV varies greatly by country worldwide. The lowest rates are observed in northern European countries, with progressively higher rates of infection noted in southern Europe, Asia and Africa.[19 20] Particularly high rates of infection are seen in Egypt, Pakistan and China.[21] Seroprevalence studies examining vertical transmission of hepatitis C in the UK

Table 1 Prevalence of hepatitis C, hepatitis B and HIV by age group

Age group	Total cohort	Reactive anti-HCV	HCV RNA positive	HBsAg detected	HIV Ag/Ab positive
15–24	184	0	0	0	0
25–34	642	4	1	7	1
35–44	170	1	0	3	2
45–54	4	0	0	0	0
Total	1000	5	1	10	3

HBsAg, hepatitis B surface antigen; HCV, hepatitis C virus; HIV Ag/Ab, HIV antibody/antigen.

Table 2 Prevalence of hepatitis C, hepatitis B and HIV by ethnicity

Ethnicity	Total cohort	Reactive anti-HCV	HCV RNA positive	HBsAg detected	HBsAg prevalence	HIV Ag/Ab positive	HIV prevalence
White (British and Irish)	121	0	0	0	0.00	0	0.00
Black (British and other)	29	0	0	1	3.45	0	0.00
White (European and other)	148	2	0	0	0.00	0	0.00
Caribbean (white and black)	30	0	0	0	0.00	0	0.00
African	110	1	1	4	3.64	3	2.73
Asian	478	2	0	3	0.63	0	0.00
Chinese	23	0	0	2	8.70	0	0.00
Middle Eastern	2	0	0	0	0.00	0	0.00
Other	59	0	0	0	0.00	0	0.00

HBsAg, hepatitis B surface antigen; HCV, hepatitis C virus; HIV Ag/Ab, HIV antibody/antigen.

have reflected this variation, with subgroup analysis demonstrating a higher prevalence of HCV in mothers born outside of the UK.[22]

We found the seroprevalence for anti-HCV to be 0.5% (0.1% viraemic) in our antenatal population, similar to the stated national prevalence of 0.4%[2] and to the prevalence observed in previous antenatal studies performed in other areas of the UK.[14 16 17] The prevalence is 2.1% lower than in the ED of the same hospital.[18] It is possible that the inclusion criteria for the current study introduced bias due to the requirement for specific sample information to be present—this information is less likely to be complete for ethnic minority populations most likely to be at risk of HCV. The HCV RNA prevalence in this group was lower than that for HIV Ag/Ab and HBsAg, both of which are currently screened for antenatally.

The small number of positive samples in this study does not allow for comparison between age and ethnic groups. Any comparisons between the ED and the antenatal cohorts are biased because of the differences in sample acquisition and because they reflect very different opportunities for identifying infection. The ED population represents a diverse population unwell and in need of emergency care prospectively sampled, whereas the antenatal cohort represents a population which is in general asymptomatic.

The US CDC currently only recommends screening for hepatitis C in persons considered to be at high risk of infection. It applies these guidelines to the antenatal population and does not recommend routine screening for hepatitis C in pregnant women. The European Centre for Disease Prevention and Control technical report on surveillance in 2010 demonstrates that antenatal HBsAg screening is widespread, but antenatal screening for hepatitis C is currently only undertaken in Spain and Norway.[23] A 2005 economic analysis based on the US setting concluded that screening of asymptomatic pregnant woman for HCV was not cost-effective for the US model at that time. The modelling used is not applicable to the UK system of healthcare, or to the current recommendations for management of pregnant women with HCV. In addition, it could not consider the new DAA treatments.[24]

Recent modelling has been performed on antenatal populations in the UK and the Netherlands with superficially contrasting results. Selvapatt and colleagues modelled the cost-effectiveness of antenatal hepatitis C screening using their data from St Mary's Hospital, London.[16] Utilising the MONARCH (Modelling the Natural History and Cost-effectiveness of Hepatitis C) model, which has previously been published and validated, they demonstrated cost-effectiveness in a variety of scenarios, including the use of newer DAAs.[25] After discussing possible underestimations, they found that the quality-adjusted life years (QALYs) associated with effective treatment far outstripped the costs of implementing screening and providing treatment. In contrast, a study of anti-HCV antenatal screening in the Dutch health system found that implementation was not cost-effective, though Selvapatt indicated that this was due to high costs of screening and treatment, and the use of outcome measures which underestimates benefits of treatment in relation to quality of life. The St Mary's group took the Dutch figures and adapted them with lower treatment costs and found the screening programme to be cost-effective for the previously applied threshold of €20 000 per QALYs. The St Mary's study and the adaptations that its authors made to the Dutch study data appear to indicate that even with the current high costs of DAAs, their high cure rate indicates probable cost-effectiveness even with active case finding.

Our study provides a snapshot of seroprevalence of anti-HCV in the antenatal population at two busy East London Hospitals. Owing to the methodology employed in sample acquisition, it is most likely that the results are an underestimation of the true size of the problem and this warrants further investigation with prospective anonymised sampling of the antenatal cohort.

Extrapolating the prevalence of our study, with over 700 000 antenatal clinic attendances nationally, 700 viraemic women could be identified annually, with potential for further viraemic individuals to be identified through contact screening. With current high throughput multiple

testing platforms, the costs of adding anti-HCV to samples that have already been acquired as part of routine antenatal screening are minimal, negating further phlebotomy equipment or services costs. From a laboratory perspective, the addition of a test to an existing sample would minimally impact on laboratory staff. With the number of positive results demonstrated in our and other seroprevalence studies, the impact on workload for those analysing results should be easily accommodated.

The face of hepatitis C treatment has completely changed in recent years and antenatal screening provides us with a unique opportunity to intervene in a population for which it has previously been deemed unproductive. Screening of pregnant women can impact multiple people at multiple points: it allows for appropriate management of the current pregnancy, reducing vertical transmission by informing the obstetric team to avoid use of obstetric interventions; babies born to mothers with HCV can be monitored and provided with treatment as necessary post-delivery; the mother herself can be provided with treatment, impacting not just her own health, but the health of future pregnancies; contact screening of partners and previous children might identify other asymptomatic carriers, allowing them to access treatment. Clinical trials using DAAs for children with hepatitis C are currently underway.[26] Identifying a hepatitis C viraemic mother at antenatal screening has the potential to impact on many more lives. The longer term advantages of reducing the hepatitis C burden as well as the personal implications for women and their families cannot be underestimated.

Prior to the advent of DAAs, HCV was not considered worthy of antenatal screening because of a lack of options for intervention. The landscape has dramatically changed and it is time that we adapt to reflect this with our screening strategies.

Contributors CO is the corresponding author and was responsible for the study concept, analysis and interpretation of data; drafting and revision of work; final approval of the version to be published. AJ-S was involved in the acquisition, analysis and interpretation of data; drafting and revision of the work, final approval of the version to be published. GRF and CYWT were involved in the analysis and interpretation of data; revising the work, final approval of the version to be published. All authors agree to be accountable for all aspects of the work.

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