HEPATITIS C SEROPREVALENCE IN THE ANTENATAL CLINIC OF TWO LONDON HOSPITALS –SHOULD WE BE SCREENING ANTENATAL WOMEN?

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<th>BMJ Open</th>
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<td>Research</td>
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<td>Date Submitted by the Author:</td>
<td>24-Nov-2015</td>
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</tbody>
</table>
| Complete List of Authors: | Orkin, Chloe; Barts Health NHS Trust, Department of Infection and Immunology
Jeffery-Smith, Anna; Barts Health NHS Trust, Department of Infection
Foster, Graham; Queen Mary University London, Blizard Institute of Cell and Molecular Science
Tong, C. Y. William; Barts Health NHS Trust, Department of Infection |
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TITLE:

HEPATITIS C SEROPREVALENCE IN THE ANTENATAL CLINIC OF TWO LONDON HOSPITALS – SHOULD WE BE SCREENING ANTENATAL WOMEN?

AUTHORS:

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KEYWORDS:

Seroprevalence, hepatitis C, pregnancy, screening

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1310 - excluding abstract, tables, references, statements
ABSTRACT:

Objectives: In 2014, an unlinked hepatitis C virus (HCV) seroprevalence survey of the emergency department (ED) at an East London hospital revealed an unexpectedly high prevalence of 2.6% (1.2% viraemic). Following that, an unlinked anonymous seroprevalence study was conducted to estimate the prevalence of HCV infection in samples derived from antenatal clinic attendees at two East London Hospitals.

Design: One thousand stored residual samples were tested for HCV antibody (Ab) 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 HCV reactivity rate was 0.5% (5/1000) with 0.1% (1/1000) confirmed viraemic. Prevalence for the other blood-borne viruses (BBVs) was higher: 1% (10/1000) were hepatitis B surface antigen (HBsAg) positive and 0.3% were HIV antigen/antibody positive (3/1000). There were no co-infections.

Conclusions: In contrast to the ED data, adding HCV testing to the existing BBV screening panel for these women would not have diagnosed any new cases of viraemic HCV. In this study there were far more hepatitis B virus (HBV) cases than HCV.

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

• Comparisons between the ED and the antenatal cohorts are confounded by age (the antenatal cohort were far younger)
• The ED population presented in need of emergency care unlike the antenatal cohort who represent a well population

• The findings in our population may not be applicable to antenatal clinics in other geographical locations; local data need to be established for local HCV screening recommendations

**Funding Statement:**

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**Competing Interests:**

All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coiDisclosure.pdf and declare: no support from any organisation for the submitted work; C.O. has received funds from companies that sell drugs for the treatment of HIV including: Gilead, GSK, Boehringer-Ingelheim, BMS, Viiv, Janssen, Johnson & Johnson, MSD, Abbott and AbbVie. G.R.F. has received funds from companies that sell drugs for the treatment of viral hepatitis including: BMS, BI, Gilead, Janssen, Novartis, Springbank, Achillion, GSK, AbbVie. C.Y.W.T. and A.J-S have no conflict of interest. No other relationships or activities that could appear to have influenced the submitted work.
BACKGROUND:

With around 130-170 million people living with HCV world-wide, 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 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] Whilst universal screening for other BBVs such as HIV is recommended in the UK and the US, no such universal recommendations exist for HCV.[6, 7] In the United States, the Centre for Disease Control and Prevention (CDC) recommends one-time HCV ‘birth cohort’ screening for those born between 1945-1965.[8] In the UK, risk-based HCV testing is recommended by the National Institute for health and Care Excellence (NICE).[9] Accurate data are important in shaping appropriate screening strategies, however in England, the estimation of HCV prevalence estimates vary widely and are informed by relatively few representative population-based sero-surveys.[10]

In 2013 there were over 700,000 attendances to ANC’s in England with 97.54% having bloods taken for HIV and 97.68% for 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 conducted in the late 1990’s. Antenatal derived seroprevalence data across the UK have revealed a prevalence in London of 0.33% (86/25940) and in the North and Yorkshire region (N&Y) of 0.22% (37/33959). The adjusted prevalence by proportion tested for London in that study was 0.43% (95% CI :0.32-0.53) and N&Y 0.21% (95% CI : 0.14-0.28).[14] Other UK cohorts have reported a range of antenatal HCV prevalence rates including 0.8% at St Mary’s hospital in London in 2000.[15] Based on this higher 0.8% prevalence demonstrated in the seroprevalence study at St Mary’s routine HCV testing was introduced at this hospital. However, a recently published retrospective review of HCV screening in pregnancies that occurred between 2003-2013 revealed a much lower prevalence of 0.003% (119/35455).[16] Methodological problems around recording of data and uncertainties about universality of uptake make these data difficult to interpret. Importantly there were four vertical transmissions in this cohort, three of which occurred in babies born to mothers with acute infections.[16] In the era of directly-acting agents against hepatitis C, at least some of these transmissions would be preventable.

In 2014, an unlinked seroprevalence survey of the emergency department at an East London hospital revealed a high HCV Ab prevalence of 2.6% (1.2% viraemic).[17] As a result of these data we sought to determine the retrospective prevalence of active HCV infection in samples derived from antenatal attendees in this hospital and in a second hospital. Both are busy ethnically-diverse East London hospitals.
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 HCV in June 2015. 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. The hospitals both serve boroughs falling within the highest deprivation index quintiles in the country. Anonymisation of samples and HCV testing were double blinded. For each sample data on age, ethnicity and HIV and HBV status were collected, and the sample was tested for HCV antibody (Ab) using an automated EIA (Architect, Abbott) assay. Reactive samples were further tested for HCV RNA (COBAS). Data were statistically analysed using the SPSS Statistics 20 software (IBM). The study was reviewed by the East Midland NRES ethics committee and approved.

RESULTS:

One thousand samples were collected during the study period. Age range was 15-49 (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 – 0.94%) of samples were reactive for HCV Ab and 1/1000 (0.1%; 95% CI: 0 – 0.3%) was HCV RNA positive. Two of the five HCV Ab positives were already known, including the HCV RNA positive individual. Four of the five reactive samples were in the 25-34 year age group.
Prevalence for the HBV was higher: 1% (10/1000; 95% CI: 0.38 – 1.62%) were HBsAg positive, whereas 0.3% were HIV antigen/antibody positive (3/1000; 95% CI: 0 – 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 [Table 1 and Table 2].

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

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Total cohort</th>
<th>Reactive HCV Ab</th>
<th>HCV RNA positive</th>
<th>HBsAg detected</th>
<th>HIV Ag/Ab positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>15-24</td>
<td>184</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
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<tr>
<td>25-34</td>
<td>642</td>
<td>4</td>
<td>1</td>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td>35-44</td>
<td>170</td>
<td>1</td>
<td>0</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>45-54</td>
<td>4</td>
<td>0</td>
<td>0</td>
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</tr>
<tr>
<td>Total</td>
<td>1000</td>
<td>5</td>
<td>1</td>
<td>10</td>
<td>3</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Ethnicity</th>
<th>Total cohort</th>
<th>Reactive HCV Ab</th>
<th>HCV RNA positive</th>
<th>HBsAg detected</th>
<th>HBSAg prevalence</th>
<th>HIV Ag/Ab positive</th>
<th>HIV Ab prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>White (British &amp; Irish)</td>
<td>121</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0.00</td>
<td>0</td>
<td>0.00</td>
</tr>
<tr>
<td>Black (British &amp; Other)</td>
<td>29</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>3.45</td>
<td>0</td>
<td>0.00</td>
</tr>
<tr>
<td>White (European &amp; Other)</td>
<td>148</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0.00</td>
<td>0</td>
<td>0.00</td>
</tr>
</tbody>
</table>
Table 2: Prevalence of Hepatitis C, Hepatitis B and HIV by ethnicity

<table>
<thead>
<tr>
<th>Ethnicity</th>
<th>HCV</th>
<th>HBV</th>
<th>HIV</th>
<th>HCV RNA</th>
<th>HBV RNA</th>
<th>HIV RNA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caribbean (White &amp; Black)</td>
<td>30</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0.00</td>
<td>0</td>
</tr>
<tr>
<td>African</td>
<td>110</td>
<td>1</td>
<td>1</td>
<td>4</td>
<td>3.64</td>
<td>3</td>
</tr>
<tr>
<td>Asian</td>
<td>478</td>
<td>2</td>
<td>0</td>
<td>3</td>
<td>0.63</td>
<td>0</td>
</tr>
<tr>
<td>Chinese</td>
<td>23</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>8.70</td>
<td>0</td>
</tr>
<tr>
<td>Middle Eastern</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0.00</td>
<td>0</td>
</tr>
<tr>
<td>Other</td>
<td>59</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0.00</td>
<td>0</td>
</tr>
</tbody>
</table>

Table 2: Prevalence of Hepatitis C, Hepatitis B and HIV by ethnicity

**CONCLUSIONS:**

To our knowledge this is the first antenatal derived seroprevalence cohort to be compared both against the HCV prevalence in a different department of the same hospital and against HIV and HBV prevalence data for this population. We found the seroprevalence for HCV Ab to be 0.5% (0.1% viraemic), similar to the stated national prevalence of 0.4% and 2.1% lower than in the ED of the same hospital.[2,17] In the ED population, the 35-54 year old age group was found to have the highest prevalence of HCV RNA. This antenatal cohort, however, was significantly younger and therefore fits into the overall picture of having a lower prevalence of active HCV infection. Furthermore, prevalence rates for HCV RNA were much lower than HBV reinforcing current guidelines which recommend antenatal HBV screening but not HCV.

Due to the small number of positive samples it is not possible to compare between age and ethnic groups. Comparisons between the ED and the antenatal cohorts are biased by age (the antenatal cohort were far younger) and therefore less likely to have HCV. In addition,
the ED population presented in need of emergency care, unlike the antenatal cohort who represent a well population.

The prevalence of HCV varies greatly by country world-wide. The lowest rates are observed in northern European countries, with progressively higher rates of infection noted in southern Europe, Asia and Africa.[18, 19] Particularly high rates of infection are seen in Egypt, India and China.[20] Seroprevalence studies examining vertical transmission of hepatitis C in the UK have reflected this variation, with sub-group analysis demonstrating higher prevalence of HCV in mothers born outside of the UK.[21]

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 only undertaken in Spain and Norway.[22] A 2005 economic analysis based on the US setting found that screening of asymptomatic pregnant woman for HCV was not cost effective.[23]

This study finds much lower seroprevalence of HCV in antenatal women compared with ED attendees at the same hospital. We also showed lower seroprevalence than for HBV and HIV. This supports current ANC screening guidance for HCV. As the findings in our
population may not be applicable to antenatal clinics in other geographical locations, local
data need to be established for local HCV screening recommendations.

AUTHOR CONTRIBUTIONS:

CO – Corresponding author responsible for study concept, analysis and interpretation of
data; drafting and revision of work; final approval of the version to be published

AJ-S – Acquisition, analysis and interpretation of data; revising the work, final approval of
the version to be published

GF - analysis and interpretation of data; revising the work, final approval of the version to be
published

WT - 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.

DATA SHARING STATEMENT:

No additional unpublished data exists for this study.

REFERENCES:


230 2012; 61:1–32. [http://www.cdc.gov/mmwr/preview/mmwrhtml/rr6104a1.htm](http://www.cdc.gov/mmwr/preview/mmwrhtml/rr6104a1.htm)

231 Accessed 24 November 2015

232 9. National Institute of Clinical Excellence. Hepatitis B and C: ways to promote and offer testing to people at increased risk of infection. 2014


238 11. Department of Health


241 12. Department of Health


245 13. Department of Health


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STROBE Statement—Checklist of items that should be included in reports of cohort studies

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<th>Item No</th>
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<td><strong>Title and abstract</strong></td>
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<td>1</td>
<td>(a) Indicate the study’s design with a commonly used term in the title or the abstract</td>
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<td></td>
<td>(b) Provide in the abstract an informative and balanced summary of what was done and what was found</td>
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<tr>
<td><strong>Introduction</strong></td>
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<td>2</td>
<td>Explain the scientific background and rationale for the investigation being reported</td>
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<td>3</td>
<td>State specific objectives, including any prespecified hypotheses</td>
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<td><strong>Methods</strong></td>
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<td>4</td>
<td>Present key elements of study design early in the paper</td>
<td>2,5,6</td>
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<td>5</td>
<td>Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection</td>
<td>6</td>
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<tr>
<td>6</td>
<td>(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up</td>
<td>6</td>
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<td>(b) For matched studies, give matching criteria and number of exposed and unexposed</td>
<td>NA</td>
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<tr>
<td>7</td>
<td>Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable</td>
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<td>8*</td>
<td>For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group</td>
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<tr>
<td><strong>Bias</strong></td>
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<td>9</td>
<td>Describe any efforts to address potential sources of bias</td>
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<td><strong>Study size</strong></td>
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<td>Explain how the study size was arrived at</td>
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<td><strong>Quantitative variables</strong></td>
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<td>11</td>
<td>Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why</td>
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<td><strong>Statistical methods</strong></td>
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<td>12</td>
<td>(a) Describe all statistical methods, including those used to control for confounding</td>
<td>6,7</td>
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<td></td>
<td>(b) Describe any methods used to examine subgroups and interactions</td>
<td>NA</td>
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<tr>
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<td>(c) Explain how missing data were addressed</td>
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<td></td>
<td>(d) If applicable, explain how loss to follow-up was addressed</td>
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<td></td>
<td>(e) Describe any sensitivity analyses</td>
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<td><strong>Results</strong></td>
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<td><strong>Participants</strong></td>
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<td>13*</td>
<td>(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed</td>
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<td>(b) Give reasons for non-participation at each stage</td>
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<td>(c) Consider use of a flow diagram</td>
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<td><strong>Descriptive data</strong></td>
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<td>(b) Indicate number of participants with missing data for each variable of interest</td>
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<td>(c) Summarise follow-up time (eg, average and total amount)</td>
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<td><strong>Outcome data</strong></td>
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<tr>
<td>15*</td>
<td>Report numbers of outcome events or summary measures over time</td>
<td>6,7</td>
</tr>
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</table>
Main results 16

(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included

(b) Report category boundaries when continuous variables were categorized

(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period

Other analyses 17

Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses

Discussion

Key results 18

Summarise key results with reference to study objectives 8

Limitations 19

Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias 2,3,8,9

Interpretation 20

Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence 9,10

Generalisability 21

Discuss the generalisability (external validity) of the study results 9,10

Other information

Funding 22

Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based 3

*Give information separately for exposed and unexposed groups.

RETROSPECTIVE HEPATITIS C SEROPREVALENCE SCREENING IN THE ANTENATAL SETTING –SHOULD WE BE SCREENING ANTENATAL WOMEN?

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AUTHORS:
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0207 377 7038(PA)

KEYWORDS:
Seroprevalence, hepatitis C, pregnancy, screening

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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 two 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 one of these hospitals.

Design: One thousand 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 (BBVs) 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 HCV screening recommendations

BACKGROUND:

With around 130-170 million people living with hepatitis C virus (HCV) world-wide, 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] Whilst universal screening for other blood borne viruses (BBVs) such as HIV is recommended in the UK and the US, no such universal recommendations exist for HCV.[6, 7] In the United States, the Centre for Disease Control and Prevention (CDC) recommends one-time HCV ‘birth cohort’ screening for those born between 1945-1965.[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 varying interpretation by both 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 sero-surveys.[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 1990’s, 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 has revealed a seroprevalence ranging from
0.21%-0.8% in different regions. [14,15] More recent London data has 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 this 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. The hospitals both serve boroughs falling within the highest deprivation index quintiles in the country. Following the acquisition of the list of patient
samples fulfilling these criteria 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 version 2). Data were statistically analysed using the SPSS Statistics 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 – 0.94%) of samples were reactive for anti-HCV and 1/1000 (0.1%; 95% CI: 0 – 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 – 1.62%) were HBsAg positive; 0.3% were HIV Ag/Ab positive (3/1000; 95% CI: 0 – 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
[Table 1 and Table 2]. It is not possible to establish from this data if any of these infections were newly identified.

Data from the seroprevalence survey in the ED showed an age-gender specific prevalence for HCV and a predominant White British ethnicity. This antenatal cohort was significantly younger than the ED cohort (median of 29 year vs 48 year, p < 0.001 Mann-Whitney U test).

However due to the very small numbers it is difficult to comment meaningfully on ethnicity.

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Total cohort</th>
<th>Reactive anti-HCV</th>
<th>HCV RNA positive</th>
<th>HBsAg detected</th>
<th>HIV Ag/Ab positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>15-24</td>
<td>184</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>25-34</td>
<td>642</td>
<td>4</td>
<td>1</td>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td>35-44</td>
<td>170</td>
<td>1</td>
<td>0</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>45-54</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>1000</td>
<td>5</td>
<td>1</td>
<td>10</td>
<td>3</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Ethnicity</th>
<th>Total cohort</th>
<th>Reactive anti-HCV</th>
<th>HCV RNA positive</th>
<th>HBsAg detected</th>
<th>HBSAg prevalence</th>
<th>HIV Ag/Ab positive</th>
<th>HIV prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>White (British &amp; Irish)</td>
<td>121</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0.00</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Black (British &amp; Other)</td>
<td>29</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>3.45</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>White (European &amp; Other)</td>
<td>148</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0.00</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Caribbean (White &amp; Black)</td>
<td>30</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0.00</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>African</td>
<td>110</td>
<td>1</td>
<td>1</td>
<td>4</td>
<td>3.64</td>
<td>3</td>
<td>2.73</td>
</tr>
<tr>
<td>Asian</td>
<td>478</td>
<td>2</td>
<td>0</td>
<td>3</td>
<td>0.63</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Chinese</td>
<td>23</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>8.70</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Middle Eastern</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0.00</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Other</td>
<td>59</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0.00</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Table 2: Prevalence of Hepatitis C, Hepatitis B and HIV by ethnicity
CONCLUSIONS:

The prevalence of HCV varies greatly by country world-wide. 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 have reflected this variation, with sub-group analysis demonstrating 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 this 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 that they reflect very different
opportunities for identifying infection. The ED population represent a diverse population
unwell and in need of emergency care prospectively sampled, whereas the antenatal cohort
represent a population who are 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]

More 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 quality-adjusted life-years (QALY). 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. Due to the methodology employed in sample acquisition it is 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 is 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 ours and other seroprevalence studies the impact upon 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 whom 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 on not only 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 upon 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 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.

**AUTHOR CONTRIBUTIONS:**

**CO** – Corresponding author responsible for study concept, analysis and interpretation of data; drafting and revision of work; final approval of the version to be published

**AJ-S** – Acquisition, analysis and interpretation of data; drafting and revision of the work, final approval of the version to be published

**GF** - analysis and interpretation of data; revising the work, final approval of the version to be published

**WT** - 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.

**FUNDING STATEMENT:**

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**COMPETING INTERESTS:**
All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: no support from any organisation for the submitted work; C.O. has received funds from companies that sell drugs for the treatment of HIV including: Gilead, GSK, Boehringer-Ingelheim, BMS, Viiv, Jannsen, Johnson & Johnson, MSD, Abbott and AbbVie. G.R.F. has received funds from companies that sell drugs for the treatment of viral hepatitis including: BMS, BI, Gilead, Janssen, Novartis, Springbank, Achillion, GSK, AbbVie. C.Y.W.T. and A.J-S have no conflict of interest. No other relationships or activities that could appear to have influenced the submitted work.

DATA SHARING:

No additional data available

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12. Department of Health


13. Department of Health


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10.1097/MOP.0000000000000313.
Title: HEPATITIS C SEROPREVALENCE IN THE ANTENATAL CLINIC OF TWO LONDON HOSPITALS –SHOULD WE BE SCREENING ANTENATAL WOMEN?

STROBE Statement—Checklist of items that should be included in reports of **cohort studies**

<table>
<thead>
<tr>
<th>Item No</th>
<th>Recommendation</th>
<th>Reported on page #</th>
</tr>
</thead>
<tbody>
<tr>
<td>Title and abstract</td>
<td>1</td>
<td><em>(a)</em> Indicate the study’s design with a commonly used term in the title or the abstract</td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>(b)</em> Provide in the abstract an informative and balanced summary of what was done and what was found</td>
</tr>
<tr>
<td>Introduction</td>
<td>2</td>
<td>Explain the scientific background and rationale for the investigation being reported</td>
</tr>
<tr>
<td>Objectives</td>
<td>3</td>
<td>State specific objectives, including any prespecified hypotheses</td>
</tr>
<tr>
<td>Methods</td>
<td>4</td>
<td>Present key elements of study design early in the paper</td>
</tr>
<tr>
<td>Setting</td>
<td>5</td>
<td>Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection</td>
</tr>
<tr>
<td>Participants</td>
<td>6</td>
<td><em>(a)</em> Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up</td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>(b)</em> For matched studies, give matching criteria and number of exposed and unexposed</td>
</tr>
<tr>
<td>Variables</td>
<td>7</td>
<td>Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable</td>
</tr>
<tr>
<td>Data sources/measurement</td>
<td>8*</td>
<td>For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group</td>
</tr>
<tr>
<td>Bias</td>
<td>9</td>
<td>Describe any efforts to address potential sources of bias</td>
</tr>
<tr>
<td>Study size</td>
<td>10</td>
<td>Explain how the study size was arrived at</td>
</tr>
<tr>
<td>Quantitative variables</td>
<td>11</td>
<td>Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why</td>
</tr>
<tr>
<td>Statistical methods</td>
<td>12</td>
<td><em>(a)</em> Describe all statistical methods, including those used to control for confounding</td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>(b)</em> Describe any methods used to examine subgroups and interactions</td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>(c)</em> Explain how missing data were addressed</td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>(d)</em> If applicable, explain how loss to follow-up was addressed</td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>(e)</em> Describe any sensitivity analyses</td>
</tr>
<tr>
<td>Results</td>
<td>13*</td>
<td><em>(a)</em> Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed</td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>(b)</em> Give reasons for non-participation at each stage</td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>(c)</em> Consider use of a flow diagram</td>
</tr>
<tr>
<td>Descriptive data</td>
<td>14*</td>
<td><em>(a)</em> Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders</td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>(b)</em> Indicate number of participants with missing data for each variable of interest</td>
</tr>
<tr>
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<td></td>
<td><em>(c)</em> Summarise follow-up time (eg, average and total amount)</td>
</tr>
<tr>
<td>Outcome data</td>
<td>15*</td>
<td>Report numbers of outcome events or summary measures over time</td>
</tr>
</tbody>
</table>
Main results

16  
(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included

(b) Report category boundaries when continuous variables were categorized

(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period

Other analyses

17  
Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses

Discussion

Key results

18  
Summarise key results with reference to study objectives

Limitations

19  
Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias

Interpretation

20  
Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence

Generalisability

21  
Discuss the generalisability (external validity) of the study results

Other information

Funding

22  
Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for exposed and unexposed groups.

Retrospective hepatitis C seroprevalence screening in the antenatal setting—should we be screening antenatal women?
Chloe Orkin, Anna Jeffery-Smith, Graham R Foster and C Y William Tong

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