Screening for asymptomatic urogenital Chlamydia trachomatis *infection at a large Dublin maternity hospital: results of a pilot study*

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ORIGINAL ARTICLE

Screening for asymptomatic urogenital *Chlamydia trachomatis* infection at a large Dublin maternity hospital: results of a pilot study

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Abstract
Background There are currently no Irish guidelines on screening for *Chlamydia trachomatis* infection in pregnancy. Prevalence rates in the antenatal population are not known which has prevented the development of screening recommendations for this group.
Aims The objective of this study was to determine the prevalence of asymptomatic urogenital *C. trachomatis* infection in young women attending for care at a large maternity hospital.
Methods All patients aged 25 years and under attending the Hospital between December 2011 and December 2013 were offered screening for urogenital *C. trachomatis* infection. Nucleic acid amplification testing of the *C. trachomatis* cryptic plasmid was performed on either endocervical swabs or first void urine samples.
Results There were 2687 women tested for *C. trachomatis* infection, 83.4 % (2241/2687) through the antenatal clinics, 7.1 % (193/2687) through the gynaecology clinic, and 9.4 % (253/2687) through the emergency department. The rate of a positive test result was 5.6 % (151/2687) overall. The rates in women ages 16–18, 19–21 and 22–25 years were 9.1 % (31/340), 6.5 % (50/774) and 4.4 % (69/1561), respectively. A positive test result was more likely in those who were unemployed ($p = 0.04$), those who were Irish ($p = 0.03$) and those who were unmarried ($p < 0.01$). There were no cases of neonatal *C. trachomatis* infection in babies born to mothers who were screened in early pregnancy.
Conclusions The prevalence rate of detected *C. trachomatis* infection was 5.6 % in the study population. Screening of antenatal patients may have a role in preventing vertical transmission of infection to the neonate.

Keywords *Chlamydia trachomatis* · Antenatal screening · *Chlamydia trachomatis* prevalence

Introduction

Chlamydia trachomatis infection is a significant problem in Ireland with the number of reported cases increasing almost 25-fold from 245 cases in 1995, to 6008 cases in 2011 [1, 2]. Recommendations for the control of urogenital *C. trachomatis* infection vary widely between countries [3]. There are currently no national guidelines on screening for *C. trachomatis* infection in Ireland and routine screening of asymptomatic individuals is generally not performed. A recent national report on the potential role of screening was limited by the fact that there is little data on the prevalence of *C. trachomatis* infection. The report stated that "priority should be given… to establish the prevalence of genital *Chlamydia trachomatis* infection in different subpopulations in Ireland to inform policy on the need for screening in Ireland" [4].

In the pregnant population urogenital *C. trachomatis* infection has been associated with miscarriage [5] and can result in vertical transmission to the neonate. There is insufficient evidence to link infection to other adverse outcomes such as pre-term birth [6].

We screened asymptomatic women aged 25 years and under for *C. trachomatis* to determine the prevalence of infection in our hospital population. We focused specifically on this age group since they are considered to be at

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increased risk by the Health Protection Surveillance Centre and current recommendations confine antenatal screening to this age group in the United States (US) and United Kingdom (UK) [4, 6, 7].

Methods

The study was performed at a tertiary University Maternity Hospital with almost 9000 deliveries annually. All women aged 25 years and under attending the Hospital over a 2 year period, from 1st December 2011 to 1st December 2013 were invited in person, to participate in the screening programme by their midwife or doctor when they attended the hospital. A patient information leaflet was given to the patients and informed consent was obtained. Ethical approval was granted by the Hospital's research ethics committee.

Socio-demographic details were collected through interview and computerised as part of standard hospital care. This included details on employment status, marital status, ethnicity and smoking status. Testing for *C. trachomatis* was performed either on samples of first-void urine or on endocervical swabs. Specimens were tested in batches using Nucleic Acid Amplification Testing (NAAT), polymerase chain reaction targeting the cryptic plasmid of *C. trachomatis* using COBAS® TaqMan®48 CT test v.1.0 (Roche Diagnostics, Switzerland). Specimens were tested according to the manufacturer's instructions using Lightmix® kit (Roche) and Lightcycler® reagents (Roche). For inhibited polymerase chain reaction tests, the sample was frozen to −70 °C and retested; if repeatedly inhibited, a new specimen was obtained.

Patients who tested positive for *C. trachomatis* infection were followed-up either in a specialist Infectious Diseases clinic (for patients aged 18 years and over) or in a specialist Adolescent Clinic (for patients aged less than 18 years). Contact tracing was organised for all patients who tested positive. All patients who tested positive were treated with 1 g azithromycin orally as a single dose, administered under direct observation by medical staff. A repeat screening test was performed at 6–8 weeks following treatment in patients who were pregnant and in patients who had an intra-uterine device in situ. For pregnant patients where repeat screening test following treatment was performed prior to the third trimester a further screening test was performed in the third trimester. All patients were advised to use barrier contraception until the repeat screening test following treatment was obtained.

Neonates with clinical signs of infection were screened as clinically indicated. Maternal and neonatal charts were reviewed from all positive cases from the first year of screening.

Results were analysed using Excel v.14 (Microsoft, Redmond, USA) and SPSS v.20 (IBM Corp, Armonk, USA). The χ^2 test was used to test for significance between proportions and Student's t test to test significance between means. A p value of <0.05 was considered significant.

Results

During the study period 32.8 % of eligible women underwent a screening test for *C. trachomatis* (2687/8199). Of these 83.4 % (2241/2687) were recruited through the antenatal clinic, 7.1 % (193/2687) through the gynaecology clinic and 9.4 % (253/2687) through the emergency department. Screening uptake was highest in the antenatal clinic with 56.5 % (2241/3967) of those eligible for screening availing of the test compared to 15.4 % (193/1251) in the gynaecology clinics and 8.8 % (253/2881) in the emergency room.

Data on employment status were available for 71.8 % (1930/2687) of the cohort, on nationality for 70.3 % (1888/2687), on smoking status for 68.3 % (1835/2687), and on marital status for 94.1 % (2530/2687).

The mean age of women undergoing screening was 21.8 years (16.2–25.9). Of those for whom data were available 38.0 % (734/1930) were employed, 13.9 % were in full-time education (268/1930), 67.2 % (1269/1888) were Irish, 13.0 % (329/2530) were married and 28.0 % (515/1835) smoked. Compared to the hospital's total antenatal population, our cohort were more likely to be Irish-born (67.2 vs 62.0 %; $p < 0.001$), less likely to be in employment (38.0 vs 77.0 %; $p < 0.001$) and less likely to be married (13.0 vs 59.0 %; $p < 0.001$) [8].

Overall the detected prevalence of *C. trachomatis* infection was 5.6 % (151/2687). The prevalence of a positive test result in those screened was 5.8 % (131/2241) in antenatal patients, 4.7 % (9/193) in gynaecology patients and 4.3 % (11/253) in emergency room patients. The prevalence of a positive test result was 8.2 % (22/268) in those in full-time education, 6.8 % (63/928) in those who were unemployed, 4.8 % (35/735) and in those in employment. Sociodemographic details of women testing negative and those testing positive are shown in Table 1. The rates in women ages 16–18, 19–21 and 22–25 years were 9.1 % (31/340), 6.5 % (50/774) and 4.4 % (69/1561), respectively. Positive test results by age are given in Fig. 1.

All women who required repeat testing following treatment received repeat testing, and all tested negative on re-testing. There were no cases of neonatal *C. trachomatis* infection in babies born to women who underwent screening in the first trimester. There were two cases of neonatal *C. trachomatis* ophthalmia in women screened in the third trimester. One woman underwent screening

Table 1 Sociodemographic characterisitcs by screening test result

	Negative test ($n = 2536$)	Positive test ($n = 151$)	p
Irish[a]	66.7 % (1200/1799)	76.4 % (68/89)	0.03
Married[a]	13.0 % (329/2530)	5.3 % (8/151)	<0.01
Smoker[a]	28.2 % (481/1705)	26.2 % (34/130)	0.62

[a] Full socio-demographic details were not available for entire cohort

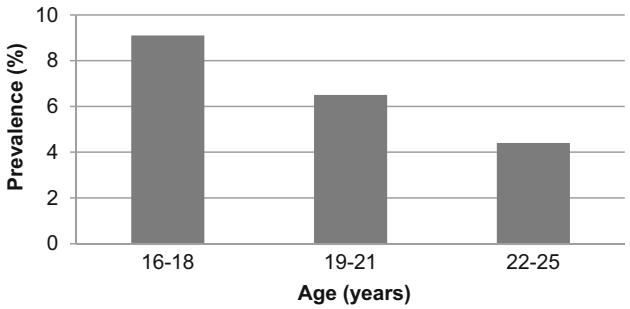

Fig. 1 Prevalence of a positive screen by age group

2 weeks prior to delivery and was treated on the day of delivery. The other woman's test result was not available until after delivery. Full data on clinical outcomes from detailed chart review were available for the first year of screening. There was no increase in the rate of pre-term delivery or small-for gestational age babies born to women who tested positive in the first trimester. However, the numbers of women experiencing these outcomes were low overall and the study was not powered to examine these outcomes.

Discussion

The prevalence of detected urogenital *C. trachomatis* infection in this study was 5.6 %. This is lower than that detected at the same hospital in a previous study carried out in 2003–2004, which found a prevalence of 8.7 % (23/263) in patients aged less than 25 years [9]. This decrease has occurred in the absence of national screening guidelines or a national screening programme for urogenital *C. trachomatis* infection but in the presence of a national sexual health awareness campaign.

An Irish study of *C. trachomatis* in cervical cytology specimens during 2003–2005 found an overall prevalence of infection of 9.6 % (18/187) in those aged less than 25 years [10]. However, other Irish groups have reported a similar detection rate to those found in our study. A recent pilot study on screening for urogenital *C. trachomatis* infection carried out in the West of Ireland in males and females aged 18–29 years, between 2007 and 2009, found an overall prevalence of detection of infection of 4.8 % (48/998) [11]. A study in three Irish third level institutions, carried out among female students of all ages (mean 20.6 years) in 2004–2005, detected a prevalence of 4.8 % (22/460) [12].

Overall, our uptake rate of 32.8 % compares favourably to the 2–9 % uptake reported for woman from an opportunistic pilot screening programme carried out in the West of Ireland [11]. The US reports screening uptake rates of about 13.6 % and the National Chlamydia Screening Programme in the UK aims for a coverage rate of about 29 % [13, 14]. We noted much higher uptake of screening in the antenatal clinics (56.5 %) compared to gynaecology (15.4 %) or emergency (8.8 %) presentations. Midwives in the antenatal clinics systematically discussed screening with eligible women. Similar structures were not in place for gynaecology and emergency room patients. This highlights the importance of ensuring that women have the opportunity to directly discuss screening with trained staff.

In our study the factors associated with testing positive were younger age, single status, Irish nationality, student status or unemployment but not cigarette smoking. Young age and cigarette smoking have been previously associated with risk of sexually transmitted infections in an Irish cohort and age, Irish nationality and single status were associated with increased risk of infection in the previous study in our hospital [7, 11]. Younger age is associated with urogenital *C. trachomatis* infection throughout the world [15]. There is evidence that partial protective immunity develops over time, however, the mechanisms by which this occurs are not well defined [16]. Younger age has also been associated with less consistent condom use [17].

Our cohort was more likely to be Irish-born and less likely to be employed or married than the general hospital population. These characteristics are all associated with a higher likelihood of a positive test result. These findings, therefore, confirm the fact that women aged 25 years and under are at increased risk compared to the general hospital population and support the argument for concentrating screening efforts in this age-group in the context of limited resources.

There is no consensus on screening asymptomatic individuals for urogenital *C. trachomatis* infection. The reasons for screening are to prevent morbidity in the person infected and to decrease the population prevalence of

infection to decrease transmission rates and to protect those not infected. Screening of pregnant women has the added benefit of preventing potential adverse pregnancy outcomes associated with infection and of preventing vertical transmission to the neonate.

It is difficult to accurately assess the role of urogenital *C. trachomatis* infection in its clinical complications; pelvic inflammatory disease, tubal factor infertility, ectopic pregnancy and chronic pelvic pain, since none of these is specific to *C. trachomatis* infection and the population prevalence of infection is rarely accurately known.

The natural course of *C. trachomatis* infection is not well understood. If complications occur early in the course of infection, then it will be necessary to treat infections soon after they are acquired to prevent morbidity. If complications develop from chronic persistent infection then there is greater potential for regular screening to reduce complication rates. Thus, the effectiveness of screening depends on the risk and timing of complications relative to the acquisition of infection and on the mean duration of infection in the population [18]. Current evidence suggests that a typical untreated genital Chlamydial infection can last a year or longer [19, 20]. However, the study of the natural history of genital *C. trachomatis* infection is limited by a lack of knowledge of when the infection was initially acquired, and by the difficulty in differentiating between repeat infections and persistent infections [21]. Mathematical modelling suggests that disease can occur throughout the course of an infection [22], suggesting that there is a window of opportunity prior to disease occurrence where screening may be able to prevent the development of complications.

Urogenital *C. trachomatis* infection in pregnancy has been associated with adverse pregnancy outcomes as well as vertical transmission of infection to the neonate. A Swiss study examining the role of *C. trachomatis* in miscarriage found a higher prevalence of immunoglobulin G against *C. trachomatis* in women who miscarried compared to those who had ongoing pregnancies. They also found *C. trachomatis* DNA more frequently in the productions of conception or placental samples from pregnancies that ended in miscarriage [5]. However, the evidence regarding the role of *C. trachomatis* in adverse pregnancy outcomes is conflicting, with some studies associating urogenital infection with low birth-weight [23, 24] and other studies finding no such association [25, 26]. A large study from the Netherlands of 3913 pregnancies found a significant increase in preterm birth in pregnancies with untreated *C. trachomatis* infection [25]. Treated urogenital *C. trachomatis* infection was associated with preterm birth in a study of 851 women in Washington State, United States of America (USA) [26] but this finding was not supported by a study of 730 women performed in Baltimore, USA [23]. Two studies from the same group in Birmingham, USA, again produced conflicting results regarding the association of urogenital *C. trachomatis* infection and preterm birth [27, 28]. Another large study in the USA of 2127 pregnant women found no association with urogenital *C. trachomatis* infection and preterm birth [29]. Despite a lack of definitive evidence associating *C. trachomatis* infection with adverse pregnancy outcome, modelling shows that for a detected chlamydia prevalence rate of 3 %, screening women aged 16–25 years in pregnancy is cost-effective [30]. Since our detected prevalence is 5.8 % in pregnant women, screening in Irish maternity hospitals can be expected to be cost-effective.

Our reporting of urogenital *C. trachomatis* prevalence in our population is important as it provides robust data to guide national screening policy. Our finding that, in an organised screening programme where all antenatal women were re-tested after treatment and again in the third trimester, the only cases of neonatal infection occurred in women who underwent screening late in pregnancy and did not receive treatment prior to delivery suggests that high intensity screening of antenatal patients may have a role to play in preventing neonatal infection. We recommend screening of women aged 25 years and under attending maternity services in Ireland.

Compliance with ethical standards

Funding No funding was received for this work.

Conflict of interest AOH declares that she has no conflict of interest. VJ declares that she has no conflict of interest. ML declares that she has no conflict of interest. DLB declares that he has no conflict of interest. GC declares that she has no conflict of interest. ME declares that she has no conflict of interest. JSL declares that he has no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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