ARTICLE

Prenatal Screening for Chlamydia and Gonorrhea: An Evidence Based Approach

Le dépistage prénatal de la chlamydiose et de la gonorrhée : une approche fondée sur les preuves

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ABSTRACT

Various North American guidelines regarding prenatal screening for chlamydia and gonorrhea provide conflicting recommendations, and reflect differences in the values underlying interpretation of the available evidence. A systematic search of the literature was conducted to identify evidence regarding the risks and benefits of prenatal screening and treatment of chlamydia and gonorrhea. The available evidence suggests that there is an overall benefit to screening in both the first and third trimesters for women with risk factors for infection or for women living in settings with a high prevalence of infection. Women with no known risk factors who live in settings with a low prevalence of infection should be offered prenatal screening in the first trimester within a context of informed choice.

KEY WORDS

chlamydia, gonorrhea, pregnancy, mass screening, prenatal screening

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RÉSUMÉ

Plusieurs lignes directrices nord-américaines relatives au dépistage prénatal de la chlamydiose et de la gonorrhée fournissent des recommandations contradictoires et reflètent des différences dans les valeurs sous-jacentes à l'interprétation des preuves disponibles. Une recherche systématique de la littérature fut effectuée pour identifier les preuves en ce qui a trait aux risques et aux avantages du dépistage et du traitement prénatals de la chlamydiose et de la gonorrhée. Les preuves disponibles suggèrent qu'il y a un avantage global à effectuer un dépistage au premier et au troisième trimestres pour les femmes ayant des facteurs de risques d'infection ou pour les femmes vivant dans des milieux ayant une prévalence élevée d'infection. On devrait offrir le dépistage prénatal aux femmes sans facteur de risque connu qui habitent dans des milieux ayant une faible prévalence d'infection, et ce, au premier trimestre et dans un contexte de choix éclairé.

MOTS CLÉS

Chlamydiose, gonorrhée, grossesse, dépistage de masse, dépistage prénatal

Cet article a été évalué par des pairs.

Introduction

Chlamydia and gonorrhea are the first and second most common sexually transmitted infections (STIs) in Canada respectively. In 2006, the Public Health Agency of Canada released national guidelines on STIs[1] which included recommendations for universal screening in pregnancy for both infections and for repeat screening in both the second and third trimesters for women with risk factors. These recommendations differ from those made by other North American organizations,[2-4] reflecting differences in the values driving the conclusions drawn from the evidence. There is also a notable absence of a national Canadian clinical guideline developed by maternity care providers on this topic.

What approach should midwives take regarding prenatal screening for chlamydia and gonorrhea in light of conflicting interpretations of the evidence? A comprehensive review of the literature regarding the benefits and harms of prenatal screening and treatment for chlamydia and gonorrhea was conducted to help address this question. This paper summarizes the literature and then discusses how midwives might provide informed choice for their clients with respect to this issue.

Methods

Systematic literature searches were conducted in Medline and the Cochrane Central Register of Controlled Trials to identify articles relevant to the topic of prenatal screening for chlamydia and/or gonorrhea. Reference lists of existing clinical guidelines were also searched. Systematic reviews addressing the issue were sought, and clinical trials and other prospective studies were examined where systematic reviews were not available.

Chlamydia and Gonorrhea

The features of chlamydia and gonorrhea are compared in Table 1. An important characteristic of both infections is that they are often asymptomatic in women – in fact, most pregnant women with chlamydia are asymptomatic.[5] Symptoms of the two infections are similar, but gonorrheal infections tend to progress much more quickly and are more likely to cause severe symptoms than chlamydial infections. The prevalence of both infections has been rising over the last decade, but while chlamydial infections are more common in females than in males (264.7/100 000 versus 137.9/100 000 in Canada in 2006), the opposite is true of gonorrhea (25.9/100 000 vs. 40.4/100 000 in females and males respectively in Canada in 2006.)[6-7] Both infections are much more common in younger women than in older women, with chlamydia affecting 1.4-1.5% of 15-24 year old women.[6] Rates of chlamydial and gonorrheal infections reported in females in Canada are shown by age in Tables 2 and 3. Care providers should keep in mind that significant variation in regional rates exists, so in some Canadian settings prevalence is much higher than the overall national rate while in others it is substantially lower.

Prevalence in pregnancy

Surveillance data on both infections in Canada do not capture information about pregnancy status, and no Canadian studies that examine the prevalence of these infections in pregnant women could be identified. While the reported rates of infection in all Canadian women are the best estimates we have of the prevalence of chlamydia and gonorrhea in pregnant Canadian women, these estimates are likely inaccurate.

Benefit from screening and treatment

There is good evidence from RCTs that antibiotic therapy is effective in treating chlamydia in pregnancy.[8] Antibiotic therapy was found to reduce the number of women with positive cultures at follow-up by approximately 90% when compared to placebo.[8] Relevant RCTs primarily measured microbiological cure, and the findings of these studies provide little evidence to support or refute the assumption that microbiological cure is the same as prevention of neonatal infection or postpartum infection in the mother.[8]

Five studies examining the impact of prenatal screening for chlamydia were identified.[9-13] These studies were conducted primarily in high risk populations in the United States during the 1980s. The first of these was a prospective cohort study of 11,544 subjects who were screened by cervical

Table 1: **Comparison of Chlamydia and Gonorrhea**

	Chlamydia	**Gonorrhea**
Causal agent	*Chlamydia trachomatis* (bacteria with multiple serotypes)	*Neisseria gonorrhoeae* (Gram-negative bacteria)
Prevalence in Canadian females	264.7/100,000 [6]	25.9/100,000 [7]
Risk Factors	• infection with *N. gonorrhoeae*[5, 23] • new sexual partner[5, 23] • >2 sexual partners in past year[5, 23] • history of an STI [5, 23] • age under 25 [5, 23] • injection drug use [5] • incarceration [5,] • sex trade work [5] • street youth [5] • late onset of prenatal care [24, 25]	• commercial sex workers and their sexual partners [15, 23] • sexually active youth <25 years of age with multiple partners [15] • street-involved youth [15] • anybody who has previously had gonorrhea or another STI [15, 23]
Incubation period	• Usually 2-3 weeks [5] • May be as long as 6 weeks [5] • 70% of women remain asymptomatic, vs. 50% of men [26]	• 2-7 days [15] • May be up to 3 weeks in women [27] • Women often remain asymptomatic for months [15, 27]
Symptoms	• vaginal discharge [5, 27] • dysuria [5, 27] • frequency [5, 27] • lower abdominal pain [5, 27] • dyspareunia [5, 27] • abnormal vaginal bleeding [5]	• vaginal discharge [15, 27] • dysuria [15, 27] • frequency [15, 27] • lower abdominal pain [15] • deep dyspareunia [15] • abnormal vaginal bleeding [15] • rectal pain and discharge [15]
Major sequelae	• salpingitis [5, 23] • peritonitis [5, 23] • reactive arthritis [5, 23] • Reiter syndrome [5, 23] • infertility [5] • ectopic pregnancy [5]	• acute pelvic inflammatory disease (rapid onset) [15, 27] • infertility [15, 27] • ectopic pregnancy [15] • bacteremia [27] • disseminated gonococcal infection [15, 23]
Perinatal complications	• preterm birth [23, 28, 29] • preterm rupture of membranes [23, 28, 29] • perinatal death [23, 28, 29] • delayed postpartum metritis [30]	• preterm birth [23] • preterm rupture of membranes [23] • chorioamnionitis [23] • postpartum infection[23] • increased risk of disseminated • gonococcal infection [23]
Neonatal complications	• conjunctivitis [31] • pneumonia [31] • asymptomatic infections of • nasopharynx and vagina [31]	• ophthalmia neonatorum [28] • disseminated gonococcal infection (may include sepsis, arthritis, endocarditis, meningitis) [28]
Treatment in pregnancy	• Amoxicillin, Erythromycin, or • Azithromycin [5] • Test of cure 3-4 weeks after completion of treatment [5]	• Cefixime or Ceftriaxone [15] • Empiric treatment for Chlamydia (20-40% rate of co-infection) [15] • Test of cure post-treatment [15]

Table 2: **Reported Rates of Genital Chlamydia in Females in 2006 in Canada by Age Group**

Age Group	15-19	20-24	25-29	30-39	40-59
Rate per 100 000 women within age group (6)	1367.4	1504.9	607.4	175.7	24.7

culture for chlamydia at their first prenatal visit.[9] The prevalence of chlamydia was 21%. Of the 2,433 women with positive chlamydia cultures, 1,323 received treatment for chlamydia and 1,110 were untreated. When compared to women who were uninfected or treated, women with untreated chlamydial infections were twice as likely to have premature rupture of membranes and small-for-gestational-age babies. The risk of perinatal mortality was four times greater for women who were untreated than for those who were treated.[9]

The second study was a retrospective cohort study of 5,875 women who were screened for chlamydia at the first prenatal visit and then every 2-3 months for the remainder of pregnancy.[10] The prevalence of chlamydia was 5.8%. Among the chlamydia positive women, outcomes were recorded for 244 women who were successfully treated with erythromycin and 79 women for whom treatment failed (5% loss to follow-up). The risk of preterm birth was significantly lower among women with successfully treated chlamydial infection (2.9%) than for women with failed treatment (13.9%) and for a control group of 244 uninfected, untreated women (11.9%). The risk of premature rupture of membranes, premature contractions, and small-for-gestational-age infants was significantly lower for successfully treated women compared to those for whom treatment was not successful.[10]

A third study of 1,082 women screened for chlamydia in the third trimester identified 85 (7.8%) to be positive.[11] The quality of the findings of this study is significantly compromised by high loss to follow-up (59%). Of the 85 women who had chlamydia, 38 were treated with erythromycin and 47 were untreated. Complications (endometritis, postpartum fever, chorioamnionitis, and an infant with growth retardation) occurred with five of the untreated women and none of the treated women. Positive nasopharyngeal and conjunctival chlamydia cultures were only found for infants born to untreated mothers.[11]

A fourth study also provided evidence for the screening and treatment of chlamydia in pregnancy. In a prospective cohort study, 184 women with cervical chlamydia infections were offered erythromycin treatment at 36 weeks.[12] Of this group, 32 refused treatment and 137 received treatment. Findings were limited by high loss to follow up (39% of infants). Maternal treatment was successful in eliminating chlamydia in 92% of cases (n=107), and intolerance to therapy was low (3%, n=152). Outcomes were available for 83 infants. Chlamydial infection developed in 4/59 (7%) of infants born to infected mothers who were treated, compared to 12/24 (50%) of infants born to women who refused treatment.[12]

A fifth study that was examined was also found to be of poor quality. In a prospective cohort of 199 women who were screened for chlamydia in the third trimester, 52 (26%) were found to be positive.[13]

Table 3: **Reported Rates of Genital Gonorrhea in Females in 2006 in Canada by Age Group**

Age Group	15-19	20-24	25-29	30-39	40-59
Rate per 100 000 women within age group [7]	137.1	122.1	58.2	21.2	4.5

Infected women and their sexual partners were offered treatment with erythromycin, counseling and post-therapy retesting. Fifty infants born to treated chlamydia positive women and 48 infants born to women with negative screening results were evaluated for conjunctivitis and respiratory tract infections. No significant differences were found between these two groups.[13] The findings of the study are limited by the small sample size and the possibility of confounding factors in the group of women with negative screening results.

Despite the weaknesses of these studies, there is a common trend in their findings of maternal and neonatal benefit with prenatal screening for chlamydia. The low quality of the studies limits the reliability of their results in accurately quantifying the benefits provided by routine screening and treatment. However, their combined findings provide fair evidence from cohort studies that prenatal screening for chlamydia followed by treatment of infected women leads to improved maternal and neonatal outcomes in populations with a high prevalence of infection. Given the level of evidence available, it is unlikely that an RCT of prenatal chlamydial screening and treatment, which would be the best method of quantifying the benefits of such an intervention, would be considered ethical in a population at high risk for chlamydia.

A Cochrane review examining the efficacy of antibiotics for gonorrhea in pregnancy[14] identified two RCTs that compared the efficacy of different antibiotics in pregnant women on the rate of microbiological cure. While these RCTs found high rates of microbiological cure with several antibiotics, it has been noted that there is a lack of research examining the impact of treatment on perinatal outcomes and the side effects associated with treatment.[14]

Effective treatment for gonorrhea was introduced in the 1940s with the discovery of penicillin. Gonorrhea was one of the first infections to be treated with antibiotics.[14] RCTs were not conducted when this intervention was introduced, and it would not be considered ethical to conduct an RCT in which pregnant women with gonorrhea were allocated to a placebo or no treatment group because the historical evidence supporting the benefits of treatment is so strong.

No studies investigating the impact of universal prenatal screening for gonorrhea in pregnancy on perinatal outcomes were identified. However, there is clear consensus that gonorrhea in pregnancy has potentially devastating consequences for both mother and baby, and that it is beneficial to treat infected women in pregnancy. Recommendations regarding prenatal screening for gonorrhea are universally supportive of screening women with risk factors.[2, 3, 15]

Repeated screening

Another aspect of screening that has been explored in a few studies is the value of repeated screening. The first such study was a prospective cohort study involving 542 women who were screened for chlamydia and gonorrhea at the first prenatal visit and in the third trimester, and who had negative initial screens.[16] Regression analysis was used to examine the relationship between identified risk factors and a positive third trimester result. The authors concluded that comprehensive risk factor based screening is effective in predicting low risk of a positive third trimester screen in an urban clinic population.[16]

Two other studies examined the value of late pregnancy screening for chlamydia (n=752) and gonorrhea (n=751) for women in a high risk population with an initial negative screen.[17, 18] Both studies were retrospective chart reviews of the records of pregnant women seen during a 29 month period at a single clinic serving a population with a high prevalence of both infections. Women were tested for both infections at the beginning of prenatal care and again at 34 weeks. Treatment was offered to all women with positive swabs.

The authors found that 105 (14.0%) had chlamydia diagnosed at their initial screen, and 29 women (3.9%) were positive only at their third trimester screen, with an overall prevalence of 17.8%. Fourteen of the 105 women with positive initial tests were positive again at 34 weeks (after treatment). Several factors were associated with an increased risk of chlamydia among the study population (younger

age, lower gravidity and parity, fewer prenatal visits, and gonorrheal infection). However, the prevalence of chlamydia for women without risk factors was still high enough to warrant repeat third trimester testing of all women in the study population.[17]

In the same population, 38 (5.1%) had gonorrhea diagnosed at their initial screen, and 19 women (2.5%) were positive only at their third trimester screen. Both tests were positive for one patient. No significant differences in the prevalence of most risk factors were found between those with negative swab results and those with positive results. Younger women were at an increased risk for positive swabs at both times, but the prevalence of infection in older women at both initial and repeat testing was considered to be high enough to warrant universal testing.[18] In both studies, the authors suggest that their findings support universal repeat testing at 34 weeks gestation in populations with a high prevalence of the infection.

Given the stigma attached to many of the risk factors and to the infections themselves, it is important to consider the implications of this stigma in potential screening strategies for "low risk" women, and to find ways to overcome it.

Harm

No studies were identified that examine the harms of universal prenatal screening for chlamydia or gonorrhea. Screening for chlamydia and gonorrhea in pregnant women typically involves a speculum examination to obtain endocervical cultures. The inconvenience and discomfort of this test are considered to be one of the potential harms of screening. No research investigating women's beliefs and experiences regarding this aspect of screening were identified. However, a multi-center cohort study investigating the sensitivity and specificity of various screening methods[19] found evidence to suggest that some of the hypothesized harms of screening could be lowered through the use of new methods of specimen collection. Multiple specimens (first catch urine, endocervical swab, and vaginal swabs) were collected from 1464 pregnant and non-pregnant women seen at nine different centres. The study population included both asymptomatic and symptomatic women. Nucleic acid amplification tests (NAATs), considered to be the most sensitive kind of tests available for the diagnosis of chlamydia[20] and gonorrhea, were used. Vaginal swabs were found to have high sensitivities and specificities for both chlamydia and gonorrhea regardless of whether specimens were collected by patients or physicians.[19] A parallel study of a subgroup of this population found that women found it easy to self-collect a vaginal swab, and the majority preferred this method over urine samples and cervical swabs.[21] These findings suggest that less intrusive screening with vaginal swabs may be just as effective as cervical swabs. NAAT testing for chlamydia and gonorrhea is available through public health laboratories; however, at present cervical swabs are required by these laboratories for NAAT testing in all cases except where women have had a hysterectomy.[22]

Another potential harm is the possibility of false positive test results, and the associated distress, potential impact on personal relationships and unnecessary treatment. Despite the fact that some tests for chlamydia and gonorrhea have been found to have highly specific findings (e.g., 99.3%),[19] when the prevalence of infection is low, the majority of positive results will be false-positives. For example, let us assume that the prevalence of gonorrhea is 0.5% in a group of 1,000 women who undergo screening in pregnancy. If the specificity of the test is assumed to be 99.3%, seven of the 995 women who are not infected with gonorrhea will have a positive test result (compared to a maximum of five true positive results if the sensitivity of the test is 100%). It is possible to reduce the likelihood of false positive tests by using additional tests to confirm

Figure 1: **Summary of Recommendations**

1. Recommend screening for chlamydia in the first and third trimester to women with known risk factors and to women living in settings with a high prevalence of chlamydia, within a context of informed choice.

2. Recommend screening for gonorrhea in the first and third trimester to women with known risk factors and to women living in settings with a high prevalence of gonorrhea, within a context of informed choice.

3. Offer screening for chlamydia and gonorrhea in the first trimester to women with no known risk factors, within a context of informed choice.

positive results (e.g., running additional tests on the original sample). The feasibility of this type of approach to prenatal screening has not been explored in the literature.

Costs

No economic analyses were identified that examined the cost of various approaches to screening for chlamydia or gonorrhea in pregnancy. More accurate estimations of the prevalence of chlamydial and gonorrheal infections in Canadian pregnant women and the associated perinatal risks would be needed in order to evaluate the cost-effectiveness of various approaches to prenatal screening for these infections.

Public Health Implications

Clarification of the value attributed to the various potential effects of prenatal screening can also help guide decision-making about the best approach for screening with low risk women. Pregnancy is sometimes viewed as a good time for opportunistic screening for infections, so prenatal screening programs may be seen as valuable components of strategies that address broad public health goals like reducing the burden of disease. There is also a precedent in prenatal care in Canada of universal prenatal screening for other much less common STIs such as syphilis and HIV. This suggests that there is high value placed on detecting potentially detrimental infections in pregnancy in order to minimize vertical transmission and other negative outcomes.

The most substantial harms associated with screening low risk women relate to the consequences of false-positive results. If maternal and neonatal benefits of the identification and treatment of these infections are highly valued by women, false-positive results may not be seen to outweigh these benefits. A comparable case that illustrates this phenomenon is prenatal genetic screening. When provided an informed choice within the context of midwifery care, which includes full disclosure of the potential for false positive results, the uptake of genetic screening test may be lower than when there is less complete disclosure of the limitations of these test; however, many women who are cared for by midwives still choose to undergo genetic screening tests because they value the information these tests can provide.

Risk Status

The available evidence suggests it may be appropriate to use different screening strategies depending on the level of risk of maternal infection. This approach raises the interesting issue of how risk status is determined. While in some cases risk factors may be readily apparent, in other cases identification of risk factors will depend on maternal disclosure. Given the stigma attached to many of the risk factors and to the infections themselves, it is important to consider the implications of this stigma in potential screening strategies for "low risk" women, and to find ways to overcome it. High uptake rates seen with universally offered prenatal HIV screening suggest that such stigma may be overcome in the context of pregnancy with the use of a screening approach that involves informed choice but does not emphasize risk factors.

Implications for practice

Recommendations for practice are summarized in Figure 1. The available evidence suggests that there

is an overall benefit to prenatal screening for chlamydia and gonorrhea in both the first and third trimesters for women with risk factors for these infections, or in settings where the prevalence of these infections is high. First and third trimester screening should be recommended to these women within a context of informed choice.

Lack of evidence about cost and potential harms make it difficult to evaluate whether there is an overall benefit to screening for women without known risk factors where the prevalence of infection is low. Until further evidence is available, a reasonable approach is to provide low risk women with information about the potential benefits and risks of screening for chlamydia and gonorrhea and offer them the option of being screened for either or both of these infections early in their prenatal care.

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CORRECTION

The image on the cover of the 2009 Canadian Journal of Midwifery Research and Practice was captured by photographer Vania Jimenez. In this photo, Lindsey Mina gives birth to Ashevak, supported by her mother Nancy Mina, with midwife Monique Paré and Inuit student midwife Margaret Mina in attendance.