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Screening characteristics for the diagnosis of genital infections with *Chlamydia trachomatis* in pregnant women

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Introduction : *Chlamydia trachomatis* infection during pregnancy can cause maternal morbidity and also neonatal infection. Screening of *chlamydia trachomatis* infection during pregnancy is warranted. However, clinical characteristics may be one of the useful screening criteria in the low resource setting.

Objective : To determine the significance of clinical characteristics of cervical infection in predicting *Chlamydia trachomatis* infection.

Setting : Prenatal Clinic, Department of Obstetrics and Gynecology, Faculty of Medicine, Chulalongkorn University and King Chulalongkorn Memorial Hospital.

Subjects : Pregnant women of 37-42 weeks gestation, who attended prenatal clinic at King Chulalongkorn Memorial Hospital.

Design : Cross sectional study.

Methods : Two hundred pregnant women were evaluated. They were recruited under the following criteria: excessive leukorrhea, endocervical mucopus, induced endocervical bleeding; excess white blood cells in endocervical smear were evaluated. Infection was determined by the combined results of *Chlamydia trachomatis* culture and multiplex polymerase chain reaction (PCR) assays for *Chlamydia trachomatis*.

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Results : *Chlamydia trachomatis* was diagnosed in 10% of the subjects by using PCR technique. With the use of culture technique, the prevalence of chlamydial infection was 2 %. All positive cultures had positive results from PCR. The sensitivity of excessive leukorrhea, endocervical mucopus, induced endocervical bleeding and excess white blood cells were 15 %, 15 %, 20 % and 20 %, respectively. The positive predictive value of excessive leukorrhea, endocervical mucopus, induced endocervical bleeding and excess white blood cells were 13 %, 9.1 %, 8 % and 13.3 %, respectively.

Conclusion : The characteristics for screening chlamydial infection of the cervix among pregnant women of gestational age of 37- 42 weeks had low sensitivity and positive predictive value for detection.

Keywords : *Chlamydia trachomatis*, Infection, Pregnant

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พิชัย โชตินพรัตน์ภัทร, สมภพ ลิ้มพงศานุรักษ์, สุรสิทธิ์ ชัยทองวงศ์วัฒนา. ลักษณะทางคลินิกในการคัดกรองการติดเชื้อคลามัยเดียที่อวัยวะสืบพันธุ์ในสตรีตั้งครรภ์. จุฬาลงกรณ์เวชสาร 2547 ก.พ; 48(2): 73 - 81

- บทนำ** : การติดเชื้อคลามัยเดียในสตรีตั้งครรภ์ มีผลเสียต่อทั้งมารดาและทารก จึงจำเป็นต้องตรวจคัดกรองระหว่างตั้งครรภ์ แต่ค่าใช้จ่ายรวมทั้งความพร้อมของห้องปฏิบัติการยังเป็นปัญหา ดังนั้นการคัดกรองโดยใช้ลักษณะทางคลินิกอาจมีประโยชน์
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- วิธีการศึกษา-วัตถุประสงค์** : สตรีตั้งครรภ์จำนวน 200 ราย ได้รับการตรวจภายในและตรวจหาเชื้อคลามัยเดียที่ปากมดลูกโดยการเพาะเชื้อ และการตรวจด้วยวิธีพีซีอาร์และได้ตรวจหาลักษณะทางคลินิกของปากมดลูกดังนี้ ตกขาวมากผิดปกติ มูกหนองที่ปากมดลูก เลือดออกที่ปากมดลูก ตกขาวมีเม็ดเลือดขาวมากกว่า 10 ตัวต่อพื้นที่เมื่อตรวจด้วยกล้องจุลทรรศน์กำลังขยายสูง
- ผลการศึกษา** : สตรีตั้งครรภ์จำนวน 200 ราย ที่ได้รับการตรวจ พบการติดเชื้อคลามัยเดียที่ปากมดลูกด้วยวิธีเพาะเชื้อ จำนวน 4 คน (ร้อยละ 2) แต่เมื่อตรวจด้วยวิธีพีซีอาร์ พบเชื้อคลามัยเดียจำนวน 20 คน (ร้อยละ 10) สตรีตั้งครรภ์ทุกคนที่เพาะเชื้อเป็นบวกจะตรวจพบโดยวิธีพีซีอาร์ด้วยเช่นกัน จากลักษณะของปากมดลูกพบว่า ตกขาวมากผิดปกติ มูกหนองที่ปากมดลูก เลือดออกที่ปากมดลูก ตกขาวมีเม็ดเลือดขาวปริมาณมาก มีความไวเท่ากับ ร้อยละ 15, 15, 20, 20 ตามลำดับ ความสามารถทำนายเมื่อผลการทดสอบเป็นบวก เท่ากับร้อยละ 13, 9.1, 8, 13.3 ตามลำดับ
- สรุป** : ลักษณะทางคลินิกสำหรับการคัดกรองการติดเชื้อคลามัยเดียที่ปากมดลูกในสตรีตั้งครรภ์ที่มีอายุครรภ์ตั้งแต่ 37-42 สัปดาห์มีความไวต่ำและความสามารถทำนายเมื่อผลการทดสอบเป็นบวกได้ต่ำ
- คำสำคัญ** : การติดเชื้อ คลามัยเดีย สตรีตั้งครรภ์

Chlamydia trachomatis infection is the most prevalent sexually transmitted disease. Untreated chlamydial infection can cause severe and costly problems in reproductive and other systems with both short-term and long-term consequences. *Chlamydia trachomatis* infection during pregnancy can cause serious complication for the woman and her newborn. It can result in premature birth, premature rupture of the membranes, low birth-weight infant and puerperal infection. ⁽¹⁾ Chlamydial infection can also transmit to infants causing neonatal eye infection and pneumonia from contacting with infected cervico-vaginal secretion. ⁽²⁾

Detection and treatment of chlamydial infection in pregnant women is crucial. Rastogi *et al.* ⁽³⁾ demonstrate that the prevalence of *Chlamydia trachomatis* infection among pregnant women in the first to third trimester was found to be 18.8 %. They also found that routine screening and treatment of *Chlamydia trachomatis* infection in pregnant women reduced the adverse effects on pregnancy outcome.

Postma *et al.* ⁽⁴⁾ performed pharmacoeconomic model analysis to estimate the cost-effectiveness of antenatal screening for *Chlamydia trachomatis*. By the use of ligase chain reaction on urine specimen as diagnostic tool and the use of erythromycin as treatment of identified infected cases, antenatal *Chlamydia trachomatis* should be screened if the prevalence rate was 3 percent or higher.

Meanwhile, Chaisilwattana *et al.* ⁽⁵⁾ reported that the prevalence of chlamydial infection among pregnant women in Bangkok was 9.2 %. In the low-resource setting like that of our situation, however, chlamydia culture or chlamydial DNA detection for every woman at their prenatal visit are not affordable.

Therefore clinical data may help us to select specific groups for further investigation and treatment among pregnant women. In this study, we aimed to determine the significance of clinical characteristics of cervical infection in predicting *Chlamydia trachomatis* infection in pregnant women.

Material and Method

From January 1995 to February 1995, 200 pregnant women in their gestational age of 37-42 weeks who attended the prenatal clinic at King Chulalongkorn Memorial Hospital, Bangkok were screened for *Chlamydia trachomatis*.

The women were identified for their presence of clinical characteristics of cervical infection: excessive leukorrhea, endocervical mucopus, induced endocervical bleeding and excess white blood cells in endocervical smear. Excess white blood cells in endocervical smear defined as the presence of white blood cells more than 10 cells per high power field in more than 5 fields.

Vaginal speculum was introduced to identify the cervix. Their cervical discharge was collected for microscopic exam. Cervical mucous was cleansed. The cotton-tipped swab was introduced through squamocolumnar junction and brushed around endocervical canal. After brushing thoroughly, the swab was placed in a plastic tube containing 1 mL of transport media. The plastic tube was frozen at -4 °C immediately. The specimen was processed for culture for *Chlamydia trachomatis* immediately and for performing multiplex polymerase chain reaction (PCR) assay within 24 hours. All endocervical specimens were tested for the presence of *Chlamydia trachomatis* with cycloheximide-treated McCoy cells culture

Figure 1. Deoxyribonucleic acid (DNA) sequences of in-house primers of plasmid DNA of chlamydia trachomatis.

Primer A : AGACTTCAGAGGAGCGTTTAC
Primer B : GGACATTTTGCGGATAGGTTA
Primer C : TAGGAAGGATGCTGTT
Primer D : AGAAATGTCGTTAGAA

and with multiplex PCR. PCR testing was performed using in-house primers of plasmid deoxyribonucleic acid (DNA) of *Chlamydia trachomatis* (Figure 1).

The statistical significance of difference was evaluated with Chi-square test or Fisher's exact test. The statistical analysis was performed with the use of SPSS for Windows[®] version 9.0. P values of less than 0.05 were regarded as statistical significance.

Results

A total of 200 term pregnant women were recruited into this study. Their mean age was 24.8 ± 4.8 years of age (ranged 15-39 years of age). The gestational age at which the test was performed was 38.0 ± 1.1 weeks, ranging from 37-42 weeks of gestation. The majority of cases were primigravida (78 %). There were two cases of twin pregnancies. Of the total, 10 % (95 % CI; 5.8 %, 14.2 %) were found to be positive for PCR test. Two percent (95 % CI; 1.0 %, 3.9 %) were positive for culture in McCoy cells. All of the positive culture results were also positive for PCR test.

Eighty pregnant women had at least one of the characteristics, listed in Table 1. There was no statistically significant difference of the clinical characteristics between positive group and negative group for chlamydial PCR (Table 1). Subsequently,

each clinical characteristic was separately analyzed. The results, however, showed that each characteristic was not correlated with the presence of chlamydial infection by PCR technique. In addition, half of positive chlamydial PCR (50 %) did not have the mentioned clinical characteristics. The predictive values of clinical characteristics of cervical infection were shown in table 2.

Discussion

Rastogi *et al.*⁽³⁾ conducted a study of chlamydial infection among pregnant women in the first to third trimester in India. By using direct fluorescent assay and PCR of endocervical specimen, the prevalence rate was found to be 18.8 %. Whereas, Swiss Sentinel Surveillance network illustrated in a cross sectional study that the prevalence of *Chlamydia trachomatis* infection among pregnant women was 2.8 %.⁽⁶⁾ The prevalence rate of *Chlamydia trachomatis* infection among pregnant women in Thailand was 5.7-9.2 %.^(5,7,8)

In 1988, Niamsanit *et al.*⁽⁷⁾ showed that the prevalence of *Chlamydia trachomatis* infection, by using cervical swab culture during the first and the third trimester was 8.5 %. Recently, Chaisilwattana *et al.*⁽⁵⁾ showed that the prevalence rate of *Chlamydia trachomatis* infection among pregnant women in

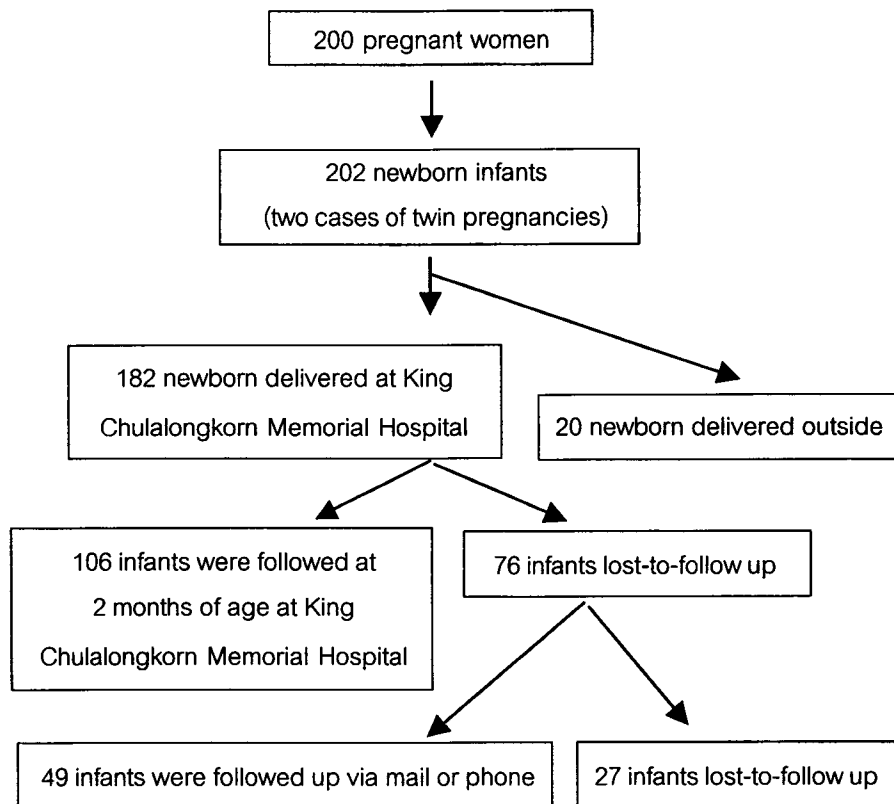


Figure 2. Illustration of newborn follow-up.

Bangkok, by using DNA probe, was 9.2%. They also found that the prevalence of *Chlamydia trachomatis* in HIV-seropositive pregnant women was higher than that in HIV-seronegative pregnant women.

In this study, the prevalence rate of *Chlamydia trachomatis*, by using PCR method, in pregnant women was 10% (95% CI; 5.8%, 14.2%) which was comparable with previous studies.

Marrazzo *et al.*⁽⁹⁾ used cervical findings to predict chlamydial infection among women attending sexually transmitted diseases (STD) clinic and found that endo-cervical mucopus, induced endocervical bleeding and inflammation on cervical gram stain were associated with the infection.

Many studies supported that clinical cervicitis (either white blood cell more than 10 per high power field or the presence of mucopus) was

associated with *Chlamydia trachomatis* infection among non-pregnant women.⁽¹⁰⁻¹²⁾

In contrast, Germain *et al.*⁽¹³⁾ performed by using algorithm for diagnosing chlamydial/gonococcal infection among female sex workers. The screening criteria consisted of endocervical mucopus, the presence of yellow swab and more than 10 polymorphonuclear cells per high power field on vaginal smear. The results were unsatisfied with low positive predictive value and low sensitivity.

Rugpao *et al.*⁽¹⁴⁾ evaluated the risk factors associated with *Chlamydia trachomatis* among gynecologic out patients who had symptoms and/or signs of lower genital tract infection in Thailand. They found that factors associated with *Chlamydia trachomatis* were *Neisseria gonorrhoea* cervicitis, among patients whose age was less than 25 years,

Table 1. The clinical characteristics between positive group and negative group (total number of cases was 200 cases).

Characteristics	Positive-chlamydial result (cases)	Negative-chlamydial result (cases)	P value
Excess leukorrhea	3	20	0.71
Endocervical mucopus	3	30	0.80
Induced endo-cervical bleeding	4	21	0.29
Excessive WBCs in vaginal smear	4	26	0.51
Either one characteristic	10	70	0.34

Table 2. Sensitivity, specificity, positive predictive value of characteristics independently predictive of chlamydial cervical infection.

Characteristics	Sensitivity	Specificity	Positive predictive value	Negative predictive value
Excessive leukorrhea	15.0 (10.1, 20.0)	88.9 (84.5, 93.2)	13.0 (8.4, 17.7)	90.4 (86.3, 94.5)
Endocervical mucopus	15.0 (10.1, 19.9)	83.3 (78.2, 88.5)	9.1 (5.1, 13.1)	89.8 (85.6, 94.0)
Induced endo- cervical bleeding	20.0 (14.5, 25.5)	88.3 (83.9, 92.8)	16.0 (10.9, 21.1)	90.9 (86.9, 94.9)
Excessive WBCs in vaginal smear	20.0 (14.5, 25.5)	85.6 (80.7, 90.4)	13.3 (8.6, 18.0)	90.6 (86.5, 94.6)
Either one characteristic	50.0 (43.1, 56.9)	61.1 (54.4, 67.9)	12.5 (7.9, 17.1)	91.7 (87.8, 95.5)

Gardnerella vaginalis vaginitis and purulent vaginal discharge.

While clinical characteristics seem to be beneficial for women, mostly attending STD clinic, the value of screening among pregnant women need evaluation. Braddick *et al.* ⁽¹⁵⁾ demonstrated that the presence of either endocervical mucopus or induced endocervical bleeding was associated with *Chlamydia trachomatis* infection among pregnant women.

Moreover, they also found that behavioral characteristics, having more than one sexual partner during pregnancy, improved sensitivity and specificity of detection.

In Thailand, Chaisilwattana *et al.* ⁽⁶⁾ conducted a prospective study in HIV-seropositive and HIV-seronegative pregnant women during their mid-pregnancy period. In their study, they also evaluated the prevalence and risk factors associated with

Chlamydia trachomatis cervicitis in both groups. The study showed different factors associated with *Chlamydia trachomatis* in each group. Among HIV-seropositive pregnant women, the young age and primigravids were associated with higher prevalence of *Chlamydia trachomatis* infection. Meanwhile, history of multiple sex partners was associated with higher prevalence of *Chlamydia trachomatis* infection among HIV-seronegative women.

However, Kilmarx *et al.* ⁽⁸⁾ performed a cross sectional study in Chiang Rai and Bangkok provinces of Thailand and demonstrated that *Chlamydia trachomatis* infection was associated with young age and higher gestational age at first antenatal clinic visit. In our study, we aimed to evaluate the clinical characteristics involving cervicitis. However, we could not show any significant difference of the clinical characteristics between positive group and negative group for Chlamydia PCR.

Furthermore, we here illustrate that our screening criteria have low sensitivity and positive predictive value. In our population, these characteristics could not serve as predictive criteria for diagnosing *Chlamydia trachomatis* infection in pregnancy. Adding behavioral characteristics may be of a little benefit in our situation because almost all of Thai pregnant women had only one sexual partner during their pregnancy. By contrast, our study showed that these clinical characteristics posed high specificity and high negative predictive value for chlamydial cervical infection.

However, the value of particular characteristics in predicting chlamydial infection is likely to vary widely from one society to the other. Therefore the predictive criteria may be useful in another

population, depend on the prevalence of chlamydial infection, the variation in clinical assessment and patient characteristics.

In conclusion, the simple screening characteristics for infection caused by *Chlamydia trachomatis* among pregnant women achieve high specificity but low sensitivity and positive predictive value. As screening criteria, these characteristics could not be implicated in our population. The effectiveness of the characteristic for screening purpose among pregnant women in other parts remains to be evaluated. An effective screening leads to identify patients who are at risk and prompt treatment for preventing maternal and neonatal complications. Therefore, efforts should be made to develop cheap, simple and reliable screening test in the low-resource situation.

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