

Towards developing a diagnostic algorithm for *Chlamydia trachomatis* and *Neisseria gonorrhoeae* cervicitis in pregnancy

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Abstract

C trachomatis and *N gonorrhoeae* are major causes of maternal and neonatal morbidity and mortality in developing countries. To identify characteristics predictive of cervical infection, we examined pregnant women attending an antenatal clinic in Nairobi, Kenya. *C trachomatis* was isolated from 14/178 (8%), and *N gonorrhoeae* from 17 (10%); cervical infection with either pathogen was present in 28 (16%). Two characteristics were independently predictive of cervical infection by logistic regression analysis; the presence of either endocervical mucopus or induced endocervical bleeding, relative risk 4.2 (95% confidence interval (CI) 2.2 to 8.0) and having more than one sexual partner during pregnancy, relative risk 3.3 (95% CI 1.4 to 7.6). A screening programme for cervical infection which tested women with one or both risk markers would have a sensitivity of 68% (95% CI 51 to 85%) and a positive predictive value of 0.35 (95% CI 0.22 to 0.47). In countries where resources are limited, diagnostic algorithms incorporating clinical signs and behavioural characteristics may be useful in identifying pregnant women at high risk of cervical infection.

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Introduction

Sexually transmitted diseases (STDs) are a global problem, yet many countries lack the resources for comprehensive control programmes and are limited to treating symptomatic patients. In pregnancy *C trachomatis* and *N gonorrhoeae* may cause a wide range of serious complications, which include post-abort sepsis, premature delivery, and post-partum endometritis, ophthalmia neonatorum and neonatal pneumonia.¹⁻⁷

Currently diagnosis depends on sophisticated laboratory techniques, and the establishment of a network of specialised clinics is an unrealistic goal in many parts of the world. Simple, inexpensive, and rapid diagnostic techniques are needed at the primary health care level to identify high risk patients for treatment or further investigation.^{4,8-9} We have examined pregnant women and tried to identify demographic, behavioural and clinical characteristics predictive of cervical infection with *C trachomatis* and *N gonorrhoeae*.

Methods

All women attending an ante-natal clinic in a lower socio-economic district of Nairobi were informed about the study and invited to participate. Women giving verbal informed consent were enrolled into the study. A demographic and pregnancy history was taken and a genital examination was performed by one examiner using pre-defined criteria. Vaginal discharge was assessed for colour: clear/white/yellow-green, consistency: normal/frothy/curdy, odour normal/malodorous, and quantity: scanty/normal/profuse (scanty = dry vagina, profuse = discharge visible at introitus prior to speculum exam).

The cervix was cleaned with cotton wool and then examined for the presence of ectopy and ulcers. Cervical swabs were taken for *N gonorrhoeae* and *C trachomatis*. The first swab was assessed for colour of endocervical secretions: clear/opaque/yellow-green (yellow-green endocervical secretions were defined as mucopus), and for induced endocervical bleeding.

Specimens for *N gonorrhoeae* were immediately inoculated on modified Thayer-Martin media and

Table 1 Relationship of demographic and behavioural characteristics, symptoms, and signs to cervical infection

Variable	Cervical Infection				p
	present (n = 28)		absent (n = 150)		
Mean Age (SD) in years	23.6	(5.3)	23.4	(5.4)	NS
Unmarried	14/27	(52%)	38/145	(26%)	< 0.02
> 1 Sexual Partner during Pregnancy	5/28	(18%)	6/150	(4%)	< 0.02
Previous STD	3/28	(11%)	21/150	(14%)	NS
Vaginal Discharge	8/28	(29%)	43/150	(29%)	NS
Dysuria	3/28	(11%)	20/150	(13%)	NS
Abdominal Pain	11/28	(39%)	65/150	(43%)	NS
Frothy Vaginal Discharge	10/28	(36%)	20/150	(13%)	< 0.01
Profuse Vaginal Discharge	10/28	(36%)	38/150	(25%)	NS
Yellow/Green Vaginal Discharge	6/28	(21%)	16/150	(11%)	NS
Induced Endocervical Bleeding	12/28	(43%)	27/150	(18%)	< 0.01
Endocervical Mucopus*	5/20	(25%)	10/139	(7%)	< 0.05
Clinical Cervicitis†	17/28	(61%)	31/150	(21%)	< 0.0001

SD denotes standard deviation.

*In 19 women endocervical secretions were obscured by induced endocervical bleeding.

†Clinical cervicitis was defined as the presence of either endocervical mucopus or induced endocervical bleeding.

incubated in candle jars at $37 \pm 2^\circ\text{C}$ within 4 hours of collection. Specimens for *C trachomatis* were placed in two sucrose phosphate medium and transported on wet ice, then stored at -70°C until cultured on cyclohexamide treated McCoy cells.

Women were informed of their results and if necessary treated with an appropriate antibiotic.

Data were analysed with SPSS/PC+ and Glim computer programmes, statistical methods used were the Chi squared test with Yates' correction, Fishers' exact test and the *t* test. Logistic regression analysis was used to identify clinical signs independently associated with cervical infection.

Ethical approval was obtained from the Kenyatta National Hospital Ethics Committee.

Results

One hundred and seventy eight pregnant women were enrolled in the study during 1987. Fifty three (30%) were primiparous, and 40 (22%) grand multipara. Most, 146 (82%), were in the third trimester and only two (1%) in the first trimester of pregnancy. Endocervical cultures for *C trachomatis* were positive in 14 (8%) of 178 women, and for *N gonorrhoeae* in 17 (10%), of which seven (41%) produced penicillinase. Twenty eight women (16%) had cervical infection with either pathogen, three women (1.7%) had dual infection.

Table 1 shows demographic and behavioural

characteristics, symptoms, and signs compared with cervical infection. Features which were significantly associated with cervical infection were unmarried status (single, widowed or divorced), more than one sexual partner during pregnancy, a frothy vaginal discharge, induced bleeding and endocervical mucopus. In 19 women endocervical secretions were obscured by induced endocervical bleeding. If either endocervical mucopus or induced endocervical bleeding was observed "clinical cervicitis" was deemed to be present. Clinical cervicitis was more strongly associated with cervical infection than either endocervical mucopus or induced endocervical bleeding alone. Clinical cervicitis was present in 17 (61%) of 28 women with cervical infection versus 31 (21%) of 150, $p < 0.0001$. Symptoms of vaginal discharge, dysuria or abdominal pain were not associated with cervical infection.

PREDICTING CERVICAL INFECTION

Logistic regression analysis was performed to determine which variables were independently associated with cervical infection. The four variables identified on univariate analysis (unmarried status, more than one sexual partner during pregnancy, a frothy vaginal discharge, clinical cervicitis) were used in this analysis. Two variables were independently associated with cervical infection; the presence of clinical cervicitis, relative risk 4.2 (95%

Table 2 Sensitivity, specificity and positive predictive value of variables independently predictive of cervical infection

Variable	Sensitivity*	Specificity*	Positive Predictive Value*
> 1 Sexual Partner during Pregnancy	18% (4-32)	96% (93-99)	0.45 (0.16-0.75)
Clinical Cervicitis†	61% (43-79)	79% (73-86)	0.35 (0.22-0.49)
Clinical Cervicitis and/or > 1 Sexual Partner during Pregnancy	68% (51-85)	93% (88-97)	0.35 (0.22-0.47)
Clinical Cervicitis and > 1 Sexual Partner during Pregnancy	11% (0-22)	86% (81-91)	0.75 (0.33-1.0)

*95% Confidence Intervals are shown in parentheses.

†Clinical cervicitis was defined as the presence of either endocervical mucopus or induced endocervical bleeding.

CI 2.2 to 8.0, $p < 0.0001$) and having more than one sexual partner during pregnancy, relative risk 3.3 (95% CI 1.4 to 7.6, $p < 0.02$). Table 2 shows the sensitivity, specificity, and positive predictive value of these two variables individually and together. A separate analysis was performed to examine clinical signs alone, and clinical cervicitis remained the only clinical sign associated with cervical infection.

Discussion

The prevalence rates of *C trachomatis* (8%) and *N gonorrhoeae* (10%) observed in this study, are comparable with previous reports from developing countries.⁹⁻¹² Pregnant women with cervical *C trachomatis* or *N gonorrhoeae* did not have an increased prevalence of abdominal pain, dysuria or vaginal discharge. Similarly these symptoms were found to be poor predictors of gonorrhoea in a study from Senegal by De Schampeliere and Van De Velden (reported in 13). Therefore if STDs are to be identified in pregnancy, screening is needed.

This study showed clinical cervicitis to be associated with cervical infection in pregnancy. Previous studies of non-pregnant women from developed countries have shown *C trachomatis* to be associated with induced endocervical bleeding,¹⁴ and with endocervical mucopus.¹⁴⁻¹⁸ *N gonorrhoeae* has been associated with endocervical mucopus¹⁸⁻¹⁹ and with cervicitis.²⁰ Since *C trachomatis* and *N gonorrhoeae* are both associated with induced endocervical bleeding and with endocervical mucopus it seems reasonable to group both infections together when trying to identify infected women clinically.

How well does this screening test meet accepted principles?²¹ STDs in pregnancy are undoubtedly an important health problem in developing countries and if diagnosed early may be treated before complications ensue. Speculum examination is likely to be acceptable to most populations but may not always be available. The presence of clinical cervicitis should be easy to recognise; however, the sensitivity and positive predictive value of this sign alone was only moderate. Incorporation of a behavioural characteristic (more than one sexual partner during the current pregnancy) into the diagnostic algorithm improved its sensitivity and specificity. In order to refine this algorithm further, we would recommend that future research inquires about the lifetime total number of partners or number of partners in the last year, presence of genito-urinary symptoms in partners, and perhaps by testing the pH of vaginal discharge.

Whilst clinical cervicitis is likely to be a useful predictor of cervical infection in societies with a similar prevalence of infection, the value of a particular demographic or behavioural characteristic

in a diagnostic algorithm is likely to vary widely from one culture to another. Therefore this algorithm cannot be automatically adopted to identify pregnant women at high risk of cervical infection in other societies. Diagnostic algorithms ought to be developed in the same setting as they will be used, and then evaluated prospectively. Their predictive value will be dependent on the prevalence of cervical infection, the observer, and local factors.

Women identified as being at high risk for cervical infection may either be treated for both *C trachomatis* and *N gonorrhoeae*, or referred for diagnostic tests. The availability of such tests and rates of return for treatment will determine the approach to be used. Although the costs of investigation or mass treatment of high risk women identified by this test are likely to be limited the use of a diagnostic algorithm should reduce the cost of diagnosis and make control of STDs in pregnancy more cost effective. Additionally if the evidence for *C trachomatis* acting as a cofactor for acquisition of infection with human immunodeficiency virus is confirmed²² then the need for STD control campaigns will become more urgent.

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