

ENDOCERVICAL CHLAMYDIAL INFECTION IN FEMALE CONTACTS OF PATIENTS WITH NONGONOCOCCAL URETHRITIS

K B Lim, T Thirumoorthy, C T Lee, E H Sng, T Tan

ABSTRACT

Eighty-five female contacts of patients with nongonococcal urethritis attending Middle Road Hospital were examined. *Chlamydia trachomatis* was isolated from the cervix in 39% of them. Forty-five per cent of the chlamydia-positive patients were asymptomatic and 79% of them showed signs of a cervicitis. None of the patients developed complications. *Neisseria gonorrhoeae* was not isolated from any of the patients.

Clinical markers other than cervicitis are not useful for detecting chlamydial infections in female contacts of NGU. Until such time when cheaper, more convenient and accurate methods of laboratory diagnosis of *C. trachomatis* are put to routine use, it would seem prudent to treat all female contacts of NGU patients after exclusion of other sexually transmitted diseases.

Key words: Nongonococcal urethritis, contacts of, *Chlamydia trachomatis*

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INTRODUCTION

In Singapore, non-specific genital infections (NSGI) are the second most common sexually transmitted disease (STD) after gonorrhoea. National STD returns for 1985 showed that there were 2141 male cases of NSGI or NGU, and only 131 female cases of NSGI; ie. a M:F ratio of 16:1 (1). NSGI is essentially an STD, and a more equitable sex ratio is expected. The present situation, therefore, suggests under-reporting, under-diagnosis and a failure to recall female contacts of patients with NGU for investigations. The sex ratio contrasts strikingly with the M:F ratio of 2.4:1 in gonorrhoea where there is active contact tracing and a gonorrhoea control program among prostitutes since 1976.

Unlike NGU in men, NSGI in the female has no distinctive clinical features or accepted criteria for diagnosis.

Chlamydia trachomatis is accepted as the most common cause of NGU in men, accounting for 30 — 52% of these cases according to studies conducted in western countries (2 — 4). In Singapore, we have isolated *C. trachomatis* from 30% of men with NGU (5) and 50% of men with postgonococcal urethritis (PGU) (6). The incidence of endocervical chlamydial infection in female contacts of NGU, however, has not been determined previously in Singapore. We therefore, conducted a study with this aim in mind.

MATERIALS AND METHODS

From January 1984 to the end of May 1986, eighty-seven female contacts of patients with NGU attending Middle Road Hospital, Singapore were investigated. A detailed history was taken with special reference to genitourinary symptoms and a careful clinical examination was made for cervicitis and pelvic inflammatory disease (PID). Cervicitis was defined clinically as cervical friability (as judged by bleeding on initial swabbing) and/or mucopurulent exudate from the os. Cervical erosions were not considered to indicate a cervicitis unless also accompanied by friability and/or a mucopurulent discharge. Pelvic inflammatory disease (PID) was diagnosed clinically on the basis of three minimum criteria of (1) cervicitis, (2) history of bilateral lower abdominal pain and (3) tenderness on palpation of the cervix or adnexae. Women who had received antibiotics during the preceding week were excluded.

Urethral and endocervical smears were taken for Gram-stained microscopic examination for Gram-negative intracellular diplococci. Specimens taken from the endocervix were also inoculated directly onto modified Thayer Martin medium for the culture of *Neisseria gonorrhoeae*. Likewise, swabs were taken for the culture of *Chlamydia trachomatis* and inoculated into 2SP transport medium containing 5% fetal calf serum, 125 ug/ml of vancomycin, 50 ug/ml of streptomycin and 25 IU/ml of nystatin. Inoculated transport media were transported in ice to the laboratory within 6 hours of collection. Chlamydiae were cultured on cell monolayers consisting of cycloheximide treated McCoy cells. After centrifugation for 1 hour at 3900g, the sample was incubated at 37°C for 48 — 72 hours. The cover slips were then stained with Giemsa stain and examined under darkground microscopy for inclusions. Vaginal swabs were also taken for

K B Lim Medical & Skin Clinic
93 East Coast Road
Singapore 1542

K B Lim
MBBS (Lond), MRCP (UK), AM (S'pore), Dip Ven (Lond)
Dermatologist

National Skin Centre
1 Mandalay Road
Singapore 1130

T Thirumoorthy
MBBS (Mal), MRCP (UK), Dip Ven (Lond), AM (S'pore)
Consultant Dermatologist

C T Lee
MBBS (S'pore), M Med, MRCP (UK), Dip Derm, Dip Ven (Lond)
Senior Registrar

E H Sng
MBBS (S'pore), Dip Bact (Manchester)
Medical Director

T Tan
MBBS (S'pore) FRACP, SM (S'pore)
Medical Director

Correspondence to: Dr K B Lim

Gram-stained microscopy for yeasts, wet-film microscopy for motile trichomonads and for the culture of both organisms in Trichosol broth (BBL, USA), supplemented with 8% horse serum. Samples were incubated for 48 hours and then examined under light microscopy. Trichomonads were recognised by their oval shape, their rapidly moving flagella and jerky movements. Candida species were identified by the presence of budding yeast cells and pseudohyphae. Positive specimens were later inoculated into rice extract and incubated for 48 hours. Candida albicans was identified on finding filamentous outgrowths (pseudo-germ tubes) radiating from the previously rounded or oval yeast cells. The culture and identification of N. gonorrhoeae have been previously described (7).

Statistical analysis of the data was performed using the Student's T-test, chi-square test with Yate's correction and the Fisher's exact probability test, where appropriate.

RESULTS

Two cases were excluded from analysis because cultures for C. trachomatis were contaminated. There remained therefore, 85 cases for evaluation. Chlamydia trachomatis was recovered from the cervixes of 33 (39%) of the 85 women examined. The isolation of C. trachomatis from the patients with genitourinary infections are shown in Table I. There was no significant difference in the isolation rate of C. trachomatis from patients with these specific infections compared to those without. Neisseria gonorrhoeae was not isolated from a single patient.

TABLE I
ISOLATION OF C. TRACHOMATIS FROM
WOMEN WITH GENITOURINARY INFECTIONS

Condition	C. trachomatis infected women/total (%)	P-value
Candidiasis		
Present	11/39 (28)	> 0.05
Absent	22/46 (48)	
Trichomoniasis		
Present	2/3 (67)	> 0.05
Absent	31/82 (38)	
Gonorrhoea		
Present	0/0	—
Absent	33/85 (39)	
Warts		
Present	1/1 (100)	> 0.05
Absent	32/84 (38)	

The age range of our patients was 17 – 38 years (mean 27.0 + 4.4). In the chlamydia-positive women, the mean age was 22.8 years compared with 27.6 years for the chlamydia-negative group ($p > 0.05$).

Fifty-one women were married/divorced or separated and 34 were single. Chlamydia trachomatis was recovered from 19 (37%) of the former group and 14 (41%) of the latter (chi-square = 0.02; $p > 0.05$).

Three women gave a past history of treatment for gonorrhoea, five gave a history of treatment for non-specific genital infection and one gave a history of treatment for both conditions. Thus nine patients gave a history of treatment for gonorrhoea and/or NSGI. Chlamydia trachomatis was isolated from 3 (33%) of these nine women and from 30 (39%) of the 76 patients without such a history ($p > 0.05$).

Fifteen (45%) of the chlamydia-positive women were totally asymptomatic. The results of chlamydial culture in

relation to symptoms are shown in Table II. No particular symptom was significantly associated with chlamydial infection. Twenty-six (79%) of the chlamydia positive women had signs of a cervicitis. Cervicitis was the only clinical sign significantly correlated with chlamydial infection ($p < 0.05$). None of the 3 patients complaining of lower abdominal pain were thought to have PID on clinical examination.

TABLE II
ISOLATION OF C. TRACHOMATIS IN
RELATION TO SYMPTOMS AND SIGNS

Symptom/sign	C. trachomatis infected women/total (%)	P-value
History of vaginal discharge		
Present	15/44 (36)	> 0.05
Absent	18/43 (42)	
Pruritus vulvae		
Present	3/9 (33)	> 0.05
Absent	30/76 (39)	
Dysuria		
Present	2/9 (22)	> 0.05
Absent	31/76 (41)	
History of bilateral lower abdominal pain		
Present	2/3 (67)	> 0.05
Absent	31/82 (38)	
Cervicitis		
Present	26/44 (59)	< 0.05
Absent	7/41 (17)	

DISCUSSION

Our chlamydial isolation rate of 39% from female contacts of NGU is comparable to the 30 – 42% isolation rates reported from western countries (2, 4, 8 – 10). Fifteen (55%) of the 33 chlamydia-positive women were symptomatic. However, no particular symptom was significantly associated with chlamydial infection. The lack of characteristic symptoms for chlamydial infection makes suspicion of disease in women difficult. The only clinical sign significantly associated with chlamydial infection was cervicitis.

The isolation of C. trachomatis from 39% of the women studied indicates that these women are at high risk for chlamydial infection. Eradication of C. trachomatis in these women is important to prevent the complications and reinfection between partners after treatment. It is noteworthy that one study conducted on women with PID in Singapore isolated C. trachomatis from 14% and N. gonorrhoeae from 8% of the patients (11).

Screening of all female contacts of NGU for chlamydial infection by tissue culture is expensive and laborious. Moreover, a single specimen tissue culture has an estimated sensitivity of 70 – 80% in women only (12). It should also be remembered that C. trachomatis can be isolated from the urethras of some 4 – 25% of women with negative cervical cultures (13 – 15). In order to detect the majority of infected women, it would be necessary to sample both the urethra and cervix. This would double the cost of screening. Direct-smear antigen detection by immunofluorescence (16) or enzyme linked immunosorbent assay (17) are possible alternatives, but the cost effectiveness of these methods needs to be evaluated.

Selective treatment of patients with cervicitis will result in those infected but with clinically normal cervixes not receiving treatment. On this basis, 7 (21%) of the 33 infected women in this study would not be treated. This cannot be justified knowing the risks of complications such as PID and infertility. It would be prudent therefore, to treat all female contacts of patients with NGU routinely after exclusion of other STD, with tetracyclines and erythromycin. There will be overtreatment and therefore the risk of side effects. However, side effects associated with tetracyclines and erythromycin are on the whole mild and generally believed to be less serious than the complications resulting from non-treatment of an infected person.

Therefore, until cheaper, more convenient and accurate methods of laboratory diagnosis became available for routine use, this and most other STD treatment centres have advocated routine treatment of all female contacts of patients with NGU.

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REFERENCES

1. National disease returns to Middle Road Hospital, 1985.
2. Holmes KK, Handsfield H, Wang SP, Wentworth BB, Turck M, Anderson JB, Alexander ER: Etiology of nongonococcal urethritis. *N Engl J Med* 1975; 292: 1199-206.
3. Alani MD, Darougar S, Burns DC MacD, Thin RN, Dunn H: Isolation of *Chlamydia trachomatis* from the male urethra. *Br J Vener Dis* 1977; 53: 88-92.
4. Paavonen J, Kousa M, Saikku P, Vesterinen E, Jansson E, Lassus A: Examination of men with non-gonococcal urethritis and their sexual partners for *C. trachomatis* and *Ureaplasma urealyticum*. *Sex Transm Dis* 1978; 5: 93-6.
5. Lim KB, Lee CT, Thirumoorthy T, Arora PN, Tan T, Sng EH: The microbiology of nongonococcal urethritis (NGU) in Singapore. *Ann Acad Med Singapore* 1985; 14: 686-8.
6. Lee CT, Thirumoorthy T, Lim KB, Sng EH, Tan T: Norfloxacin in the treatment of uncomplicated gonorrhoea in Singapore males. *JAMA (Southeast Asian Edition)* 1986; Suppl 2: 42-4.
7. Lim KB, Thirumoorthy T, Lee CT, Tham SN, Sng EH, Tan T: Single dose cefoxitin in treating uncomplicated gonorrhoeae caused by penicillinase producing *Neisseria gonorrhoeae* (PPNG) and non-PPNG strains. *Br J Vener Dis* 1986; 62: 224-7.
8. Nayyar KC, O'Neill JJ, Hambling WH, Waugh MA: Isolation of *C. trachomatis* from women attending a clinic for sexually transmitted diseases. *Br J Vener Dis* 1976; 52: 396-8.
9. Tait IA, Rees E, Hobson D, Byng RE, Tweedie MCK: Chlamydial infection of the cervix in contacts of men with nongonococcal-urethritis. *Br J Vener Dis* 1980; 56: 37-45.
10. Terho P: *Chlamydia trachomatis* infection in non-specific urethritis. *Br J Vener Dis* 1978; 54: 251-6.
11. Chaudhuri P: Benjamin Sheares memorial lecture, 1984: A prospective study of *Neisseria gonorrhoeae* and *Chlamydia trachomatis* in a non-prostitute population and their etiologic role in pelvic inflammatory disease in Singapore. *Singapore J Obstet Gynaecol* 1985; 16: 16-22.
12. Schachter J: Biology of *Chlamydia trachomatis*. In: Holmes K K, Mardh P A, Sparling P F, Weisner P J (eds). *Sexually transmitted diseases*. New York: McGraw-Hill Book Company, 1984: 243-57.
13. Bradley MG, Hobson D, Lee N, Tait IA, Rees E: Chlamydial infections of the urethra in women. *Genitourin Med* 1985; 61:371-5.
14. Woolfit JMG, Watt L: Chlamydial infection of the urogenital tract in promiscuous and non-promiscuous women. *Br J Vener Dis* 1977; 53:93-5.
15. Paavonen J: *Chlamydia trachomatis*-induced urethritis in female partners of men with nongonococcal urethritis. *Sex Transm Dis* 1979; 6: 69-71.
16. Thomas BJ, Evans RT, Hawkins DA, Taylor-Robinson D: Sensitivity of detecting *Chlamydia trachomatis* elementary bodies in smears by use of a fluorescein labelled monoclonal antibody: comparison with conventional chlamydial isolation. *J Clin Pathol* 1984; 37: 812-6.
17. Howard LV, Coleman PF, England BJ, Herrmann JE: Evaluation of *Chlamydiazyme* for the detection of genital infections caused by *Chlamydia trachomatis*. *J Clin Microbiol* 1986; 23: 329-32.