Comparison of clinical and epidemiological characteristics of pelvic inflammatory disease classified by endocervical cultures of *Neisseria gonorrhoeae* and *Chlamydia trachomatis*

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SUMMARY We compared the clinical and epidemiological characteristics of 89 women with pelvic inflammatory disease (PID) seen at a clinic for sexually transmitted diseases during 1982 and 1983. Patients were classified into four groups by having endocervical cultures positive for *Neisseria gonorrhoeae* only (24), *Chlamydia trachomatis* only (16), both organisms (14), or neither organism (35). More women with cultures positive for *N gonorrhoeae* were black ($p < 0.005$), had a sexual partner with gonorrhoea ($p < 0.005$), and had a purulent vaginal discharge ($p < 0.05$). No other significant differences were found between groups regarding age, exposure to a sexual partner with non-gonococcal urethritis, history of trichomoniasis, parity, use of antibiotics, contraceptive history, duration of abdominal pain, relation of pain to the phase of the menstrual cycle, abdominal rebound tenderness, reproductive tract signs, or febrility.

In women presenting to outpatient clinics, PID tends to be mild and the diagnosis unreliable. Though *C trachomatis* is emerging as an important aetiological agent, we found no clinical indicators that could distinguish chlamydial from gonococcal PID.

Introduction

We previously compared the clinical and epidemiological characteristics of gonococcal and non-gonococcal pelvic inflammatory disease (PID) as seen in a clinic for sexually transmitted diseases (STD) during 1978 and 1979.¹ At that time we were unable to undertake routine cultures for *Chlamydia trachomatis*. Because of increasing evidence implicating chlamydiae as a cause of PID as well as a broad range of other sexually transmitted infections,^{2,3} our clinic began performing chlamydial cultures on a

limited basis in 1981. Since 1981 we have obtained endocervical specimens for cultures for *C trachomatis* from all women suspected of having PID.

In our experience, women who present to STD clinics with abdominal pain tend to have rather mild pelvic symptoms and signs, and the diagnosis of salpingitis is often unreliable.¹ Verification by laparoscopy is seldom possible or practical. The availability of endocervical chlamydial cultures does not resolve this dilemma, but it does provide the opportunity to classify and contrast further women with a clinical diagnosis of PID based on culture results. In the study published here we compared the clinical and epidemiological characteristics of PID in women seen at the Denver Metro Health Clinic whose endocervical cultures were positive for *Neisseria gonorrhoeae* only, *C trachomatis* only, both organisms, or neither organism.

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Accepted for publication 15 November 1985

Patients and methods

The Denver Metro Health Clinic provides diagnostic and treatment services for STD on request to residents of the Denver metropolitan area. Services are available seven hours each weekday and are free and confidential. The clinic records about 23 000 patient visits a year and diagnoses and treats more than 60% of cases of gonorrhoea reported from the city and county of Denver. The population of the clinic is about 60% white, 20% black, and 17% hispanic. Other ethnic groups comprise less than 3%. A standardised form was used to collect extensive data for each woman making an initial visit to the clinic.

We conducted a retrospective chart review of all women diagnosed as having PID at the Denver Metro Health Clinic during a two year period from 1 January 1982 to 31 December 1983. PID was defined as: (1) abdominal pain in association with at least one reproductive tract sign including tenderness on cervical movement, adnexal tenderness, or an adnexal mass; or (2) two or more reproductive tract signs. All women suspected of having PID had two endocervical specimens taken for the culture for *N gonorrhoeae*, which were processed as described previously.¹ In addition, two endocervical specimens for the culture of *C trachomatis* were obtained using sterile, cotton tipped applicators (Abco, Milwaukee, Wisconsin, USA). The specimens were inoculated into 3.7 ml (1 dram) vials containing glass beads and 1 ml of 2 SP transport medium (0.2 ml/l sucrose, 0.02 ml/l phosphate, 25 mg/l nystatin, 10 mg/l gentamicin; M A Bioproducts, Walkersville, Maryland, USA) and immediately refrigerated. If specimens could not be inoculated into cells within 24 hours they were stored at -70°C, then rapidly thawed and inoculated when cells became available. Specimens were vortexed to break up cells and enhance suspensions, and 0.2 ml aliquots were inoculated into each of three 3.7 ml glass vials containing a 12 mm coverlip coated with a confluent layer of McCoy cells (M A Bioproducts). Vials were centrifuged at 3000 x g for one hour at 25-35°C, the inoculum discarded, and the monolayer rinsed once with Eagle's minimum essential medium containing 10% fetal calf serum, 5.4 mg/l dextrose, 20 mmol/l HEPES, 0.21 mg/l sodium bicarbonate, 10 mg/l gentamicin, and 0.5 mg/l cyclohexamide (M A Bioproducts). After the monolayers had been rinsed 1 ml of medium was added to each vial and the cultures incubated at 35°C. After being incubated for 48 hours monolayers from two vials were stained with iodine. The monolayer from the third vial was stained after 72 hours. Coverslips were examined under a microscope at 60 x and 40 x magnifications, and chlamydial inclusions were counted.

Patients were divided into four groups based on culture results: those yielding *N gonorrhoeae* only,

yielding *C trachomatis* only, yielding both organisms, or yielding neither organism. Clinical and epidemiological characteristics that were compared included: age; race; sexual contact with men with gonorrhoea or non-gonococcal urethritis; history and description of vaginal discharge, dysuria, or abdominal pain; number of days since last sexual contact and number of different contacts in the previous 30 days; contraceptive history; number of pregnancies; recent menstrual history; history of STDs; use of antibiotics in the previous 30 days; results of endocervical cultures; and results of a complete pelvic examination.

Statistical analysis used Yate's correction of the χ^2 test, and the normal deviate test.

Results

Of the 89 women clinically diagnosed as having PID, *N gonorrhoeae* only was isolated from the cervix of 24 (27%), *C trachomatis* only from 16 (18%), both organisms from 14 (16%), and neither organism from 35 (39%). Table I compares the epidemiological characteristics of these four groups of women. Age and recent sexual history were similar in each group. More black than white or hispanic women yielded positive endocervical cultures for *N gonorrhoeae* ($p < 0.005$). More women yielding chlamydiae only or both organisms than women in the other two groups had had recent sexual contact with a partner with gonorrhoea ($p < 0.005$). More women yielding neither organism than in the other three groups reported previous gonococcal infection, though this difference was not significant. No significant differences were seen between groups regarding exposure to a partner with non-gonococcal urethritis, history of trichomoniasis, parity, use of antibiotics, or contraceptive methods used. Furthermore, table II shows that no significant differences were found between groups regarding duration of abdominal pain, relation of pain to phases of the menstrual cycle, abdominal rebound tenderness, or reproductive tract signs. More women yielding *N gonorrhoeae* than in the other three groups had purulent endocervical discharge ($p < 0.05$). Only one of 84 women tested had a temperature higher than 38°C.

Discussion

Though the rates of gonococcal PID seem to be declining in some populations, rates of chlamydial PID may be increasing.⁴ Recent reports have implicated *C trachomatis* as the causative agent in as many as 20-60% of patients.⁵⁻⁶ Whereas gonococcal PID is seen commonly in highly symptomatic women presenting to emergency rooms or gynecological inpatient services, chlamydial disease has been characterised as having a relatively mild and protracted course, and has a greater

TABLE I Comparison of epidemiological characteristics of 89 women with pelvic inflammatory disease (PID), classified by endocervical culture results for *Neisseria gonorrhoeae* (Ng) and *Chlamydia trachomatis* (Ct), attending Denver Metro Health Clinic, 1982-3. Figures are numbers (%) of women unless shown otherwise.

Epidemiological characteristics	Ng positive Ct negative (n = 24)	Ng negative Ct positive (n = 16)	Ng negative Ct positive (n = 14)	Ng negative Ct negative (n = 35)
Median (range) age (years)	25 (19-42)	21 (16-29)	24 (19-44)	24 (16-45)
Race:				
Black	10 (41.7)	6 (37.5)	4 (28.6)	8 (22.9)
White	11 (45.8)	7 (43.8)	6 (42.9)	21 (60.0)
Hispanic	3 (12.5)	3 (18.8)	4 (28.6)	6 (17.1)
Mean (range) days since last sexual contact	4 (1-80)	4 (1-14)	6 (1-30)	4 (1-30)
Mean (range) No of sexual contacts in previous 30 days	1 (0-3)	1 (1-2)	1 (1-2)	1 (1-180)
Contact of gonorrhoea	8 (33.3)	0 (0.0)	4 (28.6)	2 (5.7)
Contact of non-gonococcal urethritis	1 (4.2)	2 (12.5)	1 (7.1)	3 (8.6)
History of gonorrhoea	9 (37.5)	6 (37.5)	5 (35.7)	22 (62.9)
History of trichomoniasis	7 (29.2)	4 (25.0)	5 (35.7)	12 (34.3)
History of pregnancy	20 (83.3)	12 (75.0)	11 (78.6)	27 (77.1)
Use of antibiotics within 30 days	4 (16.7)	1 (6.3)	0 (0.0)	4 (11.4)
Contraceptive use:				
Pill	4 (16.7)	4 (25.0)	2 (14.3)	6 (17.1)
Intrauterine device	3 (12.5)	1 (6.3)	0 (0.0)	4 (11.4)
Other	5 (20.8)	2 (12.5)	3 (21.4)	10 (28.6)
None	12 (50.0)	9 (56.3)	9 (64.3)	15 (42.9)

TABLE II Comparison of clinical symptoms and signs in 89 women with pelvic inflammatory disease (PID), classified by endocervical culture results for *Neisseria gonorrhoeae* (Ng) and *Chlamydia trachomatis* (Ct), attending Denver Metro Health Clinic, 1982-3. Figures are numbers (%) of women.

Clinical symptom or sign	Ng positive Ct negative (n = 24)	Ng negative Ct positive (n = 16)	Ng positive Ct positive (n = 14)	Ng negative Ct negative (n = 35)
Duration of abdominal pain* (days):				
≤ 14	18 (75.0)	14 (87.5)	14 (100.0)	27 (77.1)
> 14	5 (20.8)	1 (6.3)	0 (0.0)	4 (11.4)
Day of menstrual cycle pain began*:				
0 - 7	5 (20.8)	1 (6.3)	3 (21.4)	5 (14.3)
8 - 14	5 (20.8)	5 (31.3)	3 (21.4)	8 (22.9)
15 - 21	3 (12.5)	0 (0.0)	2 (14.3)	3 (8.6)
22 - 31	1 (4.2)	2 (12.5)	3 (21.4)	3 (8.6)
Before last menstrual period	9 (37.5)	7 (43.8)	3 (21.4)	12 (34.3)
Abdominal rebound tenderness	4 (16.7)	3 (18.8)	4 (28.6)	7 (20.0)
Cervical motion tenderness	15 (62.5)	10 (62.5)	10 (71.4)	16 (45.7)
Adnexal tenderness	20 (83.3)	14 (87.5)	9 (64.3)	32 (91.4)
Adnexal mass	3 (12.5)	1 (6.3)	0 (0.0)	2 (5.7)
Vaginal discharge:				
None/normal/menses	8 (33.3)	5 (31.3)	5 (35.7)	12 (34.3)
Excessive white	8 (33.3)	6 (39.5)	3 (21.4)	17 (48.6)
Purulent vaginal	1 (4.2)	2 (12.5)	2 (14.3)	4 (11.4)
Purulent endocervical	7 (29.2)	3 (18.7)	4 (28.6)	2 (5.7)

*Not all women experienced abdominal pain and numbers in each category may therefore not total "n".

incidence of serious long term medical sequelae. As most women with PID who seek treatment present to outpatient clinics, where sophisticated diagnostic and culture techniques may not be available, we thought it worthwhile to evaluate the clinical presentation of PID in women attending our STD clinic, who were classified according to endocervical culture results for *N gonorrhoeae* and *C trachomatis*.

Of 89 women identified as having PID, 38 (42.7%) yielded *N gonorrhoeae* from the endocervix and 30 (33.7%) yielded *C trachomatis*. These data compare well with published reports from Scandinavia where endocervical cultures were positive for *N gonorrhoeae* in 10-30% and for *C trachomatis* in 20-60% of patients with acute salpingitis^{5 6} and with American reports of 10-70% of patients yielding *N gonorrhoeae* from the cervix and over 20% yielding *C trachomatis*.^{7 9} In general, studies from the United States of America have shown higher rates of gonococcal and lower rates of chlamydial PID than those from Sweden, Finland, and Norway. Differences in patient populations, isolation techniques, and severity of cases, however, make direct comparisons impossible. We know of no reports that have evaluated specifically the relation of these organisms to the clinical and epidemiological characteristics of women outpatients with suspected PID.

In our clinic the proportion of all patients with PID associated with gonorrhoea has declined from 61.4% in 1978/9 to 42.7% in 1982/3, which paralleled a decrease in the overall prevalence of gonorrhoea in women attending the clinic from 19% to 11.4%. At the same time the proportion of non-gonococcal PID has risen from 38% to 57.3%. these trends have been observed in other populations⁴ and have been attributed to improved efforts to treat and control gonorrhoea in the absence of similar efforts to treat and control non-gonococcal urethritis and other chlamydial infections. We were unable to lend support to this hypothesis because both the prevalence and incidence of non-gonococcal urethritis in men attending our clinic actually declined appreciably between 1978/9 and 1982/3¹⁰ and because we found no appreciable association between a history of sexual contact with men with non-gonococcal urethritis and a diagnosis of either non-gonococcal or chlamydial PID. Our data probably failed to document the expected associations because most women are unaware that they have been exposed to a man with non-gonococcal urethritis, less than 50% of non-gonococcal urethritis is caused by *C trachomatis*, few endocervical chlamydial infections result in PID, and the clinical diagnosis of PID is not accurate.

We identified several clinical and epidemiological findings that generally agreed with prior studies. Women with gonococcal PID were more likely to be black, to have a recent history of sexual contact with a partner

with gonorrhoea, and to have a purulent endocervical discharge,^{11 12} and women with non-gonococcal PID were more likely to report a history of gonococcal infection¹¹. In contrast with previous studies, and perhaps because of the small numbers in each of our groups, we found no significant differences between groups regarding other clinical signs and symptoms. In particular, we did not find an association between PID and other well established risk factors such as nulliparity and the use of intrauterine devices.^{11 13} Neither could we confirm the reported protective effect of oral contraceptives against gonococcal PID^{11 14} or an increase in incidence of infection with *C trachomatis* in users of oral contraceptives.¹⁵

The difficulty in accurately diagnosing PID without laparoscopy probably further compromised our ability to assess the associations of certain clinical and epidemiological risk factors with endocervical culture results. Serological testing for antibodies against *C trachomatis* might have made these relations clearer, but as with laparoscopy these techniques are not routinely used. Moreover, Ripa and colleagues recently found that measuring chlamydial antibodies in serum was inconclusive in diagnosing current infection.¹⁶ Similar serological testing for gonococcal infection has also been unrewarding.

The study published here documented a strong association between *C trachomatis* and PID in an STD clinic, but also underlined the unreliability of a clinical diagnosis of PID based on mild or equivocal pelvic findings. Many traditional features of PID that have been well described in studies of inpatients are not found in outpatients. As three quarters of all PID is seen in outpatient clinics, however, and as untreated PID can result in chronic pelvic pain, infertility rates of 30% or more, and up to a tenfold increased in ectopic pregnancy,^{14 17} the need for better understanding of this disease is obvious. The role of *C trachomatis* as an aetiological agent is especially important because the organism often produces a mild and indolent infection that is very difficult to diagnose, even though sequelae are similar to those associated with gonococcal PID.

A lack of specificity argues against the use of endocervical cultures for either *N gonorrhoeae* or *C trachomatis* in selecting treatment for a patient suspected of having PID. These organisms often occur together and additional aetiological agents must be considered. Established clinical and epidemiological characteristics of women with PID are not reliable. As recommended by the Centers for Disease Control,¹⁸ optimum treatment should always include antimicrobials with proved efficacy against both *N gonorrhoeae* and *C trachomatis*. Mucopurulent cervicitis, recently described by Brunham *et al* as the ignored counterpart in women of urethritis in men,¹⁹ should also be recognised and treated appropriately to prevent the

development of PID. Finally, aggressive efforts should be made to identify and treat epidemiologically sexual partners of women suspected of having PID.

It may not be possible to generalise results from the present study to other outpatient populations where the prevalence of *C trachomatis* and other STDs may be lower and risk factors may be different. Additional larger studies are needed to clarify further the clinical presentation and optimum management of women presenting to outpatient clinics with PID.

We thank Josephine Ehret for performing chlamydial cultures, the staff of the Denver Metro Health Clinic for collecting data, Katie Andersen and Karen Martinez for secretarial help, and the Division of Sexually Transmitted Diseases, Centers for Disease Control, Atlanta, Georgia, for funding support for chlamydial cultures.

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