Signs and Symptoms of Prevalent and Incident Cases of Gonorrhea and Genital Chlamydial Infection Among Female Prostitutes in Kinshasa, Zaire

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Most studies that have examined the clinical features of gonorrhea and chlamydial infection have been based on prevalent cases (cases of undetermined onset). In our investigation, we compared signs and symptoms of incident (new) cases of these infections with those observed in prevalent cases (involving the same women) that were diagnosed at enrollment in a prospective study of female prostitutes in Kinshasa, Zaire. *Neisseria gonorrhoeae* or *Chlamydia trachomatis* was present at enrollment in 29.2% (225 of 771) of the women in the study. As they were followed during the study, 509 (66.0%) had at least one episode of gonorrhea or chlamydial infection. No symptom was significantly associated with these infections at enrollment or during follow-up. Clinical signs, such as endocervical mucopus ($P < .001$) and vaginal discharge ($P = .001$), were associated with both the prevalent and incident cases. However, none of these signs was simultaneously sensitive and specific for detection of these infections. The frequency of clinical signs was significantly reduced after successful treatment (all P values, $<.05$). This study shows that a syndromic approach to screening for gonococcal and chlamydial infections in female prostitutes is as problematic for acute incident cases as for prevalent cases. Therefore, there is still an urgent need for simple, cheap, reliable tests that could be used in sexually transmitted disease intervention programs in developing countries.

Over the last few years, sexually transmitted diseases (STDs), both ulcerative [1–8] and nonulcerative [1, 2, 4, 8, 9], have been implicated as cofactors in HIV transmission. Because of this epidemiological synergy, STD control activities, including diagnosis and treatment, offer additional strategies for the prevention of AIDS. Moreover, the World Health Organization (WHO) now recommends that STD and AIDS control efforts be combined [10].

In developing countries, it may be particularly difficult to diagnose STDs in women, especially gonococcal and chlamydial infections, since these diseases are often asymptomatic in female subjects. Furthermore, bacterial isolation techniques and immunologic methods are not widely available in resource-poor settings because of their complexity and high costs. Symptoms such as abnormal vaginal discharge and abdominal pain [11, 12] and signs such as cervical ectopy, endocervical mucopus, and cervical friability or erythema [11–19] have been associated with infection by *Neisseria gonorrhoeae* or *Chlamydia trachomatis*. However, we have previously shown that clinical algorithms (similar to those proposed at that time by the WHO [20] and based on symptoms and signs) were insensitive for screening for these diseases in pregnant women and female prostitutes in Zaire [21].

Most studies on gonococcal and chlamydial infections in women have used prevalent cases (cases of undetermined onset). One could argue that a clinical diagnostic approach could be more valid for acute, newly acquired infections (incident cases). Indeed, a previous study in the United States has shown that most cases of gonorrhea in women were diagnosed in emergency services and were symptomatic [22]. Consequently, an improvement in STD clinical services in developing countries might attract women with more recent infections, of which diagnosis could be easier with a syndromic approach.

The objectives of this study were (1) to determine the validity of using signs and symptoms as the basis for diagnosis of incident cases of gonorrhea and chlamydial infection, with use of data from a prospective study of female prostitutes in Kinshasa, Zaire [8, 9], and (2) to compare these signs and symptoms with those observed in prevalent infections in the same women, diagnosed at enrollment in the prospective study [23].

Patients and Methods

Data Collection

The study population has been described extensively elsewhere [8, 9, 23]. In brief, following a cross-sectional study of

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1,233 female prostitutes in Kinshasa, Zaire, 771 of these women were followed prospectively every month for a median duration of 28 months (range; 3–36 months). Of those, 204 were seropositive for HIV-1 at enrollment (median duration of follow-up, 29 months), 70 seroconverted during follow-up (median duration of follow-up, 28 months), and 497 remained HIV-negative throughout the whole study period (median duration of follow-up, 27 months).

At each visit, the women were interviewed regarding the following STD-related complaints: vaginal discharge, lower abdominal pain, and vaginal itching. At physical examination, the following clinical signs were systematically recorded: vaginal discharge, endocervical mucopus, and cervical motion tenderness. Physical examinations were performed by two physicians who were simultaneously trained to apply the same diagnostic criteria. The criteria for clinical signs were as follows. Vaginal discharge was defined by the observation of secretions before insertion of the speculum or in large amount on the lower part of the speculum after its insertion; endocervical mucopus was defined by yellowish or greenish discharge from the cervical os; cervical motion tenderness was defined by pain elicited on mobilization of the cervix during bimanual examination.

Every month, laboratory samples were collected to confirm the presence of STD pathogens. Women who were found to have gonorrhea were systematically treated with a single 500-mg dose of ciprofloxacin, whereas those who had chlamydial infection received doxycycline (100 mg twice daily) for 7 days. No systematic test of cure was done following treatment, but women were scheduled for their regular follow-up visit 1 month later.

Laboratory Procedures

The laboratory procedures used in this study have been previously described [9, 21]. Direct microscopic examination of a vaginal smear was performed by an experienced laboratory technician to detect *Trichomonas vaginalis* and yeasts. Detection of evidence of bacterial vaginosis on this smear was not attempted. Endocervical swab specimens were obtained for the detection of *N. gonorrhoeae* and *C. trachomatis*. Gonococci were isolated on modified Thayer-Martin medium incubated in a candle-extinction jar at 35°C for 24–48 hours. Isolates were identified on the basis of typical colony morphology, oxidase reaction, and sugar-utilization patterns. An enzyme immunoassay was used to detect *C. trachomatis* in cervical specimens. In the cross-sectional study and in the first 6 months of follow-up, the Chlamydiazyme test (Abbott Laboratories, North Chicago, IL) was used. Thereafter, the Microtrak EIA (Syva, Palo Alto, CA) was used.

Data Analysis

Analysis was restricted to the 771 women for whom prospective (follow-up) data were available. Gonorrhea and chlamydial infection were considered together in this analysis because these two conditions have similar clinical signs and symptoms [21]. In addition, the clinical algorithms recommended by the WHO to manage STD syndromes in women propose simultaneous treatment of these two infections [20].

Concerning data from the cross-sectional survey, the prevalence of recorded signs and symptoms was measured according to the presence or absence of either *N. gonorrhoeae* or *C. trachomatis*. Stratification for the presence or absence of vaginitis agents (yeasts or *T. vaginalis*) was also performed. Similar analyses were performed on prospective data. For women who had one episode of gonorrhea or chlamydial infection during follow-up, this episode was selected for analysis; for those who had more than one incident episode, one of these was randomly selected. For women who remained uninfected by the microorganisms, any follow-up visit was randomly selected. Statistical analysis to compare the prevalences of signs and symptoms was performed with the χ^2 test. The odds ratios (ORs) with 95% confidence intervals (CIs) were computed. The Mantel-Haenzel χ^2 test was also used for stratified data.

Sensitivity, specificity, and positive and negative predictive values of the different signs and symptoms were also computed. For the prospective study, we used data from all the visits of the 771 women. Indeed, to proceed with selected visits (an essential strategy to ensure the independence of samples for the measurement of the associations between signs and symptoms and the presence of *N. gonorrhoeae* or *C. trachomatis*) would have led to biases in the estimation of predictive values.

In order to assess if the presence of a given clinical sign or symptom related to an episode of gonococcal or chlamydial infection was predictive of its presence at a later episode of the same disease, additional analyses were performed on two different subsamples of women. The first subsample consisted of women positive for either *N. gonorrhoeae* or *C. trachomatis* in the cross-sectional study and who had at least one episode of infection due to either of these organisms during the prospective (follow-up) study. When two or more incident episodes affected a woman in the prospective study, one of them was randomly selected. We then performed a matched analysis with the McNemar χ^2 test to compare the prevalence of the different signs and symptoms in prevalent and incident cases involving the same women. In addition, women with or without a given sign or symptom in the cross-sectional study were considered as independent samples for the predictive aspect of this analysis. The χ^2 or Fisher's exact test was used to compare the occurrence of signs and symptoms of incident cases with their occurrence in prevalent cases. Similar analyses were performed in a second subsample consisting of women who had at least two incident episodes during the follow-up study. For women who had three or more of these episodes, two of them were chosen randomly.

Finally, to assess if treatment of gonorrhea and chlamydial infection resulted in a decrease in the prevalence of signs and symptoms, we examined data from the visit following an epi-

Table 1. Prevalence of genital symptoms and signs in relation to the presence or absence of cervicitis agents (*N. gonorrhoeae* or *C. trachomatis*) among female prostitutes in Kinshasa, Zaire, participating in both cross-sectional and prospective studies.

	Cross-sectional study participants			Prospective study participants		
	Cervicitis agents?			Cervicitis agents?		
Variable	Yes (%; n = 225)	No (%; n = 546)	OR (95% CI)	Yes (%; n = 509)	No (%; n = 262)	OR (95% CI)
Symptom						
Vaginal discharge	29.3	23.8	1.3 (0.9–1.9)	7.9	6.1	1.3 (0.7–2.5)
Lower abdominal pain	44.4	39.7	1.2 (0.9–1.7)	19.3	16.1	1.2 (0.8–1.9)
Vaginal itching	33.3	31.1	1.1 (0.8–1.5)	11.4	11.0	1.0 (0.6–1.7)
Sign						
Vaginal discharge	60.0	48.9	1.6 (1.1–2.1)*	33.6	22.5	1.7 (1.2–2.5)*
Endocervical mucopus	16.4	2.4	8.0 (4.3–16.6)*	8.8	1.1	8.4 (2.5–22.6)*
Cervical motion tenderness	10.2	10.6	1.0 (0.6–1.6)	7.6	7.3	1.1 (0.6–2.0)

* $P \leq .001$.

sode of these diseases in the prospective study. The proportion of women who did not have an infection at this visit was recorded, and a matched analysis with the McNemar χ^2 test was used to assess the change in the frequency of signs and symptoms following treatment. In addition, the χ^2 and Fisher's exact tests were used to compare the frequency of signs and symptoms observed in the visits following treatment with those seen in women who did not have any episode of gonococcal or chlamydial infection during follow-up.

In all of these analyses, stratification of data according to HIV serological status (seropositives at enrollment, seroconversions, and seronegatives during the entire follow-up) was also performed.

Results

In the cross-sectional study, 177 of the selected 771 women (23.0%) were infected by *N. gonorrhoeae,* 90 (11.7%) were infected by *C. trachomatis,* and 225 (29.2%) had either disease. In the follow-up (prospective) study, 509 women (66.0%) had at least one incident episode of either disease; the corresponding figures for gonorrhea and chlamydial infection were 411 (53.3%) and 341 (44.2%), respectively. Among the 509 women who had at least 1 episode of either disease, the median number of episodes was 2 for gonorrhea (range, 1–11) and 1 for chlamydial infection (range, 1–9). Results of all the analyses reported on below did not differ significantly when analyses were performed separately for these two diseases (data not shown).

Table 1 shows the prevalence of recorded symptoms and signs in relation to the diagnosis of cervicitis (gonorrhea or chlamydial infection) in the cross-sectional and follow-up (prospective) studies. In both the cross-sectional and follow-up study, none of the symptoms was significantly associated with cervical infection by *N. gonorrhoeae* or *C. trachomatis.* With the exception of cervical motion tenderness, all recorded clinical signs were significantly associated with gonococcal or chlamydial infection in both studies (all P values, $\leq$.001). All symptoms were more prevalent in the cross-sectional study than in the prospective study. Clinical signs were also more frequently observed at enrollment than during follow-up, but these differences were less striking than those observed for reported symptoms. However, the odds ratios for each given sign or symptom were similar in both studies.

None of the recorded signs or symptoms was simultaneously sensitive and specific for diagnosis of gonorrhea or chlamydial infection (table 2). However, the presence of endocervical mucopus was highly specific for these diseases and yielded acceptable positive predictive values (75% in prevalent cases and 59% in incident cases).

After stratification for the presence of vaginitis agents, women simultaneously infected by agents of both cervicitis and vaginitis were found to complain more often of vaginal discharge than did other subjects in the cross-sectional study (39.7% vs. 24.0%; P = .003). A similar trend was observed in the prospective study, although it failed to reach statistical significance. Table 3 shows the results of the stratified analysis with regard to clinical signs. With the exception of cervical motion tenderness in the cross-sectional study, all signs were more frequently observed among women infected simultaneously by agents of both cervicitis and vaginitis. However, vaginal discharge (as a clinical sign) and endocervical mucopus remained significantly associated with the presence of cervicitis agents, even after the presence of vaginitis agents was controlled for (all P values, $<$.01; Mantel-Haenzel χ^2 test). It should be noted that vaginal discharge was more strongly associated with yeasts or *T. vaginalis* than it was with *N. gonorrhoeae* or *C. trachomatis.*

Similar results were found concerning signs and symptoms when data were stratified according to HIV serological status (data not shown).

Table 2. Sensitivity (Se), Specificity (Sp), and positive and negative predictive value (PPV and NPV) of genital symptoms and signs for the diagnosis of gonorrhea or chlamydial infection in female prostitutes in Kinshasa, Zaire, participating in both cross-sectional and prospective studies.

Variable	Value (%) for diagnosis in cross-sectional study*				Value (%) for diagnosis in prospective study†			
	Se	Sp	PPV	NPV	Se	Sp	PPV	NPV
Symptom								
Vaginal discharge	29.3	76.2	34.4	71.7	3.9	96.3	15.6	85.0
Lower abdominal pain	44.4	60.3	32.2	72.0	15.6	87.1	17.7	85.3
Vaginal itching	33.3	68.9	31.3	70.9	10.2	90.4	15.8	85.0
Sign								
Vaginal discharge	60.0	51.1	34.3	75.0	31.8	75.4	18.6	86.2
Endocervical mucopus	16.4	97.4	75.5	73.3	6.0	99.3	59.1	85.6
Cervical motion tenderness	10.2	89.4	29.1	70.0	3.1	97.7	19.3	85.0

* Observations regarding 771 women, of whom 225 had gonorrhea or chlamydial infection.

† Observations regarding 13,462 visits from which full information was available (out of a total of 15,124 visits) for the same 771 women in the prospective study; in 2,029 of these visits (15.1%), gonorrhea or chlamydial infection was diagnosed.

In the matched analyses, 186 women with prevalent gonococcal or chlamydial infection had at least one incident episode of either disease during the prospective follow-up, whereas, overall, 320 subjects had at least two incident episodes of these infections in the prospective study. All symptoms were found significantly more often in prevalent cases of gonococcal or chlamydial infection than in incident cases (all P values, $<.001$; McNemar χ^2 test), as would be expected from the results presented in table 1. However, the only clinical sign significantly more frequent in prevalent cases than in incident cases was objective evidence of vaginal discharge ($P < .001$; McNemar χ^2 test). No such differences were observed in comparison of the frequency of signs and symptoms in two different incident episodes.

The presence of lower abdominal pain, vaginal itching, cervical mucopus, or cervical motion tenderness in prevalent cases of gonorrhea or chlamydial infection was significantly associated with the presence of the same signs and symptoms in incident cases involving the same women (table 4). Similarly, when paired episodes of incident infections were considered, significant associations were found for vaginal itching, vaginal discharge (as a clinical sign), and cervical motion tenderness. However, in most instances, the proportion of women in whom a given symptom or sign recurred in a subsequent episode of infection by *N. gonorrhoeae* or *C. trachomatis* was low. One exception to that observation was the recurrence of vaginal discharge (as a clinical sign) in paired episodes of incident infections (nearly 60%); nearly 75% of those without clinically confirmed discharge in the first episode did not have this sign at physical examination during a subsequent episode of gonococcal or chlamydial infection. The results of these analyses were not modified by stratification according to HIV serological status (data not shown).

For 432 of the 509 women with gonorrhea or chlamydial infection in the prospective study, data were available regarding

Table 3. Prevalence of genital clinical signs in relation to the presence or absence of cervicitis and vaginitis agents in female prostitutes in Kinshasa, Zaire, participating in both cross-sectional and follow-up studies.

Cervicitis agents*	Vaginitis agents†	Cross-sectional study				Prospective study			
		No. of subjects‡	% With vaginal discharge§	% With endocervical mucopus§	% With CMT‖	No. of subjects	% With vaginal discharge§	% With endocervical mucopus§	% With CMT‖
Yes	Yes	73	76.7	26.0	13.7	108	54.6	9.3	9.3
Yes	No	147	52.4	11.6	8.8	401	27.9	8.7	7.2
No	Yes	152	62.5	1.3	15.1	36	44.4	5.6	8.3
No	No	375	41.5	2.7	8.9	226	19.0	0.4	7.1

* Either *N. gonorrhoeae* or *C. trachomatis*.

† Either yeasts or *T. vaginalis*.

‡ The numbers in the cross-sectional study do not add up to 771 because of missing data regarding the presence of vaginitis agents.

§ $P < .01$ (Mantel-Haenzel χ^2 test) for comparison of the frequency of each sign according to the presence of cervicitis agents, with the presence of vaginitis agents controlled for.

‖ Cervical motion tenderness.

Table 4. Prevalence of genital symptoms and clinical signs in incident (new) gonococcal and chlamydial infections, in relation to their presence or absence in prevalent (preexistent at enrollment) infections in female prostitutes in Kinshasa, Zaire.

Variable	% (no.) of Women with symptom/sign in the incident episode, among those who:		
	Had same symptom or sign in the prevalent episode	Did not have same symptom or sign in the prevalent episode	*P* value*
Symptom			
Vaginal discharge	10.9 (6/55)	5.3 (7/131)	.210†
Lower abdominal pain	34.1 (30/88)	16.3 (16/98)	.008
Vaginal itching	17.2 (11/64)	7.4 (9/122)	.048†
Clinical sign			
Vaginal discharge	46.5 (53/114)	33.3 (24/72)	.098
Endocervical mucopus	33.3 (10/30)	7.1 (11/156)	<.001†
Cervical motion tenderness	26.3 (5/19)	9.0 (6/167)	.037†

* For comparison of the proportion with symptom/sign in the incident episode in relation to presence or absence of the symptom/sign in the prevalent episode (χ^2 or Fisher's exact test).
† Fisher's exact test.

a subsequent visit 1 month after the selected episode. The proportion who still had either infection at this follow-up visit was 18.3%. This proportion did not vary significantly according to HIV serological status ($P = .51$). Table 5 shows the distribution of clinical signs and symptoms at this follow-up visit. Vaginal discharge (as a clinical sign) was the only variable associated with gonorrhea and chlamydial infection at that time. However, women negative for these infections had significantly less vaginal discharge (both as a symptom and as a clinical sign) and endocervical mucopus than at the previous visit, at which they were found to be infected (all P values, $<.05$; McNemar χ^2 test). In addition, the frequency of symptoms and signs they had on this occasion was comparable to that for the 262 women who never had gonorrhea or chlamydial infection (see table 1), with the exception of endocervical mucopus, which was more prevalent (4.8% vs. 1.1%; $P = .02$, Fisher's exact test) but remained highly specific. In women who were still infected at this visit, the frequency of symptoms and signs was comparable to that observed at the previous visit.

Table 5. Prevalence of genital symptoms and signs, as related to the presence or absence of cervicitis agents (*N. gonorrhoeae* or *C. trachomatis*) at the visit following treatment for gonorrhea or chlamydial infection, among female prostitutes in Kinshasa, Zaire.

Variable	Cervicitis agents present? (% of women with symptom or sign)		
	Yes ($n = 79$)	No ($n = 353$)	OR (95% CI)
Symptom			
Vaginal discharge	6.3	3.4	1.9 (0.6–6.1)
Lower abdominal pain	22.8	16.7	1.5 (0.8–2.8)
Vaginal itching	13.9	11.1	1.3 (0.6–2.8)
Sign			
Vaginal discharge	45.6	27.1	2.3 (1.3–3.8)*
Endocervical mucopus	10.1	4.8	2.2 (0.9–5.7)
Cervical motion tenderness	7.6	5.4	1.4 (0.5–4.0)

* $P = .002$.

Discussion

This study shows that genital symptoms and signs are not more predictive of incident cases of gonococcal or chlamydial infection than they are of prevalent cases.

Indeed, neither prevalent nor incident cases were significantly associated with symptoms, even after stratification for the presence of vaginitis agents. This stratification was incomplete, however, as data on bacterial vaginosis were not available. Because these findings are consistent over the different strata, it is unlikely that the availability of laboratory results regarding bacterial vaginosis would have modified these conclusions. The fact that vaginitis agents were more strongly associated with vaginal discharge than were cervicitis agents might even have been reinforced if data regarding bacterial vaginosis had been obtained. Symptoms were not as frequently reported during follow-up as they were in the cross-sectional study. This is somewhat in contradiction with data from industrialized countries collected in the 1970s that suggested that most cases of gonorrhea had an acute clinical presentation with symptoms [22].

This divergence should be interpreted with caution, however. Indeed, access to high-quality clinical services in developing countries is limited, especially for female prostitutes. Thus, it

could be expected that these patients complained of all kinds of symptoms at enrollment in the cross-sectional study, since clinical services were not accessible for these women before. As they participated in the follow-up study, they had regular access to high-quality services for their health problems. Their perception of being well cared for might then have led to lower levels of reported symptoms, as these women became more and more aware of the value of clinical examination and laboratory testing for appropriate diagnosis and treatment of their STDs. Although women had access at all times to the clinic where the study was based, spontaneous consultations for STD-related complaints (during unscheduled visits) were not common (only 4.4% of the 15,124 visits of the 771 women were unscheduled). Most of these visits were for complaints not related to STDs, and consultations at other health care facilities were unlikely, as such services were practically nonexistent.

Clinical signs, especially objective evidence of vaginal discharge and presence of endocervical mucopus, were associated with both prevalent and incident infections by either *N. gonorrhoeae* or *C. trachomatis.* This is in agreement with results from previous studies [11–19] and suggests that active screening for STDs with speculum-assisted examination may be useful, at least to some extent, for female prostitutes in developing countries. The high specificity of the presence of endocervical mucopus, combined with the high prevalence and incidence of gonorrhea and chlamydial infection, results in a relatively high positive predictive value that might be the basis for a decision to treat all prostitutes with this clinical sign. However, the sensitivity of this sign was lower in our study than that previously reported with regard to prevalent cases in industrialized countries (19%–60%) [11, 14, 15], and its use for diagnosis in populations in which these diseases are less prevalent could be problematic because, in this context, the positive predictive value could be much lower than what we found.

Vaginal discharge (as a clinical sign) was more sensitive but much less specific, and it was more strongly associated with the presence of vaginitis agents than with gonorrhea or chlamydial infection. Cervical motion tenderness, a clinical sign generally associated with upper genital tract infection, such as salpingitis, was not related to infection by either *N. gonorrhoeae* or *C. trachomatis.* This may be explained by the development of a certain level of immunity to upper genital tract infections by these agents in this group of women with a very high level of recurrent infection. Indeed, it has been previously suggested that the development of antibodies to some of the outer-membrane proteins of *N. gonorrhoeae* leads to some degree of protection against gonococcal salpingitis [24].

We used an enzyme immunoassay for the diagnosis of chlamydial infection. Although its sensitivity is lower than that of culture [25], it was preferred over this latter method because of logistical constraints related to STD diagnosis in developing countries. Newly developed tests, such as PCR [26] and the ligase chain reaction [27], are even more sensitive than culture but were not available at the time of the study. The use of a more sensitive assay for the detection of *C. trachomatis* might have shown increased specificity of the different symptoms or clinical signs, as more women with such signs and symptoms could have been found to be infected with this agent.

The reason why some women are symptomatic or present with clinical signs in association with cervical infection by these pathogens remains unclear. Indeed, no personal or behavioral characteristic has ever been associated with clinical signs or symptoms of women infected by *N. gonorrhoeae* or *C. trachomatis,* and we did not find any such evidence in this study (data not shown). However, it has been recently reported that specific *C. trachomatis* serotypes were more strongly associated with clinical signs, such as cervical mucopus [28]. Although such a finding may not have obvious short-term applications in STD control programs in developing countries, it may eventually contribute to a better understanding of the mechanisms leading to the development of signs and symptoms. Similar studies should address the symptomatology associated with different auxotypes and serotypes of *N. gonorrhoeae* in women. Previous studies about such an association in men have yielded discrepant results [29, 30].

The second main conclusion from these data is that the occurrence of several symptoms and signs during a given episode of gonococcal or chlamydial infection was predictive of their occurrence during a subsequent episode. However, this finding appears to be of limited utility because the level of prediction was relatively low, with the exception of that for vaginal discharge (as a clinical sign) in paired incident episodes. This latter finding might be of some use in STD control programs within the regular clinical follow-up of female prostitutes if appropriate records are kept.

The third main conclusion is that appropriate treatment leads to a reduction in the frequency of the signs associated with the presence of either gonorrhea or chlamydial infection, such as vaginal discharge and endocervical mucopus. Indeed, in women who were found to be cured of their infection 1 month after diagnosis, such a reduction was observed, whereas the prevalence of these signs remained stable in the 18% of women who were still infected. Although some compliance problems or even treatment failures may have occurred, this proportion of women remaining infected 1 month after treatment likely could be accounted for largely by reinfection, given the very high incidence of gonococcal and chlamydial infections in this high-risk population [8].

Overall, this study suggests that a clinical approach to screening for *N. gonorrhoeae* and *C. trachomatis* in female prostitutes in developing countries may be difficult in both prevalent and incident cases. However, options combining the observation of clinical signs with risk-profiling (based, for instance, on questions concerning condom use, number of clients, etc.) and simple diagnostic tests such as microscopy or leukocyte esterase dipstick testing (shown to be useful for the diagnosis of urethritis in men [31–34] and, to a lesser extent, in pregnant women [21]) should be investigated and may offer

alternatives. Use of risk-profiling has now been proposed by the WHO to increase the validity of vaginal discharge algorithms in low-risk women [35].

In addition to purely diagnostic considerations, the broader issue of STD services for high-risk women in developing countries is of utmost importance for STD and HIV control. Indeed, health services research should address the types of services that should be provided (special clinics vs. integration into primary health care centers) and the means to attract high-risk women to these services on a regular basis in order to diminish the duration of infection, which may be crucial with regard to the development of complications (such as salpingitis, infertility, and ectopic pregnancy) and the propagation of HIV in the community [36]. In addition, such services should be designed to address all health problems of these women and should integrate health promotion activities. Whichever strategy will prove the most acceptable, feasible, and attractive, there is an urgent need for the development of cheap, reliable laboratory tests that could be used within field STD-control programs in developing countries.

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References

1. Laga M, Nzila N, Goeman J. The interrelationship of sexually transmitted diseases and HIV infection: implications for the control of both epidemics in Africa. AIDS **1991**;5(suppl 1):S55–63.
2. Wasserheit JN. Epidemiological synergy: interrelationships between human immunodeficiency virus infection and other sexually transmitted diseases. Sex Transm Dis **1992**;19:61–77.
3. Cameron DW, Simonsen JN, D'Costa LJ, et al. Female-to-male transmission of human immunodeficiency virus type 1: risk factors for seroconversion in men. Lancet **1989**;2:403–7.
4. Plummer FA, Simonsen JN, Cameron DW, et al. Cofactors in male-female sexual transmission of human immunodeficiency virus type 1. J Infect Dis **1991**;163:233–9.
5. Darrow WW, Echenberg DF, Jaffe HW, et al. Risk factors for human immunodeficiency virus (HIV) infections in homosexual men. Am J Public Health **1987**;77:479–83.
6. Holmberg SD, Stewart JA, Gerber AR, et al. Prior herpes simplex virus type 2 infection as a risk factor for HIV infection. JAMA **1988**;259:1048–50.
7. Stamm WE, Handsfield HH, Rompalo AM, et al. The association between genital ulcer disease and acquisition of HIV infection in homosexual men. JAMA **1988**;160:1429–33.
8. Laga M, Alary M, Nzila N, et al. Condom promotion, sexually transmitted diseases treatment, and declining incidence of HIV-1 infection in female Zairian sex workers. Lancet **1994**;344:246–8.
9. Laga M, Manoka A, Kivuvu M, et al. Non-ulcerative sexually transmitted diseases as risk factors for HIV-1 transmission in women: results from a cohort study. AIDS **1993**;7:95–102.
10. World Health Organization. Consensus statement from the consultation of global strategies for coordination of AIDS and STD control programmes. Geneva: World Health Organization, **1990** (WHO/GPA/90.2).
11. Handsfield HH, Jasman LL, Roberts PL, Hanson VW, Kothenbeutel RL, Stamm WE. Criteria for selective screening for *Chlamydia trachomatis* infection in women attending family planning clinics. JAMA **1986**;255:1730–4.
12. Harrison HR, Costin M, Meder JB, et al. Cervical *Chlamydia trachomatis* infection in university women: relationship to history, contraception, ectopy, and cervicitis. Am J Obstet Gynecol **1985**;153:244–51.
13. Braddick MR, Ndinya-Achola JO, Mirza NB, et al. Towards developing a diagnostic algorithm for *Chlamydia trachomatis* and *Neisseria gonorrhoeae* cervicitis in pregnancy. Genitourin Med **1990**;66:62–5.
14. Johnson BA, Poses RM, Fortner CA, Meier FA, Dalton HP. Derivation and validation of a clinical diagnostic model for chlamydial cervical infection in university women. JAMA **1990**;264:3161–5.
15. Brunham RC, Paavonen J, Stevens CE, et al. Mucopurulent cervicitis: the ignored counterpart in women of urethritis in men. N Engl J Med **1984**;311:1–6.
16. Addis DG, Vaughn ML, Golubjatnikov R, Pfister J, Kurtycz DFI, Davis JP. *Chlamydia trachomatis* infection in women attending urban midwestern family planning and community health clinics: risk factors, selective screening, and evaluation of non-culture techniques. Sex Transm Dis **1990**;17:138–46.
17. Paavonen J, Critchlow CW, DeRouen T, et al. Etiology of cervical inflammation. Am J Obstet Gynecol **1986**;154:556–64.
18. De Schampheleire I, Van de Velden L, Meheus A. Stratégies de traitement de la gonococcie à la consultation gynécologique primaire à Pikine, Sénégal. Ann Soc Belge Med Trop **1984**;64:191–7.
19. Wilmott FE. Mucopurulent cervicitis: a clinical entity? Genitourin Med **1988**;64:169–71.
20. World Health Organization. Report of a WHO Study Group: management of patients with sexually transmitted diseases. WHO Technical Report Series 810. Geneva: World Health Organization, **1991**.
21. Vuylsteke B, Laga M, Alary M, et al. Clinical algorithms for the screening of women for gonococcal and chlamydial infection: evaluation of pregnant women and prostitutes in Zaire. Clin Infect Dis **1993**;17:82–8.
22. McCormack WM, Stumacher RJ, Johnson K, Donner A, Rychwalski R. Clinical spectrum of gonococcal infection in women. Lancet **1977**;1:1182–5.
23. Nzila N, Laga M, Thiam MA, et al. HIV and other sexually transmitted diseases among female prostitutes in Kinshasa. AIDS **1991**;5:715–21.
24. Plummer FA, Chubb H, Simonsen JN, et al. Antibodies to opacity proteins (Opa) correlate with a reduced risk of gonococcal salpingitis. J Clin Invest **1994**;93:1748–55.
25. Barnes RC. Laboratory diagnosis of human chlamydial infections. Clin Microbiol Rev **1989**;2:119–36.
26. Loeffelholz MJ, Lewinski CA, Silver SR, et al. Detection of *Chlamydia trachomatis* in endocervical specimens by polymerase chain reaction. J Clin Microbiol **1992**;30:2847–51.
27. Lee HH, Chernesky MA, Schachter J, et al. Diagnosis of *Chlamydia trachomatis* genitourinary infection in women by ligase chain reaction assay of urine. Lancet **1995**;345:213–6.
28. Workowski KA, Stevens CE, Suchland RJ, et al. Clinical manifestations of genital infection due to *Chlamydia trachomatis* in women: differences related to serovar. Clin Infect Dis **1994**;19:756–60.
29. Horner PJ, Coker RJ, Turner A, Shafi MS, Murphy SM. Gonorrhoea: signs, symptoms and serogroups. Int J STD AIDS **1992**;3:430–3.
30. Ross JDC, Wardropper A, Sprott M, Moyes A, Young H. Gonococcal infection in Edinburgh and Newcastle: serovar prevalence in relation to clinical features and sexual orientation. Genitourin Med **1994**;70:35–9.

31. Tyndall MW, Nasio J, Maitha G, et al. Leukocyte esterase urine strips for the screening of men with urethritis—use in developing countries. Genitourin Med 1994;70:3–6.
32. Sellors JW, Mahony JB, Pickard L, et al. Screening urine with a leukocyte esterase strip and subsequent chlamydial testing of asymptomatic men attending primary care practitioners. Sex Transm Dis 1993;20:152–7.
33. Veeravahu M, Smyth RW, Clay JC. Detection of leukocyte esterase in urine: a new test for nongonococcal urethritis compared with two microscopic methods. Sex Transm Dis 1987;14:180–4.
34. Mayaud P, Changalucha J, Grosskurth H, et al. The value of urine specimens in screening for male urethritis and its microbial aetiologies in Tanzania. Genitourin Med 1992;68:361–5.
35. Global Programme on AIDS. Management of sexually transmitted diseases. Geneva: World Health Organization, 1994 (GPA/TEM/94.1).
36. Boily MC, Brunham RC. The impact of HIV and other STDs on human populations—are predictions possible? Infect Dis Clin North Am 1993;7:771–92.