

Assessing therapeutic management of vaginal and urethral symptoms in an anonymous HIV testing centre in Luanda, Angola

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Abstract

Introduction: This study aimed to estimate the prevalence of *Neisseria gonorrhoeae* and *Chlamydia trachomatis* infections and to assess the therapeutic management of vaginal/urethral discharge and dysuria in patients with human immunodeficiency virus in Luanda, Angola, taking into account World Health Organization recommendations for sexually transmitted infection syndromic management.

Methodology: Socio-demographic and medical data were obtained from 436 individuals, and clinical examinations were performed in 104 women and 8 men. Vaginal/cervical and urethral specimens were collected from 112 individuals for observation of *Trichomonas vaginalis*, yeasts and bacterial vaginosis, while urine samples were obtained from 415 patients (221 symptomatic and 194 asymptomatic). Diagnosis of *Neisseria gonorrhoeae* and *Chlamydia trachomatis* was performed by polymerase chain reaction assay.

Results: The prevalence of *N. gonorrhoeae* and *C. trachomatis* was 8.4% (35/415) and 7.9%, (33/415) respectively. Eight of the 35 *N. gonorrhoeae* positive cases were treated. All men and women (79) who presented a positive wet mount/Gram stain were etiologically treated according to microscopy results. In contrast, 53.3% of the female patients (16/30) and 33.3% (1/3) of the male patients who presented microscopy negative results were treated for urinary tract infection or by syndromic approach. Among non-examined patients, 15% of women (12/80) and 52.5% of men (21/40) were treated without an etiological result. Syndromic treatment was preferentially given to non-examined males (19/40–47.5%) over females (12/80–15%) ($p<0.01$).

Conclusions: The prevalence of *N. gonorrhoeae* and *C. trachomatis* found in this study was high. WHO-recommended syndromic management of vaginal/urethral discharge is not being consistently and correctly applied.

Key words: STDs; epidemiology; syndromic management; vaginal/urethral discharge

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Introduction

Sexually transmitted infections (STIs) are increasing in many countries in Europe [1-3] and they continue to be prevalent in developing countries [4-6]. As they may predispose to HIV acquisition [7-9], the World Health Organization (WHO) has recommended that efforts to decrease HIV prevalence should include programs to prevent and control other STIs [10].

In this context, prevention and control of these infections must include a patient's early and correct diagnosis and treatment, as well as follow-up of sexual contacts. Sexual health education to reduce risk behaviours and prevent future STI episodes is also necessary. To achieve these goals, the WHO recommends the use of STI syndromic management and proposes different flow-chart schemes for the management of STIs in countries or regions where laboratory facilities are not available. Syndromic management algorithms should be assessed and adapted to the specific characteristics of the regions

where they are being implemented [11-14]. In Angola, STIs are not correctly managed; specifically, these diseases are underestimated. Taking into account that many of these infections are asymptomatic, the majority of patients do not visit a doctor, clinicians do not notify the diagnosed cases, and there is no active epidemiological surveillance. Furthermore, the diagnoses are essentially made on clinical grounds with very basic laboratory support. Some years ago, a mixture of the syndromic approach with some laboratory aid was implemented in our anonymous testing centre (ATC) clinic in Angola. However, because of frequent clinic staff changes and the occasional lack of antibiotics and reagents, we recognized the need to assess how the syndromic approach was being implemented.

The aim of this study was to estimate the prevalence of *Neisseria gonorrhoeae* and *Chlamydia trachomatis* infections and to assess therapeutic management of vaginal/urethral discharge and dysuria

in patients attending an anonymous testing centre (ATC) for HIV in Luanda, Angola, taking into account the WHO recommendations for STI syndrome management.

Methodology

The study was conducted at a non-governmental organization, the Instituto Português de Medicina Preventiva (IPMP), in Luanda, Angola, that provides anonymous testing for HIV. Twice a week all patients who presented at the clinic were asked if they wanted to be included in the study. In the end, a total of 436 individuals (266 women and 170 men) were randomly assigned to participate in this study, after informed consent was obtained.

Women had two vaginal swabs taken, one of which was used in a wet preparation for identification of *T. vaginalis* and the other in a Gram-stained smear for visualization of yeasts and bacterial vaginosis, (Nugent criteria). Urethral swabs were performed in men to verify the presence of intracellular diplococci within polymorphonuclear cells or of five or more of these cells per high-power field microscope. The results of Gram-stained slides were later confirmed by two observers blinded to the initial results at the Instituto de Higiene e Medicina Tropical (IHMT) in Lisbon.

N. gonorrhoeae and *C. trachomatis* were identified at IHMT in urine samples by PCR techniques based on those described by Ho *et al.* [15] and Jalal *et al.* [16], respectively. To identify *N. gonorrhoeae* DNA, the primers HO1-5' GCTACGCATACCCGCGTTGC 3' and HO3-5' CGAAGACCTTCGAGCAGACA 3' were used to amplify a fragment of the *ccpB* gene. Positive samples were subsequently confirmed by restriction fragment length polymorphism (RFLP). The *C. trachomatis* DNA was identified by a real-time

multiplex PCR reaction with two pairs of primers amplifying a fragment of 149 bp from the cryptic plasmid and a fragment of the 218 bp from the MOMP gene (HJ-plasmid-1-5-AACCAAGGTCGATGTGATAG-3 and HJ-plasmid-2-TCAGATAATTGGCGATTCTT -3 and HJ-MOMP-1-5-GACTTTGTTTTTCGACCGTGTT-3 and HJ-MOMP-25-CARAATACATCAAARCGATCCCA, respectively).

Results

The age of the patients included in this study ranged from 15 to 51 years for women and 17 to 72 for men, with a medium average age of 28 years for each gender.

Patients were considered symptomatic if they presented one or more of the following symptoms: vaginal/urethral discharge, itching/burning sensation, dysuria and/or lower abdominal pain. The most common presenting symptoms in females were itching/burning sensation, followed by vaginal discharge, while men complained of itching/burning sensation and dysuria (Table 1). About half (53.2%; 232/436) of the 436 patients were symptomatic, and this proportion was higher in females (69.2%; 184/266) than in males (28.2%; 48/170).

Out of the 184 symptomatic females, 104 (56.5%) were examined, while 8 of the 48 (16.6%) symptomatic males were examined. Consequently, microscopy was performed only on the samples from these patients (n = 112) and they were treated according to their microscopic results.

N. gonorrhoeae DNA was identified in urine by PCR technique in 35/415 (8.4%) of the patients. The females (21/246; 8.5%) and males (14/169; 8.3%) had a similar prevalence of this infection, with 77.1% (27/35) of them being symptomatic and 22.8% (8/35)

Table 1. Patient distribution by sex and presenting symptoms

	Female N (%)	Male N (%)	Total N (%)
Asymptomatic	82 (30.8)	122 (71.8)	204 (46.8)
Symptomatic	184 (69.2)	48 (28.2)	232 (53.2)
Itching/burning	141 (76.6)	30 (62.5)	
Vaginal/urethral discharge	130 (70.9)	11 (23.0)	
Dysuria	57 (31.0)	25 (52.1)	
Lower abdominal pain	53 (28.8)		
Total	266	170	436

asymptomatic, respectively. *C. trachomatis* DNA was detected in 7.9% (33/415) of the urine samples: 18/246 (7.3%) in women (11 symptomatic and 7 asymptomatic) and 15/169 (8.9%) in men (7 symptomatic and 8 asymptomatic).

When analyzing all symptomatic patients in whom an examination had been performed (104 women and 8 men) and a microscopic result obtained, the most frequent genital infection was bacterial vaginosis (BV) followed by candidiasis, with a prevalence of 58.7% (61/104) and 31.7% (33/104), respectively. *N. gonorrhoeae* DNA was detected in 10.7% (19/177) and 18.1% (8/44) of the symptomatic women and men, respectively, while *C. trachomatis* DNA was identified in 6.2% (11/177) of the symptomatic females and in 15.9% (7/44) of symptomatic males (Table 2).

Seventy-four of the 104 (71.1%) symptomatic examined women had a positive wet mount/Gram stain and were etiologically treated, in accordance with the microscopy result. Sixteen of the 30 women who presented negative microscopy results were treated: five for urinary tract infection and 11 according to the syndromic approach. The syndromic approach covered for gonorrhoea in 20% (6/30) of these patients, and for chlamydia, trichomoniasis/BV, and candidiasis in

26.7% (8/30), 16.7% (5/30) and 3.3% (1/30) of the patients, respectively (Table 3). Fourteen of the 30 (46.7%) patients were not treated at all. Of the 80 symptomatic non-examined female patients (without a microscopy result), 12 (15%) were treated, and of these, 11 (13.8%) were treated for urinary tract infection, while the remaining one non-examined female (1.3%) was treated for chlamydia, trichomoniasis and BV using the syndromic approach. Three of the 28 treated patients (10.7%) were given triple therapy with ciprofloxacin, doxycycline/azithromycin and metronidazole, six (21.4%) were given double therapy with any two of the previous drugs, and none was covered for all causes of vaginal discharge (Table 3).

Only 8 of the 48 (16.7%) symptomatic men were examined. Of these, five had positive microscopies for intracellular diplococci and were treated accordingly. The remaining three (37.5%) presented negative results, of whom one was treated by syndromic approach for urethral discharge and two were not treated. Nineteen of the 40 (47.5%) non-examined male patients were also treated: 7 (7/40; 17.5%) for urinary tract infection and 12 (12/40; 35%) for urethral discharge. Two of these 12 (16.6%) were exclusively

Table 2. Prevalence of infections in symptomatic patients with available samples*

	Female n/N (%)	Male n/N (%)	Total N (%)
Gonorrhoea	19/177 (10,7)	8/44 (18,1)	27/221 (12,2)
Clamidiose	11/177 (6,2%)	7/44 (15,9%)	18/221 (8,1%)
Bacterial vaginosis (BV)	61/104 (58,7)		
Trichomoniasis	3/104 (2,9%)		
Candidiasis	33/104 (31,7%)		
Mixed (more than 1)	25/104 (24,0%)		

n = number of positive results; N = total number of performed tests (PCR in gonorrhoea; wet mount/gram stain in BV, candidiasis and trichomoniasis); *urine and/or genital samples

Table 3. Syndromic treatment in symptomatic patients with negative microscopy or no available microscopy

	Negative lab results [F / M]	Non-assessed [F / M]	Total [F / M]
Urinary infection	5 / 0	11 / 7	16 / 7
Syndromic management	11 / 1	1 / 12	12 / 13
Gonorrhoea	6 / 1	0 / 7	6 / 8
Chlamydia	8 / 1	1 / 10	9 / 11
Trichomoniasis/BV	5 / 0	1 / 0	6 / 0
Candidiasis	1 / 0	0 / 1	1 / 1
Total	16 / 1	12 / 19	28 / 20

treated for gonorrhoea, 5 (41.7%) only for chlamydia, and 5 (41.7%) for both infections. One of these five was further treated with metronidazol (Table 3).

When comparing the rates of observation undertaken in men and women, a statistically significant difference was found between overall syndromic treatment (even if not correctly applied) performed in the non-examined males (19/40; 47.5%) versus the non-examined females (12/80; 15%) (Fisher's Test, $p < 0.01$).

Of the 35 cases of *N. gonorrhoeae* detected by PCR, 27 were from symptomatic patients, of whom 10.7% (19/177) were females and 18.1% (8/44) were males. Eight (4.1%) of these cases were from asymptomatic patients as follows: 2/69 (2.9%) were females and 6/125 (4.8%) were males. Microscopy was performed in all males, but only in ten of the women. All six microscopy results found to be positive at the ATC clinic (indicated by the existence of Gram-negative diplococci inside polymorphonuclear cells) were also PCR positive at IHMT and were from symptomatic patients. Three males and one female were treated according to the microscopy results; two of the males were treated only with doxycycline. Fourteen individuals in whom *N. gonorrhoeae* was identified by PCR technique (10 symptomatic and 4 asymptomatic) were not detected in the Gram-stain and only 4 of these individuals were treated (3 females and 1 male). Five women with *N. gonorrhoeae* detected by PCR were not treated, since no microscopy results were available for them. Overall, of the 35 *N. gonorrhoeae*-infected patients, 8 were treated and 27 were not treated, while 14 individuals in whom *N. gonorrhoeae* was not detected by PCR technique were treated using the syndromic approach.

C. trachomatis was detected in 33 cases (33/415; 7.9%), 18 (18/221; 8.1%) from symptomatic patients (11/177, 6.2% females; 7/44, 15.9% males) and 15 (15/194; 7.7%) from asymptomatic individuals (7/69, 10.1% females; 8/125, 6.4% males). Two of these 18 symptomatic patients had a microscopy done, which had no signs representative of chlamydial infection. Two symptomatic female patients from the 18 patients in whom *C. trachomatis* was identified were treated by syndromic approach, one with ciprofloxacin and the other with doxycycline.

Discussion

Accurate management and an effective therapeutic approach to STIs is necessary to control HIV infection [10,17].

According to WHO guidelines [10] relating to STI syndromic management, every patient with vaginal/urethral/discharge/dysuria must be observed and treated when vaginal discharge or urethral discharge are present. In this study, only 50.7% of the symptomatic patients were examined and from those with urethral/vaginal discharge only 52.5% were treated, since many times these symptoms are not considered by both patients and clinicians as STIs.

STI prevalence varies around the world and with the type of population studied. In this study, the prevalence of *N. gonorrhoeae* and *C. trachomatis* (8.3% and 7.9%) was high, taking into account that some samples were taken from asymptomatic patients. In other studies in Africa, the prevalence varied from 2.5% to 6% and from 4% to 6% for *N. gonorrhoeae* and *C. trachomatis*, respectively [4,18-19]. In relation to other causes of vaginal/urethral discharge, bacterial vaginosis was the most commonly found (58.7% of symptomatic patients). In the present study, candidiasis is found in 31.7% of the individuals and trichomoniasis in 2.9%, while Blankhart *et al.* [4] and Fonck *et al.* [18] respectively found a prevalence of 46.6% and 35% for candidiasis and 9.9% and 2.5% for trichomoniasis. In this ATC clinic, clinical diagnosis was aided by Gram-stain and wet-smear test, which were observed to have a positive contribution, since they assured some kind of treatment to patients who presented a positive microscopy for an STI agent. However, risk assessment, a key step in the syndromic approach, was not applied by the health practitioners. Gram-staining on-site detected 22.2% (6/27) of *N. gonorrhoeae* symptomatic cases, meaning that 21 patients with gonorrhoea left the clinic without receiving any kind of treatment. Had a syndromic approach been correctly applied in all patients with vaginal/urethral symptoms, only the eight asymptomatic cases would not have been treated.

Gram stain performed at the ATC clinic did not detect any signs of chlamydial infection, in contrast to the 33 cases (18 in symptomatic patients and 15 in asymptomatic) detected using the PCR technique. Consequently, only two symptomatic patients were treated, in comparison with the other 16 that should also have benefitted from treatment, following the syndromic approach.

In this study, there was a difference in the observation rates between men and women. This difference could be due the higher prevalence of infection in symptomatic men. Higher risk behaviour among men attending the clinic, such as having multiple sexual partners, could also have influenced

their preferential treatment above females. Furthermore, urethral discharge in a man represents a higher chance of the individual having an STI than the presence of vaginal discharge in a woman.

Overall, only 33% (1 out of 3) of the symptomatic males and 40% (11 out of 25) of the symptomatic females presenting negative laboratory results were correctly treated using the syndromic approach for urethral or vaginal discharge, respectively. A complete treatment for all causes of vaginal or urethral discharge was not prescribed for any of the patients for whom microscopy results were not available, even when presenting symptoms. In this study, there was a very low treatment coverage for candidiasis, since only 8.3% of the infected patients were treated, while the prevalence of the infection was 31.7%. The same situation applies to bacterial vaginosis, which was only covered in half of these infected patients, when it was in fact the most prevalent STI (58.7%). Interestingly, coverage for chlamydia (75%) was the highest amongst all STIs, and this could be explained by the complete lack of means to diagnose this infection in this clinic, making the clinicians to over-treat *C. trachomatis* infections.

Conclusion

Our study indicates that, in this clinic, many patients were under-treated for all organisms studied, which can lead to the possibility of transmitting their infections to their partners. There was also over-treatment in 3.2% of our study population, since fourteen patients were treated for *N. gonorrhoeae* without actually having the infection. In addition, even when patients were treated, treatment was often incomplete, in both men and women, with only five females and one male being given triple therapy. Therefore, syndromic management of vaginal/urethral discharge as recommended by the WHO is not being consistently and correctly applied in this setting. We also feel that there is an absolute need for implementation of laboratory tests that make STI diagnosis easy, rapid and affordable.

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