Elevada Incidência de Infecções Sexualmente Transmissíveis em Doentes com Infecção por VIH

Telma Azevedo[1], Ana Brasileiro[2], Fernando Borges[1], Kamal Mansinho[1], Irene Santo[3], Jacinta Azevedo[3]
[1]Serviço de Doenças Infecciosas e Medicina Tropical/Department of Infectious Diseases and Tropical Medicine, Hospital de Egas Moniz, Centro Hospitalar de Lisboa Ocidental, Lisboa, Portugal
[2]Serviço de Dermatologia/Department of Dermatology, Hospital dos Capuchos, Centro Hospitalar de Lisboa Central, Lisboa, Portugal
[3]Centro de Doenças Sexualmente Transmissíveis/STD Center, Centro de Saúde da Lapa, Lisboa, Portugal

RESUMO – **Introdução**: As infecções sexualmente transmissíveis (IST) são um importante problema de saúde e aumentam o risco de adquirir o vírus da imunodeficiência humana (VIH). O objectivo foi identificar as ISTs diagnosticadas em doentes com infecção VIH conhecida e nos com diagnóstico *de novo*. **Métodos**: Análise retrospectiva dos processos clínicos dos utentes que recorreram a uma clínica especializada em IST de 2009 a 2013. **Resultados**: Foram incluídos 680 doentes, correspondendo a 8% dos observados no período de estudo. A maioria (638, 92%) era do sexo masculino e homens que têm sexo com homens (489, 72%). Quase metade (304, 45%) eram migrantes. Do total, 270 (40%) dos doentes tiveram diagnóstico de pelo menos uma IST, sendo sífilis a mais comum (123, 18%), seguida por infecção por *Chlamydia trachomatis* (46, 7%), *Neisseria gonorrhoeae* (42, 6%) e condilomas genitais (32, 5%). Relativamente à infecção VIH, 329 (48%) doentes tinham infecção conhecida e 351 (52%) foram diagnosticados *de novo*. Estes eram significativamente mais jovens e recorreram mais frequentemente para rastreio. Nos doentes com infecção VIH conhecida encontrou-se maior frequência de antecedentes pessoais de IST, referenciação por parceiros, sintomatologia e diagnóstico de novas ISTs. **Conclusões**: Foi diagnosticada pelo menos uma IST (excepto VIH) em 40% dos indivíduos observados. Tal facto representa um problema importante não só porque uma IST concomitante aumenta o risco de aquisição de VIH (para os indivíduos diagnosticados de novo), mas também porque demonstra que os indivíduos com infecção VIH conhecida mantêm um padrão comportamental de elevado risco.
PALAVRAS-CHAVE – *Comportamento Sexual; Doenças Sexualmente Transmissíveis; Infecções por VIH.*

High Incidence of Sexually Transmitted Infections in Patients with HIV-Infection

ABSTRACT – ***Introduction:*** *Sexual transmitted infections (STI) are an important health problem and increase the risk for acquisition and transmission of HIV. We aimed to identify STIs diagnosed in patients with known human immunodeficiency virus (HIV) infection and in newly diagnosed ones.* ***Methods:*** *Retrospective analysis of medical charts of individuals attending a specialized STI Clinic from 2009 to 2013.* ***Results:*** *A total of 680 patients were included, accounting for 8% of the patients observed during the study period. The majority (638, 92%) were male and men who have sex with men (MSM) (489, 72%). Almost half (304, 45%) were migrants. Overall, 270 (40%) patients were diagnosed with at least one STI, syphilis was the most common (123, 18%), followed by Chlamydia trachomatis (46, 7%), Neisseria gonorrhoeae infection (42, 6%) and genital warts (32, 5%). Concerning HIV status, 329 (48%) patients had known infection and 351 (52%) were newly diagnosed during the study period. The newly diagnosed patients were significantly younger (37.3±9.7 vs 32.4± 9.5 years) and more frequently sought attention for screening. Past history of STIs, partner referral, symptoms and being diagnosed with at least one concomitant STI were significantly more common in previously known HIV patients.*

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Correspondência: Telma Susana Vieira Azevedo
Serviço de Doenças Infecciosas e Medicina Tropical
Hospital de Egas Moniz, Centro Hospitalar de Lisboa Ocidental
Rua da Junqueira nº126 - 1349-019 Lisboa, Portugal
Tel.: +351 964 350 169
E-mail: telma.uwcad@gmail.com

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Conclusion: At least one new STI (other than HIV) was diagnosed in 40% of the patients. This represents an important problem not only because concomitant STIs increase the risk of HIV acquisition (for the new diagnosed cases) but also because patient with known HIV infection maintain a high-risk behaviour pattern.
***KEYWORDS** – HIV Infections; Sexual Behavior; Sexually Transmitted Diseases.*

INTRODUCTION

In order to reduce the incidence of sexually transmitted infections (STI), it is of paramount importance to diagnose and treat symptomatic and asymptomatic patients. This is especially true among high-risk individuals, such as sex workers, men who have sex with men (MSM), and bridge populations (sex workers clients and partners of high-risk patients). Evidence supporting the role of STIs as a cofactor for human immunodeficiency virus infection (HIV) is extensive, and indisputable.[1] Several studies show a clear relation between STIs and HIV transmission, particularly those that cause mucocutaneous ulceration, such as syphilis and herpes simplex virus infection (HSV).[2] STIs can increase the risk of acquiring or transmitting HIV different mechanisms, including the breaching of mechanical barriers to infection, increased inflammation and higher levels of HIV cellular targets, and increased genital tract HIV levels.[3]

Additionally, the acquisition of a new IST by a HIV

Table 1 - Characterization of the 680 patients, divided in groups of known and newly diagnosed HIV infection.

Demographic and clinical data (n–%)	**Total** (n=680)	**Known HIV infection** (n=329)	**Newly diagnosed HIV infection** (n=351)	***P***
Male gender	624 – 92%	299 – 91%	325 – 93%	NS
Median age ± SD	34.7 ± 9.9	37.3 ± 9.7	32.4 ± 9.5	<0.05
NATIONALITY				NS
Portuguese	376 – 55%	186 – 56%	189 – 54%	
Migrants	304 – 45%	143 – 44%	162 – 46%	
• Brazil	125 – 18%	50 – 15%	75 – 21%	
• PALOPs	95 – 14%	50 – 15%	45 – 13%	
• Other European country	63 – 9%	31 – 9%	32 – 9%	
• Other	22 – 3%	12 – 4%	10 – 3%	
SEXUAL ORIENTATION				<0.05
• MSM	489 – 72%	223 – 68%	266 – 76%	
• Heterosexual	186 – 27%	104 – 32%	82 – 23%	
• Bisexual	5 – 1%	2	3 – 1%	
Nº. OF PARTNERS (6 month prior to visit)				NS
• 0	112 – 17%	54 – 16%	58 – 17%	
• 1	229 – 34%	112 – 34%	117 - 33%	
• 2-4	234 – 34%	116 - 35%	118 – 34%	
• 5 or more	98 – 14%	43 – 13%	55 – 26%	
• Unknown	7 – 1%	4 – 1%	3 – 1%	
PAST OR PRESENT INTRAVENOUS DRUG USE	10 – 1%	8 – 2%	2 – 1%	NS
SEX WORKER	7 – 1%	4 – 1%	3 – 1%	NS
AT LEAST 1 STI EPISODE IN THE PAST*	242 – 36%	178 – 54%	64 – 18%	<0.05
REASON FOR VISIT				<0.05
• Symptomatic	239 – 35%	176 – 54%	63 – 18%	
• Genital discharge	63 - 9%	51 – 16%	12 – 3%	
• Genital warts	49 – 7%	38 – 12%	11 – 3%	
• Genital ulcers	59 – 9%	35 – 11%	24 – 7%	
• Asymptomatic screening	376 – 55%	97 – 30%	279 – 80%	
• Referred by partner	33 – 5%	26 - 7%	7 – 2%	
• Referred a partner	49 – 7%	14 – 4%	35 – 10%	

* Excluding HIV diagnosis.
MSM, men who have sex with men; SD, standard deviation; NS, non-significant, PALOPs Portuguese-speaking African countries.

positive individual is believed to increase viral load in the genital area, probably in relation with the activation of inflammatory mechanisms.[4] Moreover, it is also a marker of risk behaviour, with the associated possibility of HIV transmission.[5]

In Portugal, the rate of new HIV diagnoses remains high, but over the last years we have observed a slight decline in new cases. The incidence rate per 100 000 habitants declined from 5.5 in 2009 to 3.1 in 2014, with a total of 7160 new HIV cases over those 5 years.6 Series from specialized STI clinics in the country report that 4.1 to 5.5% of assisted patients were newly diagnosed HIV patients.[4,7] Nevertheless, few specialized centres in the country are able to assist patients with STI and often the HIV care settings do not promote STI screening and treatment for HIV-infected patients.

Concerning new STIs in known HIV positive patients, the available Portuguese data dates back to 2006 and points towards a high rate of new STIs acquisition – 23% (108) of a total of 469 STIs episodes occurring in HIV-infected individuals.[5] More recent data on the patterns of STIs acquisition in this population, who have an important role in the infection spreading, is lacking.

The main objective of this study was to identify STIs acquired by newly diagnosed HIV patients, as a possible co-factor, and in known HIV-infected ones, as a marker of behaviour risk. We also aimed to characterize and compare demographics and behaviour patterns in both groups, possibly identifying factors that can be addressed in order to reduce STIs spreading, contributing in this way to reduce both the transmission of HIV and other STIs.

METHODS

We conducted an observational retrospective study, reviewing medical charts from all individuals attending an open STI primary clinic in Lisbon, Portugal, during a 5-year study period (from January 2009 to December 2013). All patients with previously known HIV infection or newly diagnosed infection were included in the study. Demographic and clinical information was collected and analysed using *Stata 12.0*. Baseline characteristics were compared using *t* tests for continuous variables and $\chi 2$ tests for categorical variables. Statistical significance was defined for $p<0.05$. Formal ethical approval was waived by the local Ethics Committee as the study was non-interventional.

RESULTS

A total of 8718 patients were observed during the study period, of which 680 (8%) were found to be HIV positive (329-3.8% known infected patients, and 351-4% newly diagnosed cases) and thus included in the study (Table 1). Male gender was predominant (624, 92%), and the mean overall age was 34.7±9.9 years. Concerning nationality, the ratio Portuguese/migrants was 376/304 (55/45%). Brazilian was the most common foreign nationality (125, 18%), and Portuguese-speaking African countries (PALOPs) individuals together represented 14% of the study population.

Half of the patients (342, 50%) reported having 0 to 1 partner in the six months preceding the visit, while 332 (49%) disclosed having 2 or more. Over a third (242, 36%) had at least one confirmed STI in the past (other than HIV), most commonly syphilis (10%) and urethritis (7%). Few patients reported using intravenous drugs (10, 1%) or being sex workers (7, 1%). More than half of the patients recurred for screening (376, 55%), while 239 (35%) had specific symptoms and 33 (5%) were referred by a partner.

Overall, during the study period, 270 (40%) patients were diagnosed with at least one STI (other than HIV), and 47 (7%) of them had 2 or more diagnosis (Table 2). Bacterial infections were predominant. Syphilis (123, 18%), namely recent syphilis (101, 15%), was the most common STI (excluding HIV). *Chlamydia trachomatis* and *Neisseria gonorrhoeae* infections were diagnosed respectively in 46 and 42 patients (7 and 6%), mostly with urethral infections (43/46 and 32/42, respectively for chlamydia and gonorrhea) and urethral/rectal infections (3/46 and 10/42, respectively). Genital warts (32, 5%), an initial clinical manifestation of genital herpes (20, 3%) and *Molluscum contagiosum* (5, 1%) were the most common viral infections. Other less frequent diagnoses are described in Table 2.

Newly diagnosed HIV patients were significantly younger than patients with known HIV infection (mean age 32.4 *vs* 37.3 years, respectively), were more frequently MSM (266, 76% *vs* 223, 68%), more frequently sought attention for screening (279, 80% *vs* 97, 30%) and were more likely to refer a partner (35, 10% *vs* 14, 4%).

Patients with known HIV infection have had more frequently at least one STI (other than HIV) diagnosed in the past than newly diagnosed HIV patients (178, 54% *vs* 64, 18%), were more often symptomatic at the time of medical visit (176, 54% *vs* 63, 18%), presented more frequently with genital discharge (51, 16% *vs* 12, 3%) and were more often referred by a partner (26, 7% *vs* 7, 2%) (Table 1). Also, they were more frequently diagnosed with at least one STI (excluding HIV infection) than newly diagnosed patients (148, 45% *vs* 122, 33%, $p < 0.05$), most commonly Syphilis (49, 15%), *Neisseria gonorrhoeae* infection (26, 8%), *Chlamydia trachomatis* (23, 7%), genital warts (19, 6%), first clinical manifestation of *genital herpes* (10, 4%).

The most common IST infections in newly HIV diagnosed patients were: Syphilis (74, 21%), *Chlamydia trachomatis* (23, 7%), *Neisseria gonorrhoeae* (16, 5%), genital warts (13, 4%) and first clinical manifestation of *genital herpes* (8, 2%).

DISCUSSION

A total of 680 (8%) of the patients attending the STI clinic were HIV-infected, 3.8% with a previously known HIV infection and 4% newly diagnosed cases. Males were predominant in both groups. Newly diagnosed patients were significantly younger and more frequently MSM. Both groups showed a high-risk sexual behaviour pattern referring multiple partners and history of other STIs in the past, the latter being more common in known HIV positive patients.

Table 2 - Sexually transmitted infections diagnosed in the study population over a 5-year period (2009-2013).

STI (n - %)	**Total** (n=680)	**Known HIV infection** (n=329)	**Newly diagnosed HIV infection** (n=351)
Number of STI* diagnosed			
• 0	410 – 60%	181 – 55%	229 – 65%
• 1	223 – 33%	130 – 40%	93 – 26%
• 2	42 – 6%	16 – 5%	26 – 7%
• 3	5 – 1%	2	3 – 1%
Syphilis (total - T)	123 – 18%	49 – 15%	74 – 21%
• Recent	101 – 15%	47 – 14%	54 – 15%
• Unknown duration	22 – 3%	2 – 1%	20 – 6%
Neisseira gonorrhoeae (T)	42 – 6%	26 – 8%	16 – 5%
• Urethral	32 – 5%	18 – 6%	14 – 4%
• Rectal	10 – 1%	8 – 2%	2 – 1%
Chlamydia trachomatis (T)	46 – 7%	23 – 7%	23 – 7%
• Urethral	43 – 6%	22 – 7%	21 – 6%
• Rectal	3	1	2 – 1%
Genital warts	32 – 5%	19 – 6%	13 – 4%
Genital herpes	20 – 3%	12 – 4%	8 – 2%
Molluscum contagiosum	5 – 1%	2 – 1%	3 – 1%
Other	32 – 5%	17 – 4%	15 – 4%
• Male urethritis	11	7	4
• Proctitis	9	8	1
• Trichomoniasis	2	0	2
• HBV infection	6	1	5
• HCV infection	4	1	3

* Excluding HIV diagnosis.

The most common reason for visiting in both groups was screening, which was more notorious in newly diagnosed patients (80%). Patients with known HIV infection visited more frequently the STI clinic when symptomatic than newly diagnosed ones (54% vs 18%). More prevalent symptoms in this group were genitourinary discharge and genital warts, while in newly diagnosed patients genital ulcers were the most common clinical presentation. A high prevalence of STI was observed in both groups, with an overall rate of at least one IST (other than HIV) of 40%. Syphilis was the most common STI, and significantly more common in new HIV cases (21% vs 15%, $p<0.05$). The high rates of co-infection of new HIV cases and recent syphilis has also been found in other series, namely in Portuguese ones.[8,9]

Concomitant STI are commonly observed in newly diagnosed HIV patients and are even more frequently reported in international literature.[10,11] As previously pointed out, concomitant STI infections, especially when associated with the presence of ulcers, enhance the activation of a number of mechanisms that increase their own transmission.[3,12]

Patients with a known HIV infection maintain high-risk sexual behaviour, as shown by the high incidence of new STI in this group (45% *vs* 33%, $p<0.05$). This issue needs to be addressed not only in STI clinics, but also on HIV clinics. Diagnosis, treatment, and contact tracing of patient partners is essential to reduce the new cases of STI and HIV.[1] Other important factors need to be considered, namely the impact in infertility in both genders,[13] morbidity, and increased susceptibility to HIV infection.[12]

MSM were highly represented in both groups of patients, as often reported. The number and type of STI diagnosed in this study is in agreement with other reports where STI such as syphilis, genital warts, and gonorrhoea are also commonly diagnosed.[8,14]

Management of sexual partners is crucial to limit the spreading of STI and the impact on public health. Patients with either a known or newly diagnosed HIV infection should be important STI clinic targets.

In our study the number of partner referrals was low in both groups (4% and 10% respectively). More efforts are needed to improve these numbers. Recently, internet-based notification systems for verified diagnoses of STI/HIV have been developed. These systems seem to be a valuable novel tool for notification by patients and providers.[15]

STUDY LIMITATIONS

We acknowledge the limitations of our study, namely its retrospective nature. Data concerning virologic and immunologic status was not available, limiting a more detailed epidemiologic characterization and also the analysis of the contribution of HIV-induced immunosuppression to the clinical expression of certain STIs, namely herpes and papilloma virus infections.

Moreover, persons engaged in high-risk sexual behaviour

are more prone to return and repeat STI tests contributing to a possible selection bias.

CONCLUSIONS

Individuals with STIs are at high risk to acquire and/or transmit HIV infection to sexual partners. Several studies show the association between HIV and other STIs. Conversely, the prevalence of STIs changes according to the study population. In our study population, patients with known HIV infection had a higher number of STIs, both in the past and present, showing an over-time pattern of high-risk sexual behaviour. Newly diagnosed HIV patients were significantly younger and more frequently MSM, which may reflect an increase in the risk of sexual behaviour in this population. These patients were more often referred by partners or sought for asymptomatic screening than those with a known HIV infection; however, partner referral remains low for both groups.

Intensified and innovative efforts in prevention within these specific risk groups need to be taken, namely education programs directed to the sexually active population as well as health professionals. Another necessary intervention is to diffuse more information to seropositive patients about the risk of transmission of both HIV and other STI and a possible negative impact of a new IST on their HIV infection status. Overall, we need to put more effort into preventing STI, as well as treating and possibly reducing new HIV infections.

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