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Newly HIV diagnosed in South Sardinia: the issue of late presentation

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ABSTRACT:

— ***Background:*** Late presentation is associated with increased HIV-related morbidity and mortality, shorter survival, poor response to treatment and increased rates of HIV transmission. The aim of the study was to evaluate the extent of HIV Late Presentation and to describe demographic and clinical features among Late Presenters in an Italian hospital.

— ***Patients and Methods:*** Data were collected from the "New HIV Diagnosis Surveillance System", available since 2012. Late presentation was defined in concordance with the recommendations of the European Late Presenter Consensus working group.

— ***Results:*** We enrolled 99 patients; the male to female ratio was 4:1. The main risk factor for HIV transmission was the sexual one (71%), with a similar percentage between heterosexuals and MSM. The predominant age group was between 31-50 years old. Patients born in Italy constituted 88%.
In our population, 63 (68%) were diagnosed with a CD4 cell count below 350 cells/µl. In late presenter group, heterosexuals and MSM showed similar percentages: 37% versus 29%, respectively. However, the prevalence of heterosexual individuals was higher among AIDS-presenters.

— ***Conclusions:*** In the three years of the study we observed a steady number of new HIV diagnosis, in line with European and national data. We observed, instead, a higher number of late presenters in comparison with European data and with national data too; in our experience, this was associated with heterosexual risk.
We found that the principal reason behind a late diagnosis is the unawareness of HIV risk factors; as a consequence, more information on HIV infection and widespread testing are necessary.

— ***Keywords:*** HIV, AIDS, Late presentation, Epidemiology, Sardinia.

INTRODUCTION

The advent of HAART, available in Europe since the mid 1990s, changed the history of HIV infection. The availability of antiretroviral therapy has led to a reduction in the incidence of AIDS events and HIV-related deaths, modifying deeply the course of HIV infection, turning it into a chronic infection.

Unfortunately, these huge improvements have not been associated with analogue enhancements in prevention and early diagnosis[1,2]. In 2014, the number of new HIV diagnosis in Europe was about 30,000, with an incidence rate of 6.4 per 100,000 inhabitants. In the same year, in Italy, there were almost 4000 new diagnosis and they remained stable over the last decade[3].

A big issue on HIV diagnosis is represented by late presentation (LP)[4]. It is known that, across Europe, about half of new HIV diagnosis every year present an advanced stage of infection and, consequently, patients enter in care late. This happens because many people are still not aware of their own serostatus and discover the infection only when an opportunistic disease or another severe HIV-related condition occurs.

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Late diagnosis is an important predictor of life expectancy, as it is associated with a poor response to antiviral therapy, related to a poor CD4+ cell count recovery and a higher risk of disease progression and death[5]; the lack of awareness determines an increase in risky conducts and, consequently, in risk of transmission; furthermore, LP represents a problem in terms of economic burden[6], because of the increased morbidity of these patients in comparison to early diagnosed[7-8]. Early diagnosis of HIV infection is absolutely necessary to reduce the number of patients in a late stage and, consequently, decrease the cited risks for these people[9].

The aim of the study was to evaluate the extent of HIV Late Presentation and to describe demographic and clinical features among Late Presenters in an Italian hospital.

PATIENTS AND METHODS

Eligible for this study were patients above 18 years of age who were diagnosed with HIV at the Unit of Infectious Diseases at SS. Trinità Hospital, Cagliari (Italy), from 1 January 2012 through 31 December 2014. Demographic and epidemiological data, including age, sex, place of birth, mode of HIV transmission and the patient's medical history were taken from the medical records and International Classification of Diseases (ICD) 9 coding recorded in our Unit between 2012 and 2014, through our department database.

LP was defined as an individual diagnosed with HIV with a CD4 count below 350/mm^3 or an AIDS-defining event regardless of the CD4 count, in the six months following HIV diagnosis. LP with advanced disease was defined as an individual diagnosed with HIV with a CD4 count below 200/mm^3 or an AIDS defining event, regardless of CD4 cell count, in the six months following HIV diagnosis. LP with the very advanced disease was defined as an individual diagnosed with HIV with a CD4 count below 50/mm^3 or an AIDS-defining event, regardless of CD4 cell count, in the six months following HIV diagnosis. This is in accordance with the recommendations of the European Late Presenter Consensus working group[10,11].

AIDS was defined as an individual diagnosed with HIV with a CD4 count below 200/mm^3 or an AIDS-defining event, regardless of CD4 cell count.

RESULTS

New HIV diagnosis surveillance system started in Italy on 31th March 2008. Our Hospital (Cagliari, Sardinia) began collecting data in 2012. In our observation, 99 HIV patients were enrolled. Of 99 persons diagnosed with HIV after 1 January 2012, 93 were included in this analysis (94%). Persons were primarily excluded because of missing data on CD4 cells count at HIV diagnosis. In detail, in 2012 we registered 38 new HIV diagnosis (36 with complete data); in 2013 new diagnoses were 34 (32 with complete data), in 2014 were 27 (25 with complete data). The total of men was 75 (81%) and of women was 18 (19%) (Table 1). Median age at diagnosis was 37 years in 2012, 41 in 2013 and 39 in 2014; in more detail, in 2014 heterosexual males had a median age of 40 years, Intravenous Drug Users (IVDU) 39 years, MSM 32 years and women 37 years. Regarding sexual risk factors, the homosexuals (MSM) were 29 (31%), the heterosexuals were 31 (33%) and the bisexuals were 6 (6%). In total, 8 countries of origin were represented in the study population. Patients born in Italy constituted 88% (n = 82), followed by 9% (n = 8) from African continent and 3% (n=3) from South America. African patients were predominantly women (n=5) versus males (n=3). All African men acquired HIV through heterosexual relations. At the time of diagnosis 46/93 (49%) had a CD4 count below 200 cells/µl, 17/93 (18%) had a CD4 count between 200 and 349 cells/µl, 30 (32%) with CD4 counts above 350 cells/µl. The principal reason that induced patients to undergo HIV testing was clinical conditions associated with HIV infection (50%): in most cases, the diagnosis was done during

Table 1. Demographic characteristics in accordance with the CD4+ count at the time of HIV diagnosis.

		CD4 count/µl		
	Total (n=93)	**<200 (n=46)**	**200-349 (n=17)**	**≥350 (n=30)**
Median age, year	**39**	**44**	**37**	**35**
Sex, n (%)				
Men	75 (81)	40 (87)	14 (82)	21 (70)
Women	18 (19)	6 (13)	3 (18)	9 (30)
Risk group, n (%)				
MSM	29 (31)	11 (24)	7 (41)	11 (37)
Heterosexual	31 (33)	17 (37)	6 (35)	8 (27)
IVDU	18 (20)	8 (17)	3 (18)	7 (23)
Unknown	9 (10)	5 (11)	0	4 (13)
Bisexual	6 (6)	5 (11)	1 (6)	0
Country of origin, n (%)				
Italy	82 (88)	42 (91)	14 (82)	26 (87)
Africa	8 (9)	4 (9)	2 (12)	2 (6)
Other	3 (3)	0	1(6)	2 (7)

Table 2. CD4+ cell count characteristics (mean and median) 2012-2014.

	Trend of CD4+ cell count/µl		
	2012	**2013**	**2014**
T0 (baseline)			
Mean	316	251	314
Median	266	219	207
T12 (1 year)			
Mean	437	510	646
Median	436	477	680
Δ media/Δ median	121/170	259/258	332/473

hospital admissions. In the period of study, we observed 9 deaths (10%). All the deaths occurred in Late Presenters. Furthermore, we observed a small population of migrant patients (n=11). Among these, 8 came from Africa and 3 from South America. At the time of diagnosis, 7 patients were Late Presenters (CD4+ count <350 cell/mm^3) with 4 of them having an AIDS-related condition, and 4 patients had a count >350 cell/mm^3.

We analyzed the CD4+ count during triennium and the results are illustrated in Table 2. The mean values in 2012, 2013 and 2014 at baseline (T0) were 316/µl, 251/µl and 314/µl respectively, where the median values were 266/µl, 219/µl and 207/µl. After one year of HAART the mean was 437/µl, 510/µl and 646/µl in 2012, 2013 and 2014 and the median was 436/ µl, 477/ µl, 680/µl respectively.

In 2012 only 4 patients don't achieve the viral suppression, in 2013 were 7 and only 2 patients in 2014 (13/93 patients, 12%).

As regards HAART, all patients started the treatment immediately after the diagnosis. For the most part, our regimens considered the NUC as backbone and principal choice was NRTI in combination with boosted PI (54%), then NRTI in association with NNRTI (30%) and at least 6% is represented by NRTI associated with INI and 10% involved another regimen, like NUC-sparing.

Late Presenters

At the time of HIV diagnosis, 63/93 (68%) patients had a CD4 count below 350 cells/µl (late presenters). Among these, 29 (31%) patients had a CD4 count below 50 cells/µl (LP with a very advanced disease), while 17 (18%) had a CD4 count between 51 and 200 cells/µl (LP with an advanced disease). In the remaining group of patients, 17 (18%) were diagnosed with HIV when they had a CD4 count between 200 and 349 cells/µl (LP). Median age at diagnosis was 41 years in 2012, 43 in 2013 and 42 in 2014; in more detail, in 2014, the heterosexual male had a median age of 47 years, Intravenous Drug Users (IVDU) 38 years, MSM 29 years and women 43 years. The most frequent age group is represented by the decade 40-49. In late presenter group, heterosexuals and MSM showed similar percentages: 37% (n=23) versus 29% (n=18), respectively. All the deaths observed during our 3-year period involved Late Presenters.

AIDS

In our population, 46/93 (49%) patients had an AIDS-defining condition at the time of the HIV diagnosis (Table 3). The percentage of AIDS events remained stable during time: in 2012, 2013 and 2014, 47%, 53% and 48% of new diagnosis were, respectively, in patients with AIDS events. The prevalence of AIDS was significantly higher for men than for women. The most frequent AIDS-defining condition was *Pneumocystis jirovecii* pneumonia. The median age observed during three years of study, remained stable over time: 44 years in 2012, 43 in 2013 and 43 in 2014. In 2014, heterosexual male had a median age of 47 years; we observed only one MSM (32 yrs), two IVDUs (29 and 38 yrs) and two women (40 and 47 yrs).

DISCUSSION

The aim of our study was to evaluate the characteristics of new HIV diagnosed population at the Infectious Diseases Unit of Cagliari, Reference Centre in South Sardinia for Infectious Diseases.

Our results showed a substantial stability in this context during the last three years, both in terms of new diagnosis (a difference of only 9 patients between 2012 and 2014) and of the percentage of people diagnosed with an advanced stage of the infection (65% in 2012 *vs.* 67% in 2014). The first observation is in accordance with European data, which showed a steadiness in the number of new HIV diagnosis in the decade 2005-2014 (the rate of new HIV diagnosis on 100,000 inhabitants ranged

Table 3. Demographic characteristics of LP population in accordance with the AIDS presentation at the time of HIV diagnosis.

	Late Presenters			
	2012 (n=23)	**2013 (n=25)**	**2014 (n=15)**	**TOT (n=63)**
LP in AIDS, n (%)	17 (65)	17 (40)	12 (67)	46 (73)
Men	17 (100)	13 (76)	10 (83)	40 (87)
Women	0	4 (24)	2 (17)	6 (13)
Italy	17 (100)	15 (88)	10 (83)	42 (91)
Africa	0	2 (12)	2 (17)	4 (9)
Other	0	0	0	0

between 6.7 in 2005 and 6.4 in 2014)[12]. In Europe about half of new diagnosis involve late presenters (47%); in our study, we observed a higher percentage, in accordance with Italian LP percentage (>50% in 2014)[1].

Based on our data, it seems important to define strategies to overcome the barriers that limit accessing to HIV testing. A consistent number of individuals avoid being tested, both because they do not consider themselves to be at risk of infection and they often experience the fear of judgment from healthcare workers as well as the society[13-15]. The ECDC guidance for testing invite "normalizing testing" and maybe making it a normal screening could be a relevant way to break down barriers and to decrease stigma perception[16].

Sexual relations still represent the main risk factor for HIV infection. In our general population, MSM and heterosexuals showed almost the same percentages in new infections, on the other hand, if we consider LP, heterosexuality is a much higher risk factor than homosexuality in people with a CD4 cell count below 200 cells (37% *vs.* 24%). This could be explained by a higher awareness of HIV infection among MSM compared with heterosexuals and with a more frequent practice of HIV test[17]. Another concurrent factor is that general practitioners and hospital workers do not often recognize symptoms of HIV, or do not correlate a disease with the possibility that the patient may have HIV infection underneath[18-20]. It is necessary to improve the education of all healthcare providers in order to prevent the late diagnosis of HIV infection and increase the opportunity for these patients to have a better life quality and life expectancy[21,22]. Moreover, early diagnosis reduces the risk of onward HIV transmission. Moreover, it is necessary to improve the quantity and quality of information about HIV infection[23].

As for the migrant population, until 2014 Sardinia was out of the route of entry in Italy; this is proved by the small number of migrants we have diagnosed in the three-year period of our study: we observed only 11 patients, but 7 arrived in a late presentation stage and, among these, 4 were in AIDS. In the first months of 2015, many migrants arrived in our region and the number of new HIV patients is doubled compared with past years; taking into account HIV prevalence in the countries of origin, we believe that a complete screening for migrants at the time of presenting for care, supported by national and regional authority, is necessary in order to have an early diagnosis and to guarantee an adequate healthcare assistance[24].

CONCLUSIONS

Our study describes a regional reality which is in line with a wider national and European framework. Late presentation is an important issue, especially because it is associated with an increased rate of AIDS/deaths. Our study suggests that widespread testing is required and more information about HIV infection is necessary to reduce the fear of discrimination or stigmatization by patients, to learn what the risk factors are and to reduce the incidence of new diagnosis and LP condition.

Conflict of Interests:
The Authors declare that they have no conflict of interests.

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