

## Late presentations among HIV-infected patients

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### ABSTRACT

**Objective:** The late diagnosis of human immunodeficiency virus (HIV) infection and, therefore, initiation of antiretroviral therapy (ART) in the advanced stages of the disease is still a significant problem in many countries. This study aimed to define the prevalence of late presentation and advanced HIV disease among newly diagnosed HIV infected patients.

**Patients and Methods:** The medical records of HIV-infected patients aged 18 and over, diagnosed between January 2011 and December 2019, were analysed retrospectively. The patients were grouped into three-year periods according to the date of diagnosis.

**Results:** Of the 280 patients with HIV infection, 44 (15.7%) were female and 236 (84.3%) were male. It was found that 50.7% of the patients were late presenters, and 28.5% had advanced diseases. There was no statistical difference in the prevalence of late presentation and advanced HIV disease between the three-year periods. While there was no relationship between gender and late presentation, a statistically significant relationship was found between advanced age and late presentation.

**Conclusion:** Despite advances in the diagnosis and treatment of HIV infection, the frequency of late presentation is still quite high, in Turkey. This situation highlights the importance of broad-based HIV screening programs to control the disease more effectively.

**Keywords:** HIV, Acquired Immunodeficiency Syndrome, Late presentation, Turkey

### 1. INTRODUCTION

In 2018, 141.552 newly diagnosed human immunodeficiency virus (HIV) infections were reported from 50 of the 53 countries in the World Health Organization (WHO) European Region. Of these newly diagnosed patients, 79% were diagnosed in Eastern Europe, 16% in Western Europe, and 5% in Central Europe. Turkey is among the fifteen Central European countries, namely Albania, Bosnia and Herzegovina, Bulgaria, Croatia, Cyprus, Czech Republic, Hungary, North Macedonia, Montenegro, Poland, Romania, Serbia, Slovakia and Slovenia. HIV infection prevalence remains relatively low in Central Europe, but the number of new diagnoses is growing faster than in other regions. A total of 6519 patients were newly diagnosed with HIV infection in the central region; 3800 of them were diagnosed in Turkey in 2018 [1].

During the natural course of HIV infection, there is a progressive loss of the CD4 T lymphocyte count, leading to a severe weakening of the infected patients' immune system.

Antiretroviral therapy (ART) alters the natural course of HIV infection and significantly reduces morbidity and mortality [2,3]. However, the late diagnosis of HIV infection and ART initiation in the advanced stages of the disease is still a significant problem in many countries. Late diagnosis of HIV infection has significant consequences both for individuals and society. Morbidity and mortality rates are ten times higher in patients with the late diagnosis than in patients diagnosed in the first year after infection [4]. Besides, long-term outcomes of late diagnosis include an increased risk of neurocognitive impairment and permanent impairment in the restoration of CD4 T lymphocyte count [5]. Also, unawareness of the HIV infection causes an increased risk of transmission in the community and is a critical factor in spreading the disease [6].

This study aimed to define the prevalence of late presentation and advanced HIV disease among newly diagnosed HIV infected patients for a three-year period for nine years.

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## 2. PATIENTS and METHODS

The medical records of HIV infected patients who are eighteen years and older diagnosed between January 2011 and December 2019 at the university hospital were retrospectively analysed for late presentation and advanced HIV disease. According to the diagnosis date, the patients were divided into three groups of three years, including the 2011-2013, 2014-2016, and 2017-2019 periods. Patients whose CD4 T lymphocyte count was not studied before ART initiation were excluded.

Late presentation and advanced HIV disease definitions were based on the European Late Presenter Consensus working group report. Late presentation was defined as a presentation with a CD4 T lymphocyte count below 350 cells/mm<sup>3</sup> or acquired immunodeficiency syndrome (AIDS), defining illness, regardless of CD4 T lymphocyte count. Presentation with advanced HIV disease is defined as a CD4 T lymphocyte count below 200 cells / mm<sup>3</sup> or with an AIDS-defining illness, regardless of CD4 T lymphocyte count [7]. In this present study, patients were evaluated on initial CD4 T lymphocyte count irrespective of their AIDS-defining illnesses.

This study was approved by the university's local ethics committee. (Approval number: B.30.2.ODM.0.20.08/407-475)

### Statistical Analysis

The analyses were performed using the IBM SPSS Statistics 23 software (SPSS; Chicago, IL, USA). Continuous variables between groups were compared with the Mann-Whitney U test or Kruskal-Wallis H test when appropriate. In contrast, categorical variables were compared with Chi-square or Fisher Exact test, when applicable. The statistical significance was defined as  $p < 0.05$ .

## 3. RESULTS

Between January 2011 and December 2019, a total of 280 patients, 44 (15.7%) females and 236 (84.3%) males, were diagnosed with HIV infection.

The mean ages of the newly diagnosed patients in the 2011-2013, in the 2014-2016, and in the 2017-2019 were  $41.4 \pm 11.0$  years,  $36.0 \pm 11.6$  years, and  $38.2 \pm 11.4$  years. The overall mean age of patients was  $38.2 \pm 11.5$  years. There was a significant difference in mean ages between the periods ( $p: 0.033$ ), and the mean age in the 2011-2013 period was significantly higher ( $p: 0.048$ ).

The CD4 T lymphocyte mean counts at the time of diagnosis were  $426.9 \pm 309.7 / \text{mm}^3$  in the 2011-2013 period,  $364.1 \pm 206.0 / \text{mm}^3$  in 2014-2016 period,  $358.5 \pm 248.1 / \text{mm}^3$  in 2017-2019 period, and the overall mean was  $373.8 \pm 251.0 / \text{mm}^3$ . There was no statistically significant difference between the mean CD4 T lymphocyte counts of the periods ( $p: 0.465$ ).

When comparing late and advanced HIV disease presentation prevalence between periods, no statistical difference was detected ( $p: 0.545$  and  $p: 0.252$ , respectively).

There was no statistically significant difference between the patients who applied with late presentation and those with CD4 T lymphocyte count  $> 350$  cells / mm<sup>3</sup> in terms of gender ( $p: 0.091$ ).

The mean age of the late presenters ( $38.8 \pm 11.4$  years) was higher than the mean age of patients with CD4 T lymphocyte  $> 350 / \text{mm}^3$  ( $36.5 \pm 11.9$  years), and the difference was statistically significant ( $p: 0.015$ ) (Table I).

**Table 1.** Demographic and laboratory characteristics of patients according to three-year periods

Periods	2011-2013	2014-2016	2017-2019	2011-2019
Number of patients (n)	56	83	141	280
Mean age $\pm$ SD (years)	$41.1 \pm 11.0$	$36.0 \pm 11.6$	$38.2 \pm 11.4$	$38.1 \pm 11.5$
Mean CD4 T lymphocyte count $\pm$ SD (mm <sup>3</sup> )	$426.9 \pm 309.7$	$364.1 \pm 206.0$	$358.5 \pm 248.1$	$373.8 \pm 251.0$
Prevalence of late presenters	44.6%	49.3%	53.1%	50.7%
Prevalence of advanced HIV disease	26.7%	21.6%	31.9%	28.5%

SD: standard deviation

## 4. DISCUSSION

From 1985 until June 2019, 20,202 HIV infected patients and 1786 AIDS cases were identified in Turkey. Of them, 79.98% were male, and 49.7% of these patients were in the 25-39 years age group [8]. In a study performed at five training hospitals in Istanbul, which the most populous city in Turkey, 829 naive HIV infected patients participated, 84.4% of the patients were male, and the mean age was 37 years [9]. In a study conducted in Ankara, the second-most populous city in Turkey, 255 HIV-infected patients were evaluated. It was reported that 75.6% of the patients were male, and the mean age was 38 years [10]. The gender distribution under male dominance and mean age of HIV-infected patients in our study are comparable to national data.

The mean age of patients diagnosed in the 2011-2013 period in our study was significantly higher than in the later periods, which is thought to be a good indicator of early diagnosis in the last years in terms of early diagnosis. However, it was found that there was no statistical difference in the immunological status of the patients in the following periods.

A recently published study from Istanbul, Turkey, including 1,673 newly diagnosed (86% males, median age: 35 years) HIV/AIDS patients, reported that half of the patients (49.4%) were late presenters and a quarter (25.5%) of the patients presented with advanced HIV disease [11].

High late presentation and advanced HIV disease prevalence have also been reported in studies from European countries. In Greece, among 107 HIV infected patients diagnosed between

2010 and 2018, 49.5% were reported to be late presenters and 33.6% with advanced HIV disease. [12]. More than half (57.6%) of the 3972 HIV-infected patients who followed up in Polish HIV treatment centers between 2000 and 2015 were late presenters, while 35.6% had advanced HIV disease [13]. An Italian cohort study including 19,391 antiretroviral-naïve adults reported that of total patients, 54 % were late presenters, and 37.6 % were with advanced HIV disease [14]. Among the 20,496 patients, 53.9% were late presenters, and 31.2% had advanced HIV disease in a French cohort [15]. European Centre for Disease Prevention and Control (ECDC) 2018 HIV/AIDS surveillance reported that among 15 of the WHO central European Region, including Turkey, 55% of the patients were late presenters and 32% with advanced HIV disease [1]. Although, there were differences in prevalence, our data also supported that generally, at least half of HIV-infected patients were late presenters, and half of them were with advanced HIV disease across Europe and Turkey.

Our study also determined that there was no statistically significant difference in CD4 T lymphocyte mean count in late presentation and advanced HIV disease prevalence between all three-year periods. According to data from a total of 30454 HIV infected patients from 34 European countries, there was no change in late presenters and advanced HIV disease prevalence between 2010 and 2013 [16]. In a study conducted in Belgium in which 687 HIV patients participated between January 2006 and July 2017, 44% of patients found to be late presenters and 24% with advanced HIV disease, and no decrease observed in these prevalences during the study period [17]. In a study conducted in Poland between January 2009 and December 2016, the prevalence of late admission was 62.86%, and admission with advanced HIV disease was 43.20%. The percentage of late presenters remained constant over the period 2009–2015 [18]. In a study of 2,507 newly diagnosed HIV infected patients in Barcelona, Spain, the late presentation prevalences were 62.7% in 2001-2003, 51.9% in 2004-2005, 52.6% in 2006-2007 and 52% in 2008-2009. The study reported that only a decrease was observed between 2001-2003 and 2004-2005, but this ratio remained constant later [19]. Despite all development efforts related to diagnosis and treatment, it is worrisome that European-based studies do not report a significant decrease in late presentation prevalences over the years.

In our study, the mean age of late presenters was higher than the mean age ( $36.5 \pm 11.9$ ) of patients with CD4 T lymphocyte count  $> 350$  cells / mm<sup>3</sup>, and the difference was statistically significant. However, there was no statistically significant difference between these two groups regarding gender. In a review where publications between 1999 and 2010 from fifteen countries in Europe, eight countries in the Asia / Pacific region, eleven countries in North America, and two countries in South America, were evaluated in terms of predictors of late presentation, in all of the studies, advanced age determined as a risk factor for late application [20]. Among HIV-infected patients followed up between 2000 and 2015 in Poland, both the late presentation and advanced HIV disease were significantly associated with older age [13]. Older individuals may be considered to be at low risk for HIV infection by healthcare service providers, or a lower

level of knowledge or risk perceptions about the disease by older patients may be the reason for their diagnosis in the later stages of the disease.

## Conclusion

The findings of our study indicate that, despite advances in the diagnosis and medical treatment of HIV infection, late presentations are quite common and still a significant problem, in Turkey. This situation highlights the importance of broad-based HIV screening programs to control the disease more effectively.

## Compliance with Ethical Standards

**Ethical approval:** This study was approved by the University's Ethics Committee (approval number B.30.2.ODM.0.20.08/407-475). The procedures used in this study adhere to the tenets of the Declaration of Helsinki.

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