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ORIGINAL ARTICLE

AIDS-Defining Illnesses and Mortality in a Cohort of 336 HIV-Infected Patients

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Abstract

Introduction: Human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) continues to be a serious worldwide public health problem despite widespread efforts to control the disease. Today, with the introduction of high-active antiretroviral therapy, AIDS-related mortality rates are significantly reduced and life expectancy for HIV-infected patients has increased. In this study, it was aimed to evaluate AIDS-defining illnesses during the clinical course of HIV infection and the effects of immune status on clinical outcomes.

Methods: The medical records of HIV infected patients who were followed up between January 2005 and November 2018 were retrospectively investigated.

Results: During the study period, 336 HIV-infected patients were followed up. Among 336 patients, 45 (13.3%) had experienced one or more, a total of 59 episodes of AIDS-defining illnesses during follow-ups. Of 45 patients who had experienced AIDS-defining illnesses, 42 (93,3%) were male, the mean age was 41.1±9.7 years and 12 of them were found to have died when this study conducted. The median count of CD4 T lymphocytes and the mean age at the time of diagnosis of 33 alive and 12 died patients were 106 cells/mm3, 40.1±9.9 years, and 94 cells/mm3, 43.9±8.5 years, respectively. There was no statistically significant difference between the median count of CD4 T lymphocytes and the mean age of alive and died patients. The most common AIDS-defining illness was *Pneumocystis jirovecii* pneumonia with 28.8%. The most common diagnosed cause of mortality was AIDS-related carcinomas with 33%.

Discussion and Conclusion: These findings reveal that the most important preventive measure for survival in HIV-infected patients is the early diagnosis of the disease and the initiation of antiretroviral therapy before the emergence of AIDS-defining illnesses due to severe immune deficiency.

Keywords: Acquired immunodeficiency syndrome; AIDS-defining illnesses; CD4; human immunodeficiency virus; mortality.

Acquired immunodeficiency syndrome (AIDS) is the name of the clinical conditions caused by the human immunodeficiency virus (HIV). HIV infection and AIDS continue to be serious worldwide public health problems despite widespread efforts to control the disease[1]. There were approximately 37.9 million HIV-infected people living in the world by the end of 2018[2]. According to the HIV/AIDS surveillance report which has been published jointly by the European Centre for Disease Prevention and Control and the World Health Organization (WHO) Regional Office for Europe, there were 141,552 newly diagnosed HIV infections from 50 countries in the WHO European Region in 2018[3]. Of these newly diagnosed infections, 3800 reported from Türkiye in the same year.[4] Today, with the in-

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troduction of highly active antiretroviral therapy (HAART), AIDS-related mortality rates are significantly reduced, and life expectancy for HIV-infected patients has increased. Between 2000 and 2018, the number of new HIV infections decreased by 37%, and HIV-related deaths decreased by 45%, and 13.6 million lives were saved due to HAART. However, even in industrialized countries, HIV-infected patients continue to have higher mortality rates than the general population. One of the main reasons for this is the negative effect of AIDS-defining illnesses that occur in HIV-infected patients[3,5-8].

This study aimed to evaluate the immun status of patients who had experienced AIDS-defining illnesses during the clinical course and the effects of immune status on mortality.

Materials and Methods

The medical records of HIV-infected patients who were followed up between January 2005 and November 2018 were retrospectively investigated on clinical course, epicrisis, and laboratory data.

An automated electrochemiluminescent immunoassay method (Cobas e411, Roche Diagnostics) was used to detect serologic markers of HIV infection during the study period. The definitive diagnosis of HIV infection was considered as reactive HIV 1/2 antigen/antibodies verified with a confirmatory method (Western blot, line immunoassay, or indirect immunofluorescence) at the central public health laboratory.

Patients who had microbiological, radiological, and/or histopathological supportive findings for an AIDS-defining illness and therefore specific treatment was initiated were included in the study. AIDS-defining illnesses were defined according to CDC's Definitions of Revised Surveillance Case for HIV Infection in 2014[9].

Mann–Whitney U analysis was performed for statistical analysis. The study was approved by the Regional Scientific Ethics committee.

Results

During the study period, 336 HIV-infected patients were followed up. Among 336 patients, 45 (13.3%) had experienced one or more, a total of 59 episodes of AIDS-defining illnesses during follow-ups. Of 45 patients who had experienced AIDS-defining illnesses, 42 (93.3%) were male, and the mean age was 41.1±9.7 years. The median count of CD4 T lymphocytes was 106 cells /mm^3 (min:2, max:798). Twelve of the patients were found to have died during the study conducted. The median count of CD4 T lymphocytes and the mean age at the time of diagnosis of 33 surviving and 12 deceased patients were 106 cells/mm^3 (min:2, max:798), 40.1±9.9 years, and 94 cells/mm^3 (min:14, max:342), 43.9±8.5 years, respectively. There was no statistically significant difference between the median count of CD4 T lymphocytes and the mean age of alive and died patients (p=0.257 and p=0.970, respectively) Figure 1.

The most frequent episodes of the AIDS-defining illnesses were 28.8% *Pneumocystis jirovecii* (previously known as *Pneumocystis carinii*) pneumonia (PCP), 27.1% mycobacterial infections, 13.5% candidal esophagitis, 8.4% Kaposi sarcoma (KS), 6.7% cytomegalovirus (CMV) disease with organ/tissue involvement, 6.7% cryptococcal meningitis, 3.3% lymphoma, 3.3% central nervous system toxoplasmosis, and 1.6% HIV encephalopathy, respectively Table 1.

Of the 12 patients who died, nine of the deaths occurred while being treated at the hospital. The diagnosed causes of the deaths were 33.3% AIDS-related carcinomas (KS in two patients, Diffuse large B-cell lymphoma in one patient), 22.2% pulmonary tuberculosis and toxoplasma encephalitis, 11.1% pulmonary tuberculosis and CMV ventriculitis, 11.1% toxoplasma encephalitis, 11.1% HIV-encephalopathy, and 11.1% acute myocardial infarction Table 2.

Discussion

AIDS-defining illnesses were detected in 13.3% of 336 HIV-infected patients in the study. There are large variations in the rates of AIDS-defining illnesses at the time of diagnosis from different countries. While two studies from Poland and Denmark reported the rates of AIDS-defining illnesses

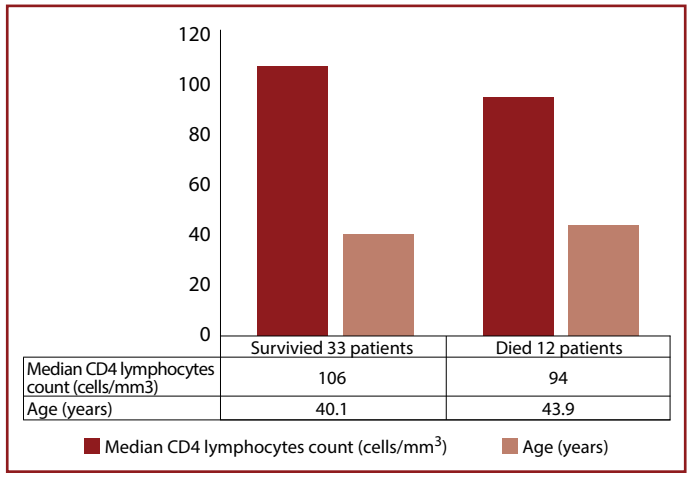

Figure 1. The median CD4 T lymphocyte counts and ages of alive and died patients.

Table 1. The number of episodes and clinical forms of AIDS-defining illnesses

AIDS-defining illnesses	Clinical form	Number of episodes	Percent
Pneumocystis jirovecii infections	Pneumonia	17	28.8
Mycobacterial infections	Pulmonary	11	27.1
	Millier	1	
	Pleurisy	2	
	Central nervous system	1	
	Lymphadenitis	1	
Candidal infections	Esophagitis	8	13.5
Kaposi sarcoma (KS)	Cutaneous	3	8.4
	Lymph node	1	
	Mucocutaneous	1	
CMV disease with organ/tissue involvement	Retinitis	1	6.7
	Colitis	1	
	Ventriculitis	1	
	Encephalitis	1	
Cryptococcal infections	Meningitis	4	6.7
Lymphoma	Diffuse large-cell B lymphoma (DBLC)	1	3.3
	Plasmablastic lymphoma	1	
Toxoplasmosis	The central nervous system (brain)	2	3.3
HIV encephalopathy		1	1.6

Table 2. The causes of mortality among HIV-infected patients

The diagnosed causes of deaths	Number of patients	Percent
AIDS-related malignancies	3	33.3
Pulmonary tuberculosis and toxoplasma encephalitis	2	22.2
Pulmonary tuberculosis and CMV ventriculitis	1	11.1
Toxoplasma encephalitis	1	11.1
HIV-encephalopathy	1	11.1
Acute myocardial infarction	1	11.1

as 8.7% and 14.6% at the time of diagnosis; higher rates reported (25.3% and 33%) from Guatemala and Brazil[10-13]. In two studies, this rate was found to be 44.4% and 22% from Türkiye[14,15]. The different rates determined between the reviews from different geographical regions may be due to the different characteristics of the patient groups constituting the study population, such as the immunological status, the incidence of tuberculosis in the community, access to health-care services, and common transmission routes that pose a risk in terms of the defining illnesses.

In our study, the two most common AIDS-defining illnesses were PCP (28.3%) and mycobacterial infections (27.1%). Pulmonary tuberculosis was the most common form of tuberculosis infection among HIV infected patients. The most-reported AIDS-defining illnesses in studies from Türkiye had been; miliary tuberculosis (40%) and PCP (26%) by Taşdelen-Fışgın et al.,[16] pulmonary tuberculosis (18.4%), and PCP (16.3) by Erbay et al.,[17] pulmonary tuberculosis (25%), and Wasting syndrome (11%) by Kaya et al.[14], candidal infections (12%), and tuberculosis (11%) by Kaptan et al.[18] respectively. In our study, as being the most frequently detected AIDS-defining illness, PCP usually occurs when the CD4 T lymphocyte count is below 200 cells/mm^3. PCP is reported worldwide at varying rates, but mainly affects individuals who are unaware of their HIV infection, diagnosed at a late stage, or who are not regularly cared for HIV infection [19-22]. The studies have reported that about 48–52.4% of HIV-infected patients in Türkiye are diagnosed late (CD4 T lymphocytes <350 cells/mm^3), and 24–30.6% of cases are diagnosed at advanced (CD4 T lymphocytes <200 cells /mm^3 and/or AIDS-defining illnesses) stage of the disease[23,24]. The median count of the initial CD4 T lymphocytes counts of 45 patients with AIDS-defining illnesses was 106 cells/mm^3, which was the most important reason explains that why PCP is the most common AIDS-defining illness in our study. As being the other most common AIDS-defining illness, mycobacterial infections pose a significant problem for public health in both developing and industrialized countries[25]. Globally, it is estimated that about 30% of HIV-infected people have a (usually latent) infection with *Mycobacterium tuberculosis*, this rate varies from 14% in Europe to 46% in South-east Asia[26]. In the 2017 Global Tu-

berculosis Report, HIV prevalence in newly diagnosed and relapsed tuberculosis cases in Türkiye reported ranging from 0 to 4.9%[27]. In our study, the prevalence of tuberculosis among HIV-infected patients was found to be 4.7% in a comparable ratio. Pulmonary tuberculosis was also found to be as the major or as a complicating factor in 33.3% of patients who died during clinical follow-ups. Although national studies have reported different rates of prevalence, tuberculosis is still one of the major causes of AIDS-related mortality and morbidity in Türkiye.

Between 6% and 49% of HIV-infected patients develop some neoplasms during the disease, and KS and non-Hodgkin's lymphomas (NHL) are the most common carcinomas in AIDS-defining illnesses[28-30]. Although the incidence of NHL and KS among HIV-infected patients has decreased during the HAART period, these illnesses are still more common in HIV-infected patients than in the normal population[31,32]. In our study, AIDS-defining carcinomas were detected in 2% of all HIV-infected and 15.5% of patients with AIDS-defining illnesses. The incidence of carcinomas in our patient group is relatively low. As different factors such as genetic characteristics, gender, and environmental factors play a role in the emergence of carcinomas, the incidence may be expected to be different among the patient groups.

Among 45 patients who had experienced AIDS-defining illnesses, 12 (26.6%) were found to have died as of the date of the survey conducted. AIDS-defining carcinomas were the most common causes of mortality with a rate of 33.3%. Opportunistic infections of the central nervous system associated with pulmonary tuberculosis have been the other most common illnesses related to mortality. In high-income countries, the causes of mortality in HIV-infected patients have gradually changed with the prolongation of survival, and a significant proportion of deaths are associated with solid organ cancers, complications related to viral hepatitis, and cardiovascular events[33-35]. The most common causes of mortality were still associated with AIDS-defining illnesses rather than chronic comorbidities in our cohort. The reason for this result may be that the CD4 T lymphocytes counts were significantly low at the time of diagnosis.

Conclusion

In our study, the initial CD4 T lymphocytes median count, both in patients who survived and died, who had experienced AIDS-defining illnesses, was found to be at the level of severe immunodeficiency. The detected causes of mortality were all associated with severe immune deficiency, while the AIDS-defining illness itself was determinative for survival. These findings indicate that the most important preventive measure in HIV-infected patients is the early diagnosis and initiation of HAART before the emergence of AIDS-defining illnesses.

Ethics Committee Approval: From Ondokuz Mayıs University Clinical Research Ethics Committee, Date/Number: 29.06.2020/2020: 438.

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