Opportunistic Infections and Other AIDS-defining Illnesses in Poland in 2000–2002

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Abstract

Background: The introduction of highly active antiretroviral therapy (HAART) led to a decreased incidence of the most severe opportunistic infections (OIs) in HIV-infected patients. In Poland, HAART became widely used in 1998.
Materials and Methods: This study was based on data from medical records data collected in the years 2000–2002 from medical centers for HIV-infected patients in Poland. The aim of the study was to determine the incidence of opportunistic infections (OIs) and other AIDS defining illnesses (ADIs). The χ^2 test was used to determine any significant trends.
Results: The incidence of ADIs was 6.8, 6.5 and 4.8/100 persons/year in 2000–2002, respectively. The most common diagnosed OIs were: fungal infections, tuberculosis, recurrent pneumonia, PCP and toxoplasmosis. In patients receiving HAART (HAART+) the incidence of ADIs was significantly lower than in non-ARV-treated as well as in all HIV+ ($p < 0.02$, $p < 0.001$, $p < 0.001$, respectively). A significant decrease in the incidence of ADIs in HAART+ patients between 2000 and 2002 ($p < 0.0001$) was observed. From 25% to 30% of ADIs among HAART+ patients were diagnosed within the first 3 months of antiretroviral therapy. In HAART+ patients the most common ADIs were fungal infections and tuberculosis. The diagnosis of ADIs resulted in the recognition of HIV status in 8.7–8.9% of patients.
Conclusions: Five years after the introduction of HAART the incidence of ADIs had declined. Fungal infections and tuberculosis were the most common OIs in HIV+ patients in Poland.

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Introduction

The introduction of highly active antiretroviral therapy (HAART) led to a decreased incidence of the most severe opportunistic infections (OIs) in HIV-infected patients [1–4]. In Poland, HAART became widely used in 1998. There are many regional differences in incidence of OIs which reflect the overall epidemiological situation, socio-economic status, differences in distribution of various pathogens, main routes of transmission of HIV and other factors [5, 6].

Aims of the Study

The aims of the study were: (1) to assess the incidence of OIs and other AIDS-defining illnesses (ADIs) in Polish patients in the period of 2000–2002, and (2) to characterize the ADIs occurring in patients receiving HAART.

Material and Methods

Data were collected annually from 2000 to 2002 and originated from the analysis of all medical records. Notifications were made by hospital-based clinicians, involved in the medical care of HIV-infected persons in all ten centers in Poland. Data included information about: number of patients in care and number of patients receiving HAART in each center, all ADIs which occurred during last 12 months, CD4 lymphocyte count and viral load (if available) at ADI diagnosis, exposure to HAART and the

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number of cases when diagnosis of ADI was the cause of recognition of HIV status.

Each patient was designated as being "in the care" of a particular center if at least one visit to an out- or inpatient clinic for HIV-positive persons was recorded. HAART was defined as prescription of at least three antiretroviral (ARV) drugs: two nucleoside inhibitors of reverse transcriptase (NRTI) and at least one protease inhibitor (PI), or two NRTIs and one non-nucleoside inhibitor of reverse transcriptase, or three NRTI, or two PIs boosted by low dose of ritonavir (in selected cases). Patients taking no ARVs were classified as "HAART(–)", while patients who initiated HAART were designated as "HAART+" even if they discontinued ARV therapy. Adherence to prescribed regimens was not evaluated.

AIDS-defining illnesses were diagnosed and recorded according to the CDC 1993 revised classification [7]. Diagnoses of ADIs were established in each individual center and were not verified before including in collection. The χ^2 test was used to determine any significant trends.

Results

From 2000 to 2002, 4,375, 5,016 and 5,156 HIV+ patients were registered, respectively, in all ten centers. Twenty-five percent (in year 2000) to 30% (in year 2002) of them received ARV therapy.

Among all HIV-positive patients "in care" the overall incidence of ADIs was 6.8, 6.5 and 4.8/100 persons/year (100 p/y) in 2000, 2001 and 2002, respectively. The most commonly diagnosed OIs were: fungal infections (mostly esophageal candidiasis), tuberculosis, recurrent bacterial pneumonia, *Pneumocystis jiroveci* pneumonia (PCP) and central nervous system (CNS) toxoplasmosis. Figure 1 shows the number of cases of all ADIs and the percentage of the most common of them.

Among patients receiving ARV treatment, the incidence of ADIs was significantly lower than in HARRT (–) as well as in all HIV+ in care in all analyzed years and reached 4.8; 2.4; 2.2 ADIs/100 p/y ($p < 0.02$, $p < 0.001$, $p < 0.001$). Additionally, there was a significant difference between the incidence of ADIs in ARV+ patients between year 2000 and 2002 ($p < 0.001$). Data regarding the incidence of ADIs among HAART+ and HAART(–) are presented in Figures 2 and 3.

Fungal infections were the most common ADI in HAART+ persons. In this group of patients 25–30% of all diagnosed ADIs occurred within the first 3 months and 30–53.3% during the first year of ARV therapy. No correlation between duration of ARV therapy and probability of ADIs occurrence was found.

In HAART-treated patients, most (62–80%) of the ADIs, occurred when CD4+ lymphocyte count was below 200 cells/mm^3. In the group of patients with good immunological response to ARV therapy (CD4+ lymphocyte count above 500 cells/mm^3) ADIs were diagnosed in two cases in 2000 – one recurrent bacterial pneumonia and one esophageal candidiasis; in 2002 in five patients – two with tuberculosis, two with esophageal candidiasis and one with recurrent bacterial pneumonia; in 2001 there were no ADIs

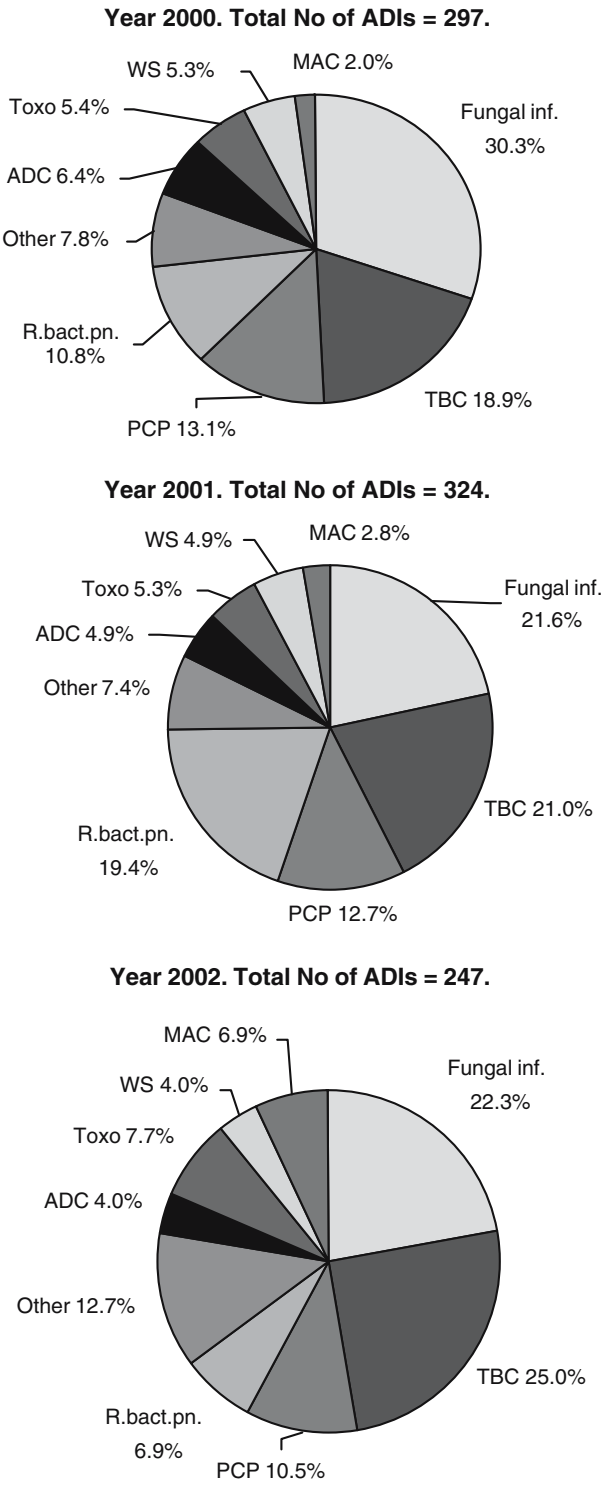

Figure 1. The total number (No.) and the percentage of the most common AIDS-defining illnesses (ADIs) in Poland in 2000–2002. MAC: *Mycobacterium avium* complex infections; ADC: AIDS dementia complex/HIV-encephalitis; HIV-WS: HIV-related wasting syndrome; Toxo: toxoplasmosis of central nervous system; PCP: *Pneumocystis jiroveci* pneumonia; Fungal inf.: fungal infection; R. bact. pn.: recurrent bacterial pneumonia; TBC: tuberculosis.

in persons with CD4+ count above 500 cells/mm³. The CD4+ cells counts and HIV RNA viral load at ADI diagnosis in HAART+ patients are presented in Table 1.

The incidence of HIV-related malignances was low: 0.0–0.18/100 p/y for Kaposi's sarcoma, 0.0–0.27/100 p/y for non-Hodgkin lymphoma and 0.0–0.03/100 p/y for invasive cervical carcinoma. No statistic differences either between particular years or between ARV(–) and ARV+ patients in any year were found.

The diagnosis of ADI preceded the detection of HIV infection in 8.7–8.9% of all newly diagnosed and registered cases in 2000–2002. The most frequent were tuberculosis and PCP.

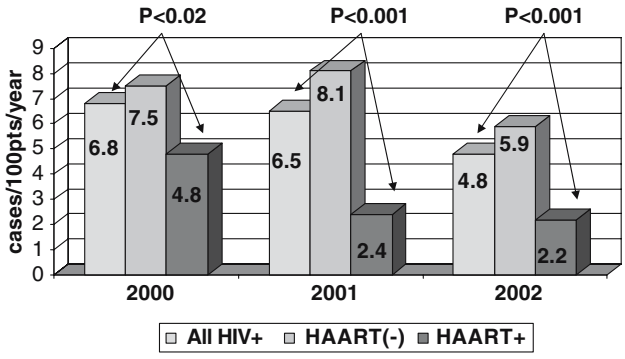

Figure 2. The differences in incidence of ADIs among all HIV+, HAART+ and HAART(–) patients. All HIV+: all patients in care; HAART+: patients receiving HAART; HAART(–): patients without antiretroviral treatment.

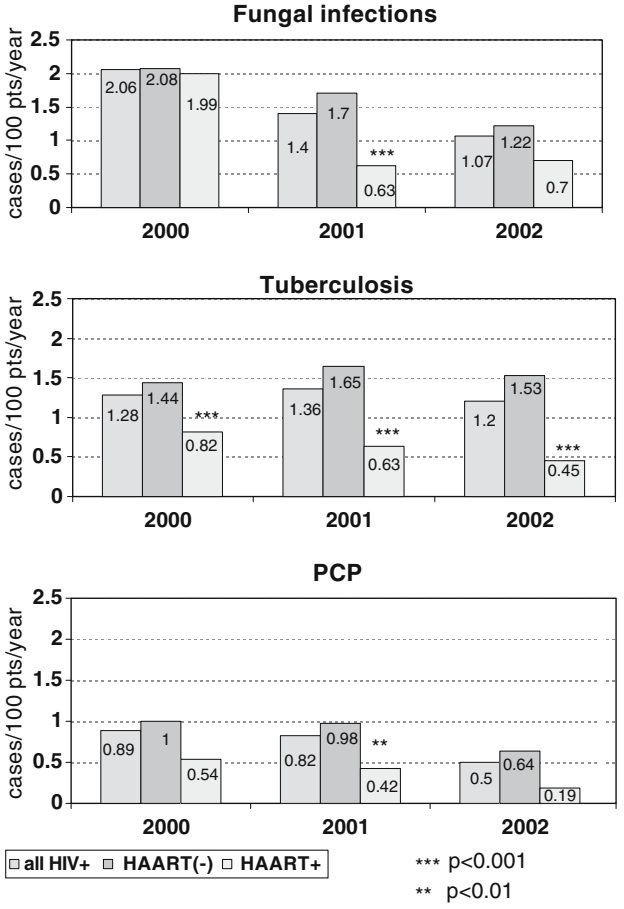

Figure 3. The incidence of the most common ADIs in HAART+ and HAART(–) patients. All HIV+: all patients in care; HAART+: patients receiving HAART; HAART(–): patients without antiretroviral treatment.

Discussion

In Poland, medical care for HIV-infected adults is provided in ten centers with out- and inpatient clinics. In the period analyzed, the proportion of HIV-infected persons provided with specialist medical care was high, reaching over 70% of cumulatively registered cases of HIV infection [8]. Free of charge HAART was available for all patients fulfilling criteria similar to European ARV treatment guidelines [9]. According to data from EuroSIDA, in 2002, proportion of HIV+ patients receiving HAART varied in different regions of Europe (Eastern, Northern, Southern and Central) and ranged through 63–81% [10]. The relatively low proportion of Polish HIV+ patients treated with HAART (25–30%) reflects three facts. First, ARV therapy was generally not offered to active drug-users who in Poland comprise the majority of HIV-infected persons (in 2000, 2001 and 2002 – 63.5%, 62.5% and 60.4%, respectively [18]). Second, according to our data, HIV infection was diagnosed and patients sought specialist medical care quite early, in more than 90% of cases, before progression to AIDS occurred. Third, medical centers for HIV-infected patients very often serve as a primary medical care institutions for people living with HIV, especially, for those living in small towns or rural areas who do not want to disclose their HIV status due to fear of social rejection. These people are therefore "in the care" of HIV centers much earlier than the implementation of ARV treatment is indicated.

Table 1
The CD4+ cells count and HIV viral load at AIDS defining illnesses (ADI) diagnosis in HAART+ patients.

	2000	2001	2002
CD4+ (cells/mm³):			
Average	165	143	244
< 200 (%)	61.2	80	62.1
200–500 (%)	34.7	20	17.2
> 500 (%)	4.1	0	17.2
Not available (%)	0	0	3.5
HIV RNA (copies/ml):			
< 1,000 (%)	32.7	36.7	51.7
> 1,000 (%)	51	56.7	37.9
Not available (%)	16.3	6.6	10.3

Tuberculosis was the most common ADI in 2001 and 2002, and the second most common in 2000; it accounted for 19–25% of all diagnosed ADIs. This fact might have contributed to the pattern that, in Poland, tuberculosis is endemic with a prevalence of 30/100,000 p/y – twice to four times higher than in countries of Western Europe or in the United States of America [11–13]. In contrast, in the developing countries, the proportion of tuberculosis among all OI can be as high as 47% [6]. In Poland, similar to other countries, morbidity due to *Mycobacterium tuberculosis* in HIV+ persons is much higher than in the overall population; and in 2000–2002 it reached, respectively, 1.28, 1.36 and 1.2/100 p/y. In the EuroSIDA cohort, in the era of HAART, the prevalence of tuberculosis was 0.3/100 p/y [14], and in the ASD Project cohort it was 0.5/100 p/y [1]. In parallel with other studies [5, 14–16] in our group the frequency of tuberculosis among HAART+ patients was statistically lower ($p < 0.001$) than in HAART(–) but a steady upward trend was observed in the overall diagnosis of tuberculosis in HIV+ in the all analyzed years.

Regardless of the fact, that the correlation between frequency of particular ADIs and route of HIV infection was not analyzed in our study, the high proportion of recurrent bacterial pneumonia in all ADIs (6.88–19.4%) seems to reflect the predominance of injecting drug-users among HIV+ persons in Poland. Many of those pneumonias occurred in the course of bacteriemia caused by the use of home-made "Polish heroin", produced in septic environments, from poppy straw or the juice of poppy heads and administered intravenously [17].

The extremely low incidence of HIV-related malignancies in our study is contrary to results presented by the ART Cohort [18] and the EuroSIDA [19, 20]. This may reflect the fact that in Western Europe HAART was implemented approximately 2 years earlier than in Poland, and there are more HIV+ patients living with long-lasting HIV infection which can escalate the development of neoplasms.

In patients receiving HAART the ADIs were statistically less frequent than in HAART(–) group ($p < 0.02$, $p < 0.001$ and $p < 0.001$ in 2000—2002, respectively), and in 2002 the overall incidence of ADIs in the HAART+ group was similar to the EuroSIDA and Swiss HIV Cohort Study [3, 19]. Among patients treated with HAART, most (62.1–80%) of the ADIs occurred, when CD4+ counts were below 200 cells/mm^3, and HIV RNA above 1,000 copies/ml (66.3–48.3%). The abovementioned high percentage of drug-users among HIV-infected patients in Poland, with approximately 100% co-infection with HCV in this group [21], may be associated with more rapid clinical progression, toxicity and poor adherence to antiretroviral therapy as well as worse immunological and virological responses than those reported by other authors [22, 23].

Conclusions

Five years after the introduction of HAART the incidence of ADIs had declined. Tuberculosis and fungal infections were the most common OIs in HIV+ patients in Poland.

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