HIV Infection/Acquired Immunodeficiency Syndrome at Siriraj Hospital, 2002 : Time for Secondary Prevention

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The authors retrospectively reviewed the medical records of HIV/AIDS patients who were admitted to the medical service, Siriraj Hospital from January 1, 2002 through December 31, 2002. Demographics, CD4 lymphocyte counts, discharge diagnoses, the incidence of *Pneumocystis carinii* pneumonia (PCP), cerebral toxoplasmosis and cryptococcosis in patients who received and did not receive appropriate chemoprophylaxis against those opportunistic infections when indicated, and outcome of the patients were collected. Three hundred medical records of 286 HIV/AIDS patients were available for review. One hundred and seventy two patients (60.1%) were male. Mean age of the patients was 36.8 ± 9.91 years (range 14-74). The mean CD4 lymphocyte count that was determined in 165 patients was 74.7 ± 134.21 cells/mm^3 (range 0-894). Of the 300 admissions, 36 per cent were newly diagnosed HIV infection. Only 23 (7.7%) patients had received antiretroviral drugs at the time of hospitalization. The leading HIV-related diseases were tuberculosis (29.3%), *Pneumocystis carinii* pneumonia (18.7%), and cryptococcosis (15.7%). The rest of them included cytomegalovirus diseases (6.3%), lymphoma (6.3%), *Salmonella* bacteremia (6%), cerebral toxoplasmosis (5.7%), cryptosporidiosis (5.3%), disseminated *Mycobacterium avium* complex infection (1.0%), extrapulmonary histoplasmosis (1.0%), *Candida* esophagitis (1.0%), progressive multifocal leukoencephalopathy (1.0%), and rhodococcosis (0.7%). Among those for whom HIV infection was established and chemoprophylaxis for PCP, cerebral toxoplasmosis and cryptococcosis were indicated, 9.8 per cent *vs* 28.2 per cent, 3.6 per cent *vs* 5.1 per cent, and 10 per cent *vs* 15.2 per cent of whom received and did not receive the appropriate chemoprophylaxis developed PCP, cerebral toxoplasmosis and cryptococcosis respectively. One hundred and ninety (63.3%) patients were alive at discharge, 84 (28.0%) had died, 21 (7%) were referred to other hospitals, and 5 (1.7%) left hospital against medical advice. The mortality rate in newly diagnosed HIV and in known HIV without antiretroviral treatment were comparable but much lower in known HIV-infected patients who received antiretroviral therapy. Secondary prevention by

detection of HIV-infected patients while they are asymptomatic and providing them with appropriate chemoprophylaxis against specific opportunistic infections as well as appropriate antiretroviral treatment would decrease morbidity, mortality, and improve the quality of life of HIV-infected patients in Thailand.

Key word : HIV Infection, Acquired Immunodeficiency Syndrome, Secondary Prevention, Thailand

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Opportunistic diseases are the most common cause of death in AIDS patients. A series of clinical studies in the late 1980s and through the 1990s led to the conclusion that prophylactic therapy for opportunistic infections (OIs) associated with acquired immunodeficiency syndrome (AIDS) was effective and could, in certain circumstances, prolong life[1]. Guidelines for the management of HIV/AIDS patients in Thailand, 2002 issued by the Ministry of Public Health, Thailand, recommended that prophylaxis for *Pneumocystis carinii* pneumonia (PCP), toxoplasmosis, cryptococcosis and disseminated *Mycobacterium avium* complex (DMAC) infection, should be the standard of care for patients with advanced HIV diseases when CD4 lymphocyte counts were below certain thresholds of risk (< 200 cells/mm^3 for PCP, < 100 cells/mm^3 for toxoplasmosis and cryptococcosis, and < 50 cells/mm^3 for DMAC infection)[2]. The incidence of OIs in patients with HIV infection and AIDS has dramatically decreased in the past several years because of improved recognition of opportunistic disease processes, improved therapy for acute and chronic complications, and the introduction of chemoprophylaxis against key opportunistic pathogens[3-6]. However, many HIV-infected patients have been admitted to Siriraj Hospital, a 2,400-bed university hospital in Bangkok, Thailand, each year. This study was done retrospectively to characterize the nature of HIV-infected patients who were admitted to Siriraj Hospital from January to December 2002.

PATIENTS AND METHOD

Medical records of HIV/AIDS patients (age ≥ 13 years old) who were hospitalized in the medical service, Siriraj Hospital, from January 1, 2002 through December 31, 2002 were reviewed by at least 2 of the authors. The data were collected for demographics, CD4 lymphocyte counts, discharge diagnoses, the incidence of PCP, cerebral toxoplasmosis and cryptococcosis in patients who received and did not receive appropriate chemoprophylaxis against those opportunistic infections when indicated according to national guidelines[2], and outcome of the patients. The list in the 1993 CDC clinical definition of AIDS with the addition of disseminated *Penicillium marneffei* infection was used as an AIDS-defining illness[7]. If the definite diagnosis by histology, or cytology was not possible, the presumptive diagnoses of cerebral toxoplasmosis and PCP was made on the basis of clinical history, physical examination, radiographic findings and response to treatment. Descriptive statistics were used for analysis. Groups of patients were compared with the use of χ^2 analysis. A p-value of < 0.05 was considered significant.

RESULTS

Three hundred medical records of 286 cases of HIV-infected patients were available for review. Fourteen patients were hospitalized twice during the study period. The demographic data are shown in Table 1. One hundred and seventy two patients (60.1%)

Table 1. Demographic characteristics of 300 hospitalized adult HIV/AIDS patients.

Characteristic	No. of patients	%	Mean ± SD	Range	Median
Age (years)	300	100	36.8 ± 9.91	14-74	35
Sex					
Male	172	60.1			
Female	114	39.9			
CD_4 + T cell count (cells/mm^3)	165	57.7	74.7 ± 134.21	0-894	23
HIV status on admission					
Newly diagnosed	108	36			
Known	192	64			

Table 2. HIV/AIDS-related diseases among the 300 hospitalized adult patients.

HIV-related Diseases	No.	%
Tuberculosis	88	29.3
Pneumocystis carinii pneumonia	56	18.7
Cryptococcosis	47	15.7
Cytomegalovirus diseases	19	6.3
Non-Hodgkin's lymphoma	19	6.3
Salmonella bacteremia	18	6.0
Cerebral toxoplasmosis	17	5.7
Cryptosporidiosis	16	5.3
DMAC infection	3	1.0
Candida esophagitis	3	1.0
Extrapulmonary histoplasmosis	3	1.0
Progressive multifocal leukoencephalopathy	3	1.0
Rhodococcosis	2	0.7
Kaposi's sarcoma	1	0.3
Nocardiosis	1	0.3
AIDS dementia complex	1	0.3
Others	63	21.0

DMAC = disseminated *Mycobacterium avium* complex.

were male. Mean age of the patients was 36.8 ± 9.91 years (range 14-74). Of 165 patients for whom CD4 lymphocyte counts were determined, the mean CD4 count was 74.7 ± 134.21 cells/mm^3 (range 0-894). Of the 300 admissions, 36 per cent were newly diagnosed HIV infection who had never received medical care for their illnesses before. Sixty-four per cent of the patients were aware of their HIV. Only 23 (7.7%) patients had received antiretroviral drugs at the time of hospitalization. The HIV-related clinical diagnoses at discharge are shown in Table 2. The leading HIV-related diseases were tuberculosis (29.3%), PCP (18.7%), and cryptococcosis (15.7%). The rest included cytomegalovirus diseases (6.3%), non-Hodgkin's lymphoma (6.3%), *Salmonella* bacteremia (6%), cerebral toxoplasmosis (5.7%), cryptosporidiosis (5.3%), DMAC infection (1.0%), extrapulmonary histoplasmosis (1.0%), *Candida* esophagitis (1.0%), progressive multifocal leukoencephalopathy (PML) (1.0%), and rhodococcosis (0.7%). Overall, 51 (17.0%), 3 (1.0%), and 1 (0.3%) patients had 2, 3, and 4 concurrent HIV-related conditions on admission respectively. Twelve (4%) patients had PCP and tuberculosis co-infections. The incidence of major opportunistic infections (PCP, toxoplasmosis, and cryptococcosis) stratified by chemoprophylaxis is shown in Table 3. Of the established HIV-infected patients for whom chemoprophylaxis against PCP, toxoplasmosis, or cryptococcosis were indicated, 9.8 per cent *vs* 28.2 per cent, 3.6 per cent *vs* 5.1 per cent, and 10 per cent *vs* 15.2 per cent of the individuals who received and did not receive appropriate chemoprophylaxis developed PCP, toxoplasmosis, and cryptococcosis respectively. All of the patients who developed break through cryptococcosis while taking chemoprophylaxis were cases with relapsed cryptococcosis. The outcome of the patients is summarized in Table 4. Of these, 190 (63.3%) patients were alive at discharge, 84 (28.0%) had died, 21 (7.0%) were referred to other hospitals, and 5 (1.7%) left hospital against medical advice. The mortality rate in newly diagnosed HIV, known HIV without highly active antiretroviral therapy (HAART), and known HIV with HAART was 29.6 per cent, 24.5 per cent, and 2.6 per cent respectively.

DISCUSSION

Although the HIV epidemic began more than 20 years ago, the majority of adult HIV-infected patients in Thailand who had a CD4 lymphocyte count of < 200 cells/mm^3 have not received antiretroviral drugs. In the highly active antiretroviral therapy (HAART) era, most HIV-infected patients in the US who need hospitalization are not receiving HAART and have AIDS. The spectrum of diseases which led

Table 3. Incidence of major opportunistic infections in established HIV-infected patients stratified by chemoprophylaxis.

	With chemoprophylaxis	%	Without chemoprophylaxis	%	P-value
PCP	6/61	9.8	35/124	28.2	0.004
Toxoplasmosis	2/55	3.6	6/123	5.1	0.71
Cryptococcosis	4/40	10*	21/138	15.2	0.40

* All were taking secondary chemoprophylaxis to prevent relapsed disease.

Table 4. Outcomes of the patients at discharge.

Outcome	No.	%
Alive	190	63.3
Died	84	28.0
Newly diagnosed HIV	32	29.6
Known HIV without HAART	47	24.5
Known HIV with HAART	5	2.6
Referred	21	7.0
Left hospital against medical advice	5	1.7

to hospitalization has significantly modified over the last 5 years and the number of admissions has decreased. The total rate of mortality and morbidity has also decreased. More than one-third of them were not aware of their HIV status and the diagnosis of HIV infection was determined at the first presentation with HIV-related opportunistic infection[8]. In the present study, the mean age of the patients was 36.8 years which is the productive age group. The median CD4 lymphocyte counts put the patients at risk for common OIs including tuberculosis (pulmonary and extrapulmonary), PCP, extrapulmonary cryptococcosis, and cerebral toxoplasmosis. In the present study, the most common OI is tuberculosis which remains the most common OI among patients with HIV infections in many developing countries (29.3% in the present study compared to 28.9%-41.9% in other Thai studies and 49%-76% in India)[9-14]. The incidence of tuberculosis in the present study was lower than that of HIV-infected patients admitted during 1985-1993 in the same hospital (29.3% *vs* 41.9%)[14]. The use of HAART for the treatment of HIV infection has been associated with a marked reduction in the incidence of most OIs, with an 81 per cent reduction in the risk of tuberculosis[12]. The second most common OI was PCP, the incidence of which was 18.7 per cent compared to 4.8 per cent - 19.8 per cent in other studies[9,14]. The incidence of PCP in the present study was similar to that of a previous study in the same center (17.7%)[14]. In developed countries, the rate of PCP has decreased with routine use of prophylaxis for PCP when HIV-infected individuals have CD4 lymphocyte count below 200 cells/mm^3. The incidence of PCP in Thai AIDS patients remains high probably because of the lack of knowledge about HIV infection and its consequence, late presentation to medical care, lack of chemoprophylaxis for OIs and being inaccessible to HAART. The third leading OI in the present study was extrapulmonary cryptococcosis which consisted of 15.7 per cent compared to 18.5 per cent - 38.4 per cent in other studies[9,11,14]. This number was lower than that of a previous study in the same hospital (20.2%)[14]. Other less common HIV-related conditions included cytomegalovirus (CMV) diseases (6.3% compared to 0.6-3.7% in other studies), non-Hodgkin's lymphoma (6.3% compared to 0.3-0.4% in other studies)[9,11]. There was no reported cases of CMV diseases with only 1 per cent of lymphoma in a previous study of AIDS at the same hopital[14]. The incidence of *Salmonella* bacteremia was 6.0 per cent compared to 0.1-5.9 per cent in other studies[9,11,14]. Other rare HIV-related conditions were DMAC infection, extrapulmonary histoplasmosis, PML, rhodococcosis, and Kaposi's sarcoma, the incidence of which was consistently low in Thai AIDS patients[9,11,14]. Interestingly, there was no patient with penicillosis in the present cohort during the study period whereas the incidence was 3.0-3.7 per cent in other studies[9,11]. The striking difference in the incidence of HIV-related conditions in the present study compared to a study during 1985-1993 in the same center were: cryptosporidiosis, DMAC infection, PML and rhodococcosis were not reported in the previous study; the incidence of non-Hodgkin's lymphoma in the present study was 6.3 per cent compared to 1 per cent in the previous study[14]. Up to 17 per cent of the presented patients had at least 2 HIV-related conditions. The percentage of individuals with

PCP who were co-infected with tuberculosis was 4 per cent compared to 13 per cent-66 per cent in other studies[15]. The rate of established HIV-infected patients who had not received appropriate chemoprophylaxis was unacceptably high (67%, 69%, and 78% for prophylaxis against PCP, toxoplasmosis, and cryptococcosis respectively). The effectiveness of chemoprophylaxis against PCP has been demonstrated in this study (Table 3). The incidence of toxoplasmosis was not different between patients with and without chemoprophylaxis, probably due to a very low event rate. Of those who received chemoprophylaxis against cryptococcosis, none in the primary chemoprophylaxis group developed disease, whereas all patients who developed breakthrough cryptococcosis were in the secondary chemoprophylaxis group. The mortality rate of the patients in the present study was 28.0 per cent compared to 12.3 - 43.3 per cent in other studies[10,11,14] and highest in newly diagnosed HIV and known HIV-infected who had not received HAART but much lower in known HIV-infected patients who had received HAART. Although primary preventive measures to prevent healthy people from HIV infection have been operated at full capacity (i.e., behavior modification, and condom use), there are approximately 15,000 new cases of HIV infection each year. Currently there are at least 400,000 Thai people living with HIV who will gradually become symptomatic in the near future. If we wait for HIV-infected patients to seek medical attention when they become ill, they may be very sick with various kinds of opportunistic infections (as shown in Table 2 and 3) and have a very high mortality rate as demonstrated in the present study (Table 4). Primary preventive measures are not applicable for patients who have already been infected with HIV, thus secondary prevention by identifying asymptomatic HIV-infected patients and providing them with appropriate chemoprophylaxis against opportunistic infections and antiretroviral treatment would drastically reduce morbidity and mortality of HIV-infected patients in Thailand in the near future. Currently, fewer than 5 per cent of persons needing antiretroviral drugs in resource-limited settings have access to these medicines[16]. HAART has reduced the incidence of OIs and extended life substantially. In the area with the highest tuberculosis rates, HAART provides substantial protection against this disease[17]. HAART is the most effective approach to prevent OIs and should be considered for all HIV-infected persons who qualify for such therapy[1,6]. However, certain patients are not ready or able to take HAART, and others have tried HAART regimens but the therapy failed. Such patients will benefit from prophylaxis against OIs. In addition, prophylaxis against specific OIs continues to provide survival benefits even among persons who are receiving HAART[18]. In the era of HAART, on the basis of French data, prophylaxis against PCP, toxoplasmic encephalitis, and *Mycobacterium avium* complex bacteremia is cost-effective[19].

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โรคติดเชื้อเอ็ชไอวี/เอดส์ในโรงพยาบาลศิริราช พ.ศ. 2545 : ถึงเวลาที่จะให้การป้องกันแบบทุติยภูมิ

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การศึกษาแบบย้อนหลังจากรายงานของผู้ติดเชื้อเอ็ชไอวี/เอดส์ที่ได้รับการรักษาตัวในแผนกอายุรกรรมโรงพยาบาลศิริราชตั้งแต่ 1 มกราคม 2545 ถึง 31 ธันวาคม 2545 โดยศึกษาข้อมูลพื้นฐาน จำนวนเม็ดเลือดขาว ซีดี 4 การวินิจฉัยโรคเมื่อจำหน่ายจากโรงพยาบาล อุบัติการณ์ของปอดอักเสบจากเชื้อ *Pneumocystis carinii* สมองอักเสบจาก *Toxoplasma* และโรคจากเชื้อ *Cryptococcus* ในผู้ป่วยที่ได้และไม่ได้รับยาป้องกันโรคติดเชื้อฉวยโอกาสดังกล่าวเมื่อมีข้อบ่งชี้ และผลของการรักษา จากการทบทวนรายงาน 300 รายงานจากผู้ป่วยที่ติดเชื้อเอ็ชไอวี/เอดส์ทั้งหมด 286 ราย พบว่าผู้ป่วย 172 ราย (ร้อยละ 60) เป็นเพศชาย อายุเฉลี่ย 36.8 $\pm$ 9.91 ปี (14–74 ปี) ค่าเฉลี่ยของเม็ดเลือดขาวซีดี 4 ของผู้ป่วย 165 รายเท่ากับ 74.7 + 134.21 เซลล์/ลบ.มม (0–894) จากผู้ป่วยที่ได้รับการรักษาในโรงพยาบาลทั้งหมด 300 ครั้ง ร้อยละ 36 เป็นผู้ป่วยที่เพิ่งได้รับการวินิจฉัยว่าติดเชื้อเอ็ชไอวี ผู้ป่วย 23 ราย (ร้อยละ 7.7) ได้รับยาต้านไวรัสอยู่แล้วขณะที่รับตัวไว้ในโรงพยาบาล การวินิจฉัยโรคที่เกี่ยวข้องกับการติดเชื้อเอ็ชไอวีที่พบบ่อยได้แก่ วัณโรค (ร้อยละ 29.3) ปอดอักเสบจาก *P. carinii* (ร้อยละ 18.7) และโรคจากเชื้อ *Cryptococcus* (ร้อยละ 15.7) การวินิจฉัยโรคอื่น ๆ ได้แก่โรคจาก CMV (ร้อยละ 6.3) lymphoma (ร้อยละ 6.3) การติดเชื้อ *Salmonella* ในกระแสเลือด (ร้อยละ 6) สมองอักเสบจาก *Toxoplasma* (ร้อยละ 5.7) โรคติดเชื้อ cryptosporidium (ร้อยละ 5.3) หลอดอาหารอักเสบจาก *Candida* (ร้อยละ 1) progressive mutifocal leukoencephalopathy (ร้อยละ 1) และโรคติดเชื้อ *Rhodococcus* (ร้อยละ 0.7) ในผู้ป่วยที่ทราบว่าติดเชื้อเอ็ชไอวีอยู่ก่อนแล้วและมีข้อบ่งชี้ในการให้ยาป้องกันปอดอักเสบจาก *P. carinii* สมองอักเสบจาก *Toxoplasma* และเยื่อหุ้มสมองอักเสบจาก *Cryptococcus* พบว่าผู้ป่วยร้อยละ 9.8, ร้อยละ 3.6 และร้อยละ 10 ในกลุ่มที่ได้รับยาป้องกันเปรียบเทียบกับผู้ป่วยร้อยละ 28.2, ร้อยละ 5.1 และร้อยละ 15.2 ในกลุ่มที่ไม่ได้รับยาป้องกันเกิดโรคติดเชื้อฉวยโอกาสดังกล่าวตามลำดับ ผู้ป่วย 190 ราย (ร้อยละ 63.3) ยังมีชีวิตอยู่ขณะจำหน่ายจากโรงพยาบาล 84 ราย (ร้อยละ 28) เสียชีวิต 21 ราย (ร้อยละ 7) ได้รับการส่งต่อไปยังโรงพยาบาลอื่นและ 5 ราย (ร้อยละ 1.7) ไม่สมัครใจรับการรักษาในโรงพยาบาล อัตราตายในผู้ป่วยที่เพิ่งตรวจพบการติดเชื้อเอ็ชไอวี และผู้ป่วยที่ไม่ได้รับยาต้านไวรัสใกล้เคียงกัน แต่ผู้ป่วยที่ทราบว่าติดเชื้อเอ็ชไอวีมาก่อนและได้รับยาต้านไวรัสอยู่แล้วมีอัตราตายต่ำกว่ามาก การป้องกันแบบทุติยภูมิ โดยการตรวจพบผู้ติดเชื้อเอ็ชไอวีในขณะที่ยังไม่มีอาการและให้ยาป้องกันการติดเชื้อฉวยโอกาสอย่างเหมาะสมตลอดจนให้การรักษาด้วยยาต้านไวรัสจะช่วยลดความพิการ อัตราตาย และเพิ่มคุณภาพชีวิตของผู้ติดเชื้อเอ็ชไอวีในประเทศไทย

คำสำคัญ : การติดเชื้อเอ็ชไอวี, โรคภูมิคุ้มกันบกพร่อง, การป้องกันแบบทุติยภูมิ, ประเทศไทย

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