Trends of HIV Seropositivity at Siriraj Hospital: 13 Year's Observation from 1992-2004

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Objective: *The aim of the present report was to observe the trend of seroprevalence rates of HIV seropositivity for routine services at Siriraj Hospital for 13 years.*
Material and Method: *The prevalence rate of HIV seropositivity was analyzed in three groups of subjects: 1) patients who attended the hospital with HIV related diseases; 2) pregnant women at first visit to the antenatal care clinic; 3) emigrating workers who have applied for employment in foreign countries.*
Results: *Of the 13 year-observation, HIV seroprevalence rates in the groups of patients, pregnant women and emigrating workers was 10.6% (95%CI 8.9-12.3%), 2.0% (95%CI 1.8-2.2%) and 0.6% (95%CI 0.4-0.8%), respectively.*
Conclusion: *The low prevalence of HIV seropositivity in the group of emigrating workers may be due to self selection, whereas the prevalence in pregnant women, which was rather consistent at about 2.0%, may represent the infection rate in the general population. The seroprevalence rate measured in the group of pregnant women demonstrates that Thailand should increase efforts to confine the spread of HIV infection in the community.*

Keywords: *Anti- HIV, Thailand, Seroprevalence, Pregnant women, Emigrating workers*

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After the first AIDS case was imported into Thailand in 1984, the Division of Epidemiology, Ministry of Public Health, in collaboration with the Department of Microbiology, Faculty of Medicine Siriraj Hospital, Mahidol University, initiated the first serosurveillance survey. This demonstrated a 1% prevalence of HIV infection in a high risk group of Men who have Sex with Men (MSM)[1,2]. Annual sentinel surveys revealed the occurrence of the first wave of an HIV epidemic among Injecting Drug Users (IDU) was such that the HIV seropositive rate of 1% observed in late 1987 increased to 30% by the end of 1988[3]. Since then, blood screening for HIV infection was initiated among blood donors in Thailand[4]. Around the mid-1990s, the second and third waves of HIV prevalence were demonstrated in Female Sex Workers (FSW) and their male clients, respectively. The fourth wave of the epidemic was the heterosexual spreading of HIV to women and their newborn children in 1991[3,5].

At Siriraj Hospital, blood testing for HIV infection was first conducted in patients in 1985 and in emigrating workers who applied for jobs in the Middle-East or other Asian countries in 1986[4,6]. In 1987, the Department of Microbiology was designated as the WHO Collaborating Centre on AIDS in Southeast Asia[4]. The Centre conducted several related activities including the organizing of several national and international workshops for training laboratory personnel in HIV testing procedures. Siriraj Hospital expanded anti-HIV testing to include pregnant women who attended antenatal care in 1991. Since the years of anti-

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HIV testing service, a variety of anti-HIV test kits have evolved from the first generation of development to the fourth generation. In addition to serological assays for anti-HIV testing, additional techniques have been introduced into routine service such as Polymerase Chain Reaction (PCR) for the detection of the HIV-DNA provirus in 1994, and molecular techniques for quantitative assays of HIV viral load in 1997. Siriraj Hospital is the oldest and the largest hospital in Thailand and probably the third biggest hospital in the world. At present, the hospital accommodates approximately 2,000 in-patient beds and more than 3,000 out-patients a day. The data recorded at Siriraj may well reflect the state of the HIV epidemic in the central region of the country. High prevalence of HIV in heterosexual may consequently spread this throughout other countries in Southeast Asia[7]. Therefore, the present study aimed to report HIV seropositivity of patients, pregnant women and emigrating workers who visited Siriraj Hospital over the past 13 years from 1992-2004.

Material and Method

From 1992 to 2004, the HIV seropositive rate was analyzed in 3 groups of subjects; 1) 264,006 patients; 2) 170,180 pregnant women who attended the Ante Natal Care (ANC) Unit and voluntarily consented to be tested after counseling; and 3) 158,220 emigrating workers who required HIV-free certification for job applications. All sera/plasma were kept at 4-8 C until tested within 18 hours.

During the investigation period, several commercial kit assays with different systems were employed for HIV antibody testing (HIV-1/HIV-2 and/or HIV-1 subtype O) by using; 1) second generation ELISAs (Genelavia mixt, Sanofi Pasteur, France; Innotest, Innogenetics, Belgium; Enzygnost, Behring, Germany; and Vironostika, Organon, Belgium) from 1986 to 1989; 2) third generation ELISAs (Access, Pasteur Institute, France; and AxSYM, Abbott, USA/Germany, Vitros Eci, Ortho-Clinical Diagnostics, USA; CobasCore and Elecsys, Roche, Switzerland; Vidas, Biomeriux) from 1987 up to now; 3) fourth generation ELISAs (Dade, Behring, Germany) since 1998; 4) non-ELISA assays by gelatin particle agglutination test (GPA, Serodia HIV-1, Fujirebio Inc, Tokyo, Japan) from 1986 up to now and rapid assays (Determine, Abbott, USA; Latex, Cambridge, USA) since 1997. In Thailand, all anti-HIV Ab test kits launched in the market have passed an evaluation with Thai blood samples to give a sensitivity of 99.5% and specificity of 98% as per the recommendation from the Thai Food and Drug Administration since 1991[8].

Before 1994, HIV strategy was performed with the first screening assay, using either ELISA or non-ELISA, and confirmed by a Western Blot assay (HIV Blot II, Diagnostic Biotech, Singapore; LAV Bot, Diagnostic Pasteur, France)[4,9]. Testing in our Siriraj Virology laboratory lies within the WHO strategy III: testing for diagnostic purposes[10-12]. The WHO Strategy III is based on the algorithm from the WHO recommendation and the Thai National Guideline for anti-HIV. Therefore, a non-reactive result on the first screening assay will be considered as negative HIV infection, and any reactive result is further investigated with the second and third assays (ELISA or non-ELISA). Concordant results of all 3 tests are considered positive. However, analysis of a second blood sample is recommended in order to avoid any error. An indeterminate result will require a follow-up specimen at 1-6 months later.

Internal controls from kits have been performed in every test run to provide internal quality control. External quality control in combination with an in-house control preparation has been performed in 1998. In addition, external Quality Assessment Program (QAP) or Proficiency Testing (PT) with a panel of serum samples has been provided 2-3 times annually from the Department of Medical Sciences (Thailand), NRL (National Serology Reference Laboratory, Australia), CDC (Centers Disease Control, USA), WRAIR (Water Reed Army Institute of Research, USA) and CAP (College of American Pathologists) since, 1996, 1997, 1998 and 2003, respectively[13]. Number and% HIV seropositive distribution were presented with average ($X \pm SD$) and 95% Confidence Interval (CI).

Results

The data presented herein did not include the results obtained from infants born to HIV infected mothers, the second samples tested for confirmation, and the referral samples from outside Siriraj Hospital. Over the 13 year-period, an average of 20,000 sera/plasma patients was tested annually. The average HIV seropositive rate in routine service was 10.6% (95%CI 8.9-12.3%). The HIV seropositive rate was markedly high in the group of patients particularly during 1993 and 1996 when the prevalence was as high as 16.2% and 15.3%, respectively (Table 1). Nevertheless, a gradual decline of the HIV seropositive rate has been noticed since 1997, a declining to 4.9% was shown in 2004.

The HIV seropositive rate in pregnant women seemed to increase slowly during 1992 to 1999 with the range of 1.2 to 2.5%. However, a trend of a decrease in infection rate was noticed since 2000 (Fig. 1). The

Table 1. Numbers of HIV-1 seropositive samples by years, Siriraj Hospital, 1992-2004

Year	Number of cases (% HIV seropositive)			
	Patients	Pregnant women	Workers	Total
1992	19,240 (11.4)	19,281 (1.2)	12,869 (1.2)	51,390
1993	19,103 (16.2)	20,292 (1.7)	19,326 (1.0)	58,721
1994	20,953 (12.6)	21,079 (2.0)	12,624 (0.7)	54,656
1995	21,055 (13.6)	20,481 (2.0)	12,065 (0.6)	53,601
1996	22,331 (15.3)	17,693 (2.4)	8,301 (1.0)	48,325
1997	18,500 (11.1)	11,796 (2.5)	11,056 (0.9)	41,352
1998	16,820 (11.0)	10,308 (2.1)	15,583 (0.5)	42,711
1999	17,564 (10.6)	9,201 (2.5)	14,954 (0.4)	41,719
2000	24,571 (10.0)	9,188 (2.0)	13,138 (0.3)	46,897
2001	20,690 (8.2)	8,148 (2.0)	8,260 (0.3)	37,098
2002	20,018 (7.4)	7,721 (1.7)	11,827 (0.3)	39,566
2003	20,839 (5.9)	7,620 (1.7)	8,736 (0.2)	37,195
2004	22,322 (4.9)	7,372 (1.6)	9,481 (0.3)	39,175
Total	264,006	170,180	158,220	592,406
($\bar{X} \pm$ SD)	(10.6 ± 3.2)	(2.0 ± 0.37)	(0.6 ± 0.33)	-
Total (average)	20,308 (10.4)	13,091 (2.0)	12,171 (0.6)	45,570
95%CI	8.9-12.3%	1.8-2.2%	0.4-0.8%	-

average rate of HIV infection in the group of pregnant women who received ANC was 2.0% (95% CI 1.8-2.2%) during the 13 years of observation.

The rate of HIV infection in emigrating workers was low with an average prevalence rate of 0.6% (95%CI 0.4-0.8%) over the past 13 years (Table 1). A trend towards a gradual decrease in HIV positivity rate among workers has been observed throughout the study period. Comparative data from all three groups of subjects has shown a trend of the decrease in the HIV infection rate since 2000 (Fig. 2).

Discussion

The first AIDS case was imported into Thailand in 1984[1]. In 1985, the finding of one HIV infected case among 101 MSM caused the authors to predict the spread of HIV among gay men[2]. However, this mode of transmission was not the primary cause of the initial increase in HIV seropositivity. Instead, the first wave of the HIV epidemic occurred amongst IDUs in 1988, followed by the second wave among FSW in 1990, and the third wave in sexually active heterosexual men in 1991[3]. Nevertheless, the finding of indigenous HIV infected cases in 1985 alerted the authors that HIV infection had been silently established in the Thai community[6]. Two subtypes of HIV-1, subtype B and subtype CRF_01 AE (subtype E), have been circulated in Thailand since 1988[14,16]. In the early period of the HIV-1 epidemic, subtype CRF_01 AE infection occurred predominantly among heterosexuals while subtype B was mainly found in IDUs after an explosive spread in 1988. From 1994-1995, it was demonstrated that the heterosexually infected subjects were of subtype E in > 95%. An increase in the prevalence rate of subtype E in IDU infection was also on the increase (from 2.5% in 1988-1989 to 45% in 1994-1995)[16]. Interestingly, not only the changing molecular epidemic of CRF_01 AE in IDU but also CRF01_AE/B recombinants was found[17]. Only some reports of HIV-1 subtype CRF01_AE/B, CRF15_01B and C/CRF01_AE recombinants were documented[18-20]. Therefore, CRF01_AE and subtype B of HIV-1 are still circulating in Thailand until now.

In the present study, the authors report the HIV seropositive rate in the Thai population starting from 1992 (after several waves of HIV epidemic in Thailand, IV drug users, sex workers, male clients, female partners of infected men and infants of infected women)[6]. In 1992, the HIV infection rate in the patients

Fig. 1 HIV-1 seropositive rate among pregnant women by year

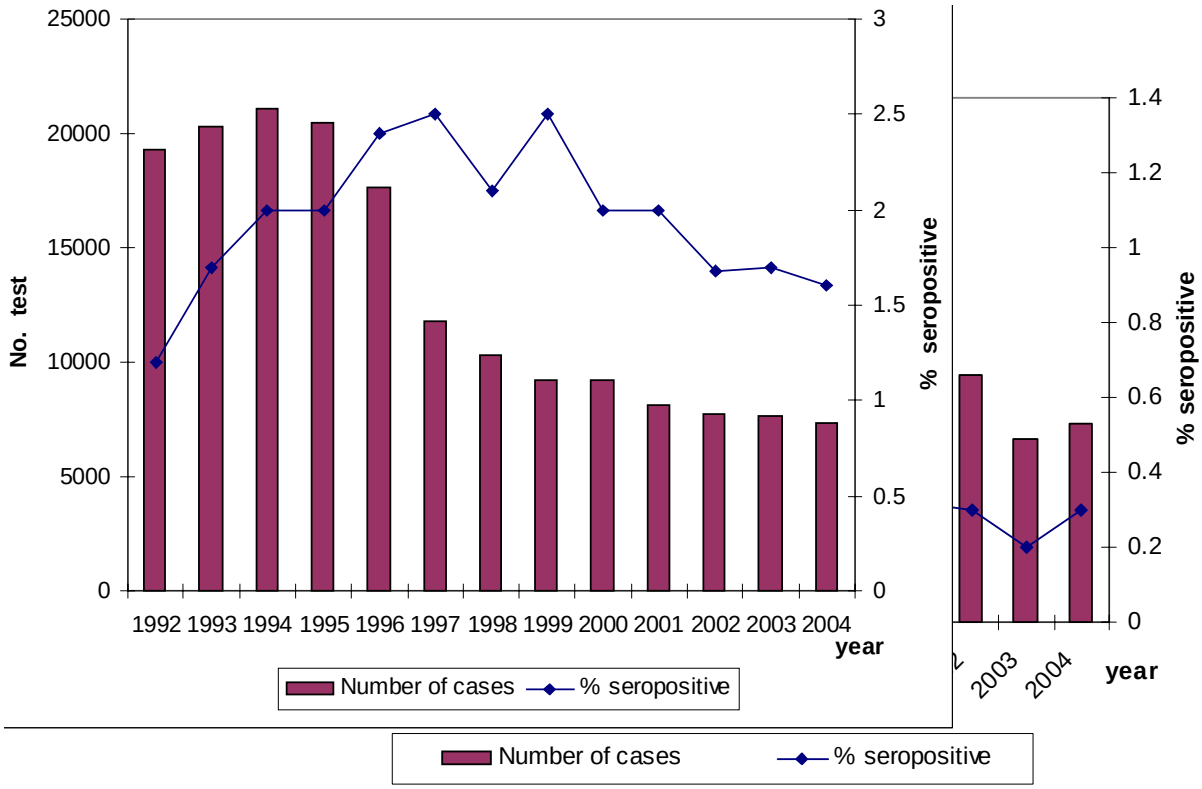

Fig. 2 HIV-1 seropositive rate among emigrating workers by year

who attended Siriraj Hospital was as high as 11%. The prevalence of HIV infection had risen during 1993 (16.2%) to 1996 (15.3%) with some fluctuation in 1994 (12.6%) and 1995 (13.6%), then, slowly declined thereafter. This corresponds to seropositivity data reported for the whole country, where the prevalence of AIDS patients per 100,000 people increased from 3.18 in 1992 to 11.72 in 1993[21]. The number of AIDS cases per 100,000 people linearly increased since then and reached 41.39 in 1996, 44.39 in 1998 and slowly declined thereafter. A sharp decrease of 10.43 AIDS cases per 100,000 people was noticed in 2003 compared to 32.17 in 2002. The situation in the central part of Thailand was also similar, where the prevalence of 43.89 per 100,000 people in 2002 decreased to 14.9 in 2004. The boom of AIDS patients in 1993 after the unrecognized spreading of HIV infection in the country since 1985 suggested that the period of clinical disease progression took about 8 years on average in Thailand.

Previously, only hepatitis B virus and Treponema pallidum was voluntarily screened in pregnant women at Siriraj Hospital. Screening for anti-HIV was initiated in pregnant women who attended the ANC clinic in 1991[22,23]. In Thailand, a second blood sample for retesting was requested from pregnant women who were HIV seropositive at first screening to avoid misdiagnosis. Those who were seronegative were retested during the third trimester of gestation for HIV seroconversion. Excluding data from the second blood sample, a rising in peak of prevalence of HIV infection in pregnant women occurred later than that in the group of patients with AIDS-related diseases. HIV seropositivity among women attending the ANC increased from 0.8% in early 1991 to 2.3% by the end of 1996[24]. The prevalence of HIV infection among this group has declined since 2000. In 2002, the prevalence rate of 1.7% was demonstrated, and it was about the same as the data reported for the country as a whole. It has been notified that the number of pregnant women who attended Siriraj Hospital decreased substantially between 1997 and 1999 according to reconstruction of the Outpatient Clinic, which limited space for the labor room. 7.3% of pregnant women did not receive ANC and thus were not included in the present analysis. Interestingly, the HIV seropositivity rate in this group was as high as 5.7% compared to 2.2% in those who attended the ANC during the same study period[25]. The prevalence of about 2% in pregnant women should be able to represent the HIV infection rate in the general population.

Anti-HIV testing has also been expanded to healthy Thai workers who apply for employment in the Middle East and other Asian countries in 1986, since it was first required that the entry visas would be issued to HIV-free persons only[4]. From the authors' observations, HIV seroprevalence rate among workers was lower (0.6%; 95%CI 0.4-0.8%) than those of pregnant women (2.0%; 95%CI 1.7-2.2%) and was probably due to self-selection.

In Thailand, the HIV vertical transmission rate was reduced from 25% to less than 10% with a combination of zidovudine with other anti-retroviral drugs, and with the use of infant formula to replace breastfeeding[26,27]. As a consequence, the Thai Ministry of Public Health has recommended and successfully implemented a program of antenatal voluntary counseling and anti-HIV testing with a short-course anti-retroviral drug regimen in all provinces since 2000[28,29]. Use of anti-retroviral prophylaxis in HIV infected mothers and their children have been shown to reduce the rate of HIV vertical transmission. Besides a national program to prevent mother-to-child HIV, the 100% condom use program has been extended to all provinces for implementation since 1992[30]. This program will approach the prevention of sexual transmission of HIV as the incidence rate of Sexually Transmission Disease (STD) decreased from 6.5 infections/1000 population to 2.1/1000 in 1989-1992.

Based on the present data, however, HIV infection is still a tremendous problem in Thailand. Although anti-retroviral drug therapy has been expanded to HIV infected cases, there is still a pressing need for a vaccine with protective immunity to provide the ultimate approach to control the HIV infection.

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แนวโน้มการพบ HIV Seropositivity ที่โรงพยาบาลศิริราช: ในระยะเวลา 13 ปีช่วง พ.ศ. 2535 - พ.ศ. 2547

สุดา ลุยศิริโรจนกุล, สนทนา ศิริตันติกร, อุไรวรรณ โฆษิตตานนท์, วรรณี กัณฐกมาลากุล, รวงผึ้ง สุทเธนทร์, ประเสริฐ เอื้อวรากุล, รัตน์ เชื้อชูวงศ์, จันทพงษ์ วะสี, พิไลพันธ์ พุธวัฒนะ

วัตถุประสงค์*: ศึกษาแนวโน้มความชุกของการตรวจพบ HIV seropositivity ในงานบริการ ณ โรงพยาบาลศิริราช ในระยะเวลา 13 ปี*

วัสดุและวิธีการ*: วิเคราะห์อัตราการตรวจพบ HIV seropositivity ในตัวอย่างตรวจจาก 3 แหล่งคือ 1) ผู้ป่วยที่มารับบริการด้วยโรคที่เกี่ยวข้องกับเชื้อเอชไอวีในโรงพยาบาลศิริราช; 2) หญิงตั้งครรภ์ที่มาคลินิกฝากท้อง; 3) ผู้ใช้แรงงานเพื่อไปทำงานในต่างแดน*

ผลการศึกษา*: อัตราการตรวจพบ HIV seropositive ในกลุ่มผู้ป่วย หญิงฝากครรภ์ และ ผู้ใช้แรงงานพบร้อยละ 10.6 (95%CI 8.9-12.3%), ร้อยละ 2.0 (95%CI 1.8-2.2%) และร้อยละ 0.6 (95%CI 0.4-0.8%) ตามลำดับ*

สรุป*: HIV seropositivity ในกลุ่มผู้ใช้แรงงานมีความชุกต่ำน่ามาจากการคัดกรองตนเอง ในขณะที่หญิงตั้งครรภ์มีความชุกของการตรวจพบคงที่ประมาณร้อยละ 2 ซึ่งน่าจะเป็นภาพลักษณ์ของอัตราการติดเชื้อเอชไอวีในประชากร ความชุกในกลุ่มนี้แสดงถึงการติดเชื้อที่ยังสูงอยู่ในประเทศ*
