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■ REVIEW ■

Epidemiology of HIV Infection in the Republic of Korea

Since the first case of human immunodeficiency virus (HIV) infection in the Republic of Korea (ROK) was detected in 1985, 876 HIV-infected patients have been reported, as of December 1998. The male to female ratio was 6.8:1, and 87% of the patients were between 20 and 49 years of age. The major modes of transmission were sexual contacts, accounting for 86% of the cases (65% heterosexuals and 21% homosexuals). Transmission through blood and blood products accounted for 28 cases (3.2%), and vertical transmission for one case. No cases among intravenous drug abusers were reported. The seroprevalence among the blood donors was approximately one in 100,000. Subtypes A, B, C, D, E, and G of HIV-1 have been introduced into the ROK, and subtype B is the most predominant subtype. The frequency of the a deletion in the CCR5 gene, a coreceptor of HIV-1, was less than 1% among Koreans.

Key Words: *HIV; Acquired immunodeficiency syndrome; Epidemiology; Receptors, CCR5; Korea*

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INTRODUCTION

Since the beginning of the acquired immunodeficiency syndrome (AIDS) epidemic in 1981, the number of patients infected with the human inmmunodeficiency virus (HIV) has increased dramatically all over the world. By the end of 1998, more than 13.9 million people had already died of HIV infection, with 2.5 million deaths during 1998 alone. Approximately 40 million people in the world are now living with HIV infection, and AIDS is one of the top five killers worldwide (1).

The center of the AIDS epidemic has been in sub-Saharan Africa, with 22.5 million people living with HIV/AIDS. Until the late 1980s, the Asian continent appeared immune to the AIDS epidemic. However, many Asian countries, led by Thailand, were facing an increasing number of HIV infections by 1992. More than seven million Asians are now infected with HIV, and HIV is spreading very rapidly throughout the continent, especially in India and China. Asia will become a major HIV/AIDS disaster area in the next decade (1).

It has been 15 years since the first case of AIDS was reported in the Republic of Korea (ROK). As of June 1999, the cumulative number of documented HIV-infected patients in Korea was 964, with 208 deaths. The rate of HIV infections remains low in the ROK (population 45 million). In this paper, we reviewed the epidemiology of HIV/AIDS in the ROK.

REPORTED HIV/AIDS CASES IN THE REPUBLIC OF KOREA

Since the beginning of the AIDS epidemic, confirmatory (i.e., western blot) tests for HIV infection have been done exclusively at the Korean National Institute of Health (Korean NIH). If a patient is found to have HIV infection, the Korean NIH report the result directly to the Ministry of Health and Welfare. Here, we analyzed the 876 cases reported to the Ministry of Health and Welfare by December 31, 1998 (Fig. 1).

Case detection

The AIDS Prevention Law was enacted in December 1987. According to the law, screening tests for HIV infection were performed for certain groups, including overseas sailors and those working at restaurants, coffee shops, barbershops, bars, and other entertainment industries. The latter group could get permission to work only when they were free of communicable diseases, including HIV infection. Community health centers provided the HIV testing for this group (Table 1).

Overseas sailors, who were employed as merchant seamen and traveled all over the world, were screened for HIV infection at quarantine laboratories on returning home. This mandatory testing stopped on June 1, 1993. As a result of the mandatory testing, many HIV infec-

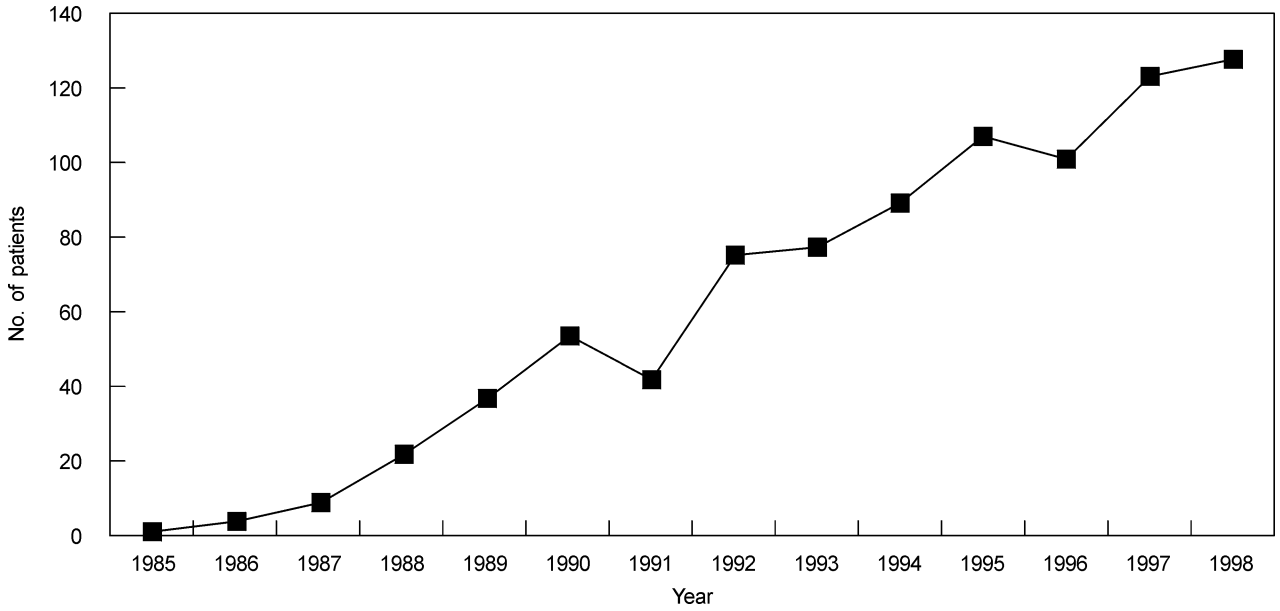

Fig. 1. Number of HIV-infected patients reported annually. Since the first case of AIDS was reported in the Republic of Korea, the number has been increasing year by year. The cumulative number of HIV-infected patients is 876, as of December 1998.

tions were detected among overseas sailors. Indeed, overseas sailors are responsible for 18.4% (161/876) of the HIV infections in the ROK, and 73% (118/161) of them were detected at quarantine laboratories.

Only 18 HIV-infected individuals were detected out of all of the female commercial sex workers tested; three in 1986, five in 1987, three in 1988, one in 1993, two in 1994, one in 1995, zero in 1996, two in 1997, and one in 1998. The decreasing number of cases detected among these individuals suggests that many of the commercial sex workers have gone underground, and are not being tested for HIV infection.

The number of HIV-infected patients detected at clinics and hospitals has been increasing every year. Of the newly reported cases of HIV infection in 1998, 43% (56/129) were detected among patients who visited clinics and hospitals.

Age and sex distribution

Patients between the ages of 20 and 49 accounted for 87% of the total HIV-infected patients, reflecting the

Table 1. Number of HIV-infected patients reported in the Republic of Korea, by detecting institution

	Community health center	Quarantine laboratory	Screening for blood donors	Clinics and hospitals	National Institute of Health	HIV diagnosed in foreign countries	Total
1985	0	0	0	0	0	1	1
1986	3	0	0	1	0	0	4
1987	5	0	1	2	0	1	9
1988	4	7	2	8	0	1	22
1989	1	21	10	4	1	0	37
1990	15	25	11	3	0	0	54
1991	10	18	2	7	5	0	42
1992	30	14	14	15	3	0	76
1993	37	13	11	17	0	0	78
1994	47	9	14	20	0	0	90
1995	50	6	20	30	0	2	108
1996	55	3	17	27	0	0	102
1997	76	0	8	40	0	0	124
1998	44	2	24	56	2	1	129
Total	377	118	134	230	11	6	876
(%)	(43.0)	(13.5)	(15.3)	(26.3)	(1.3)	(0.7)	(100.0)

Source: Ministry of Health and Welfare, Republic of Korea Government

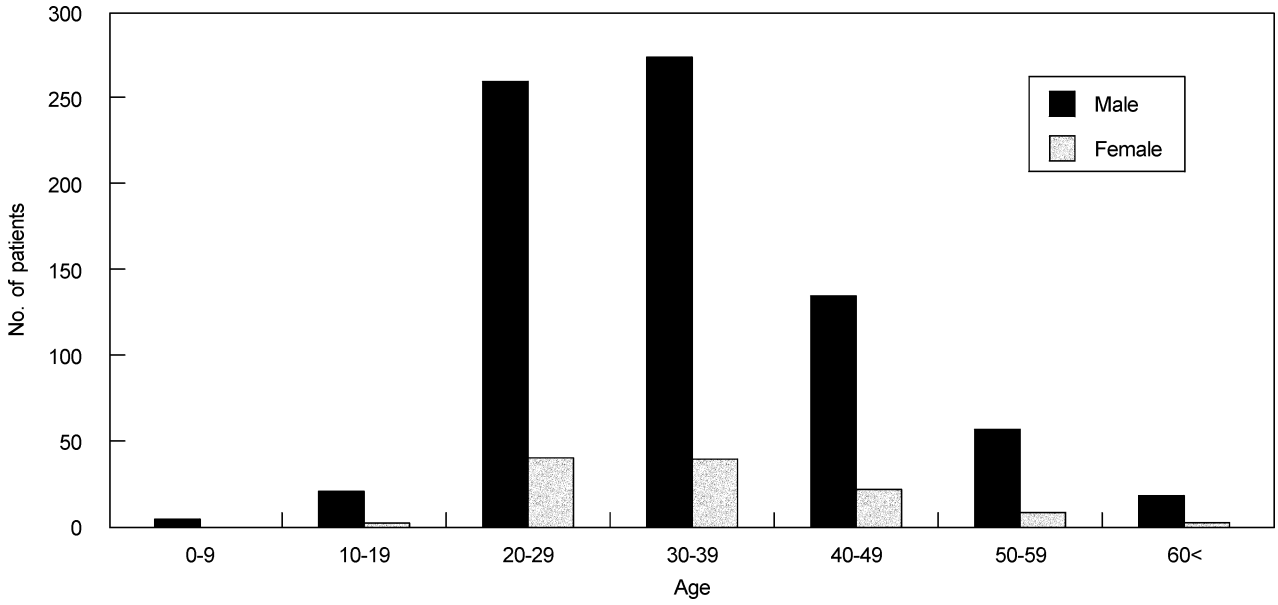

Fig. 2. Age and sex distribution of 876 HIV-infected patients reported in the Republic of Korea. The male to female ratio is 6.8:1, and those between the agos of 20 and 49 accounted for 87% of total patients.

age distribution pattern characteristic for sexually-transmitted diseases. Most of those under 20 years of age were hemophiliacs.

The male to female ratio was 6.8:1 (764 male:112 female). The marked predominance of males may be due to the fact that pre- and extramarital sexual relationships are more common in men than in women in the ROK. The selection bias, such as screening tests for overseas sailors, may also contribute to the predominance of males (Fig. 2).

Mode of transmission

The modes of transmission are shown in Table 2. The major mode of transmission was sexual contact. Heterosexual contacts accounted for 65%, and homosexual contacts for 21%. Of note here is how the mode of transmission was ascertained. Heterosexual transmission was presumed if the patient's sex partner was known to have HIV infection or the patient admitted to having multiple sexual contacts with prostitutes. Homosexual transmis-

Table 2. Number of patients with HIV infection reported in the Republic of Korea, by the mode of transmission

	Heterosexual	Homo/bisexual	IVDU	Blood	Perinatal	Unknown/Other	Total
1985	1	0	0	0	0	0	1
1986	4	0	0	0	0	0	4
1987	6	0	0	3	0	0	9
1988	18	2	0	2	0	0	22
1989	27	7	0	3	0	0	37
1990	48	5	0	1	0	0	54
1991	29	5	0	8	0	0	42
1992	41	26	0	9	0	0	76
1993	54	13	0	5	0	6	78
1994	57	21	0	5	0	7	90
1995	77	20	0	3	1	7	108
1996	52	29	0	0	0	21	102
1997	73	26	0	0	0	25	124
1998	88	37	0	0	0	4	129
Total	575	191	0	39	1	70	876
(%)	(65.6)	(21.8)	(0.0)	(4.5)	(0.1)	(8.0)	(100.0)

IVDU, intravenous drug abuser; Blood, including blood and blood products; Unknown, including cases under investigation
Source: Ministry of Health and Welfare, Republic of Korea Government

sion was presumed only if male patients admitted to having sex with other men. Because homosexuality is culturally unacceptable in the ROK, many homosexuals will not disclose their sexual preferences. Therefore, the rate of heterosexual transmission might be overestimated.

HIV seroprevalence is usually high among intravenous drug abusers, because needle sharing is quite common among these individuals. It might seem surprising that not a single case of HIV transmission through intravenous drug abuse has been documented in the ROK, considering that there is a large number of intravenous drug addicts (probably in the range of 100,000) in the country. However, clean needles and syringes are available at drug stores to anyone in the ROK, and this might explain the low prevalence of HIV infection among intravenous drug abusers in this country.

Transmission through transfusion of contaminated blood accounts for 2% (21/964) of the cases. Of the 21 HIV-infected patients who were infected through blood transfusion, ten were infected domestically and 11 were infected in foreign countries.

The estimated number of hemophiliacs is approximately 1,500 in the ROK. Of those individuals, only 17 have been reported to have HIV infection. The HIV seroprevalence among hemophiliacs in the ROK is relatively low compared to that in other countries. In the ROK, antihemophilic factors produced by a Korean pharmaceutical company have been available since the mid-1980s, and this might have protected Korean hemophiliacs from the possibility of being exposed to HIV-contaminated factors imported from Western countries.

Maternal-to-infant transmission of HIV is quite rare in the ROK. There have been only one documented case of vertical transmission of HIV infection.

SURVEILLANCE DATA

As described previously, some high risk groups were screened for HIV infection according to the AIDS Prevention Law. Because of the selection bias, however, the prevalence of HIV infection in a given group cannot be estimated by analysis of the results obtained from the mandatory testing. Limited data are available on the incidence and prevalence of HIV infection in the ROK.

Prevalence among blood donors

In the ROK, a system of voluntary blood donation has been in place since 1975, and donated blood has been screened for HIV since July 1, 1987. Table 3 shows the number of HIV-infected patients detected among blood donors. The estimated prevalence is approximately one in 100,000 blood donors, and this has not increased over the last ten years. Because young students account for one third of all blood donors, the risk of HIV infection among blood donors is believed to be less than that among the general population.

Table 3. The prevalence of HIV infection among blood donors in the Republic of Korea

Date	No. tested	No. positive	Prevalence (per 100,000 donors)
1987	458,989	1	0.2
1988	999,444	3	0.2
1989	1,046,165	9	1.0
1990	1,154,241	8	0.8
1991	1,161,377	3	0.3
1992	1,204,143	19	1.5
1993	1,540,466	16	0.9
1994	1,635,197	18	1.0
1995	2,007,691	23	1.2
1996	2,145,043	17	0.8
1997	2,323,269	8	0.3
1998	2,485,029	24	1.0

Source: Ministry of Health and Welfare

Prevalence among male military recruits

HIV screening is not compulsory for military recruits. However, many of them have been screened for HIV infection through the blood donation program. Indeed, soldiers account for one third of all blood donors in the ROK, and almost 100% of the military recruits donate blood when they begin their military service. The number of soldiers found to be infected with HIV was zero in 1993, zero in 1994, two in 1995, two in 1996, zero in 1997 and one in 1998. This suggests an estimated prevalence of HIV infection among military recruits of less than one in 100,000.

Prevalence among hospitalized patients

It has been 15 years since the first case of AIDS was reported in the ROK. Many HIV-infected individuals are now expected to develop symptomatic diseases, as they have already passed the clinical latency period of ten years. Indeed, the number of HIV infections detected at clinics and hospitals has been increasing every year.

Table 4 shows the number of patients who were found to be infected with HIV at the Seoul National University Hospital, a 1600-bed, university-affiliated tertiary hospital.

Prevalence among patients with sexually transmitted diseases

Sentinel HIV surveillance of patients with sexually

Table 4. The prevalence of HIV infection among in-patients admitted to the Seoul National University Hospital. Those already known to have HIV infection were excluded

	No. tested	No. HIV ELISA (+)	No. confirmed HIV(+)	HIV (+) per 100,000 in-patients
1992	15,420	23	0	0.0
1993	31,273	48	1	3.2
1994	31,272	23	3	9.6
1995	32,397	28	2	6.2
1996	34,276	26	2	5.8
1997	35,065	24	5	14.3
1998	40,849	23	3	7.4

transmitted diseases is very scanty in the ROK. We screened 530 patients with sexually transmitted diseases who visited STD clinics in Seoul between April 1993 and October 1993, and none of the patients were found to have HIV infection (2).

Estimated number of patients with HIV infection in the ROK

The World Health Organization estimated the prevalence of HIV infection in the ROK to be 0.01%, and the total number of HIV-infected individuals to be 3,100 (1). Ahn YO et al. predicted that the number of patients newly infected with HIV would be approximately 250 in the year 2000, and that this number would remain stable until 2005. They also predicted that the cumulative number of patients infected with HIV would be 2,350 by the end of 2005 (Ahn YO, unpublished data).

MOLECULAR EPIDEMIOLOGY OF HIV

Subtypes of HIV

HIV-1 is classified into two groups, a major "M" group and an outlier "O" group. The "M" group includes at least ten different subtypes (A to J) (3). The geographic distribution of different genetic subtypes of HIV-1 varies from country to country. Subtype B is prevalent in Europe and the United States, and subtype E is prevalent in Central Africa and Thailand. Information on the subtypes of HIV is essential for the development and evaluation of HIV vaccines.

We determined the subtypes of HIV-1 isolated from Korean patients by analyzing the nucleotide sequences of the *env* gene of HIV-1. Of 19 HIV isolates, 18 (95%) fell into subtype B and one (5%) into subtype A (4). Lee JS et al. also determined the subtypes of 35 HIV isolates using a heteroduplex mobility assay. Of the 35 HIV isolates 23 (65.7%) were subtype B, six (17%) subtype A, one subtype C, one subtype D, two subtype E, and two were subtype G (5). GPGR and GPGS were the most predominant tetrameric motifs at the tip of the V3 loop (4, 6). Souza et al. also reported finding five subtype Bs and one subtype A (7). Kang MR et al. analyzed the *nef* gene sequences from 46 Korean patients with HIV-1 infection, and found that A subtypes comprised 7%, B subtypes 89%, and D subtypes comprised 2% (8). These studies suggest that various subtypes of HIV-1 have been introduced into the ROK, and that subtype B is the most predominant of these.

Mutation in the CCR5 gene

The β-chemokine receptor 5 (CCR5) has recently been demonstrated to be a co-receptor for macrophage-tropic HIV-1 strains (9, 10). A 32-nucleotide deletion within the CCR5 gene results in a frame shift, and generates a non-functioning receptor that does not support fusion or infection by macrophage-tropic HIV-1 strains (11). Homozygotes for the deletion have been described in subjects who remain uninfected despite extensive expo-

Table 5. CCR5 genotype frequencies in Koreans

Subjects (No.)	CCR5/CCR5	CCR5/Δccr5	Δccr5/Δccr5
HIV seronegative subjects			
Healthy individuals (239)	239	0	0
Spouse of HIV patients (5)	5	0	0
HIV seropositive subjects			
HIV patients (10)	10	0	0
Spouse of HIV patients (5)	5	0	0
Total	259	0	0

sure to HIV-1 (12).

We studied the frequency of this deletion within the CCR5 gene in Koreans to elucidate whether a high frequency of the deletion is responsible for the low prevalence of HIV-1 infection in the ROK (Table 5). DNA was isolated from the peripheral blood mononuclear cells of 239 (165 male and 74 female) healthy persons not infected with HIV-1, ten HIV-1-infected patients, and the ten (five infected and five non-infected) spouses of the HIV-1-infected patients. All of these subjects were homozygous for the wild type. This suggests that the frequency of Δccr5 was less than 1%, and that factors other than mutation in the CCR5 gene might be responsible for the low prevalence of HIV infection among Koreans (Unpublished data).

CONCLUSION

The rate of HIV infection in the ROK remains relatively low. Cultural, behavioral, or genetic differences may be responsible for the low incidence of HIV infection in the ROK. However, there is no sanctuary from the global spread of the AIDS epidemic. We have already witnessed a rapid increase in HIV-infected patients in neighboring Asian countries, including China, India, and Thailand (1, 13). Sentinel HIV surveillance of high risk groups, such as homosexuals, intravenous drug users, and patients with sexually transmitted diseases are warranted in order to monitor trends in HIV infection.

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