

The Demography, Clinical Manifestations and Natural History of Human Immunodeficiency Virus (HIV) Infection in an Older Population in Singapore

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Abstract

In this retrospective study, we report 43 cases (41 males and 2 females) of human immunodeficiency virus (HIV) infection in the Singapore population aged 50 years and above at first presentation. We found an increasing proportion of these older individuals among our HIV-seropositive patients; from 4.8% in 1991 to 16.7% by mid-1996. The mean age at presentation was 59.2 years (range 50 to 75 years). They were mainly heterosexuals (93%) and the majority (79.1%) were previously or currently married. Thirty-six (83.7%) patients had multiple sexual exposures to commercial sex workers. Nearly all had acquired the infection through the sexual route. The majority (76.7%) were symptomatic at presentation. Common clinical presentations were weight loss (72%), respiratory symptoms (60%) and oral candidiasis (56%). More than half (58.1%) of the patients had acquired immunodeficiency virus (AIDS) at the time of first presentation with a low median CD4 count of 17 cells/mm³. Pneumocystis carinii pneumonia and tuberculosis were the common AIDS-defining diseases. Survival in patients presenting with AIDS (median survival 3 months) is poorer compared to younger HIV-seropositive patients (<50 years; median survival 1 year). No increase in age-related infection or malignancy was seen. Common causes of death were pneumonia and septicaemia. Physicians should consider HIV infection in older patients particularly when he/she presents with unexplained weight loss, respiratory symptoms and oral candidiasis. A history of high-risk sexual behaviour must be sought in all patients, including the elderly.

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Introduction

Early literature on human immunodeficiency virus (HIV) infection and acquired immunodeficiency syndrome (AIDS) have focused on young homosexual men, and intravenous drug abusers. HIV-infected females and children, and the prevention of HIV through vertical transmission have lately garnered much attention. Recent reports have revealed a substantial and increasing number of elderly patients infected with HIV.¹⁻⁷ Separate description or analysis on this group of individuals were few and had originated mainly from the West.¹⁻⁷ In Thailand, out of 22 890 confirmed cases of HIV/AIDS cases, 538 (2.4%) cases were over 60 years of age.² In America, about 10% of the 253 448 cases of AIDS reported up to 1992 were patients more than 50 years of age.³ AIDS has been called the new great imitator of diseases; the presentation of HIV-associated conditions in the elderly can even be more non-specific with their

concurrent medical illnesses and the association of their symptoms with age-related illnesses including occult malignancy, myelodysplasia or Alzheimer's disease. Diagnosis of HIV infection / AIDS in the elderly may be delayed or missed totally if the condition is not considered.^{4,5} We were therefore interested in reviewing the demography, clinical characteristics and natural history of patients aged 50 years and older who were diagnosed with HIV infection in Singapore.

Materials and Methods

The Department of Infectious Diseases at Tan Tock Seng Hospital is the clinical referral centre for all individuals tested seropositive for HIV infection in Singapore. The Department of Clinical Epidemiology manages the national HIV notification registry in Singapore. Patients were identified from a computerised search of all patients aged 50 years and above tested seroposi-

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TABLE I: NUMBER OF HIV INFECTIONS DIAGNOSED IN THE SINGAPORE POPULATION FROM 1985 TO 1996

	'85	'86	'87	'88	'89	'90	'91	'92	'93	'94	'95	'96 (till June)
Total	2	7	10	15	10	17	42	55	64	86	111	60
Number >50 years old	0	2	0	0	0	0	2	4	5	8	12	10
Percentage							4.8	7.3	7.8	9.3	10.8	16.7

tive from 1985 when the first case of HIV infection was detected until June of 1996. Clinical charts were reviewed in this retrospective study. For those who defaulted follow-up, attempts were made to contact them by telephone and admissions to other hospitals were also traced.

Results

Demography

There was a total of 43 patients aged 50 years or older at presentation. An increasing proportion of such individuals presenting with HIV infection or AIDS were noted from 1991 (4.8%) to mid 1996 (16.7%) (Table I). The mean age of these patients at the time of diagnosis was 59.2 years (range 50 to 75 years). Table II shows the racial constitution of these individuals compared with that of the general population. Only 2 of the 43 patients were females. Of the 34 patients who were married, 8 were widowed, 2 were separated, 15 had no sexual relations with the spouse for more than 6 years and only 8 were sexually active with their spouse for the last 2 years at the time of diagnosis; history was unavailable for 1 case. Twelve spouses (all females) were contact traced and tested for HIV infection. The other eleven spouses whose HIV status were not pursued had no sexual contact with their infected husbands for more than 8 to 10 years. Only one spouse was tested seropositive.

Occupation

Of the 35 patients whose previous and current occupations were known, there were 8 drivers, 5 self-employed,

4 labourers, 4 technicians, 3 teachers, 2 clerks, 2 prostitutes, 2 seamen, 2 hawkers and 3 others. Eleven patients were still employed at the time of diagnosis.

Modes Of Transmission

Forty cases were infected through sexual intercourse (Table III). Two were homosexuals and one was a bisexual; all had multiple sexual partners. Of the 2 females, one was the spouse of a patient and the other worked as a prostitute. The remaining 35 heterosexuals had high-risk sexual contacts with commercial sex workers. Thirty of these 35 cases had visited sex workers while overseas. After epidemiological investigations, one was thought to have acquired the infection through a blood transfusion in Florida, USA in the early 1980s. The mode of transmission was undetermined for 2; the history was unavailable for one while the other reported no high-risk behaviour. At least 20 patients had a prior history of other sexually-transmitted diseases as suggested by clinical history taking or a positive serology for syphilis (*Treponema pallidum* haemagglutination test). A positive hepatitis B serology antigen or antibody was detected in at least 20 patients. There was no case of transmission via injecting drug use in our study cohort.

Clinical Manifestations

Clinical AIDS: Twenty-five patients (59.2%) had clinical AIDS at first presentation and 5 of them had more than one AIDS-defining illness at presentation. *Pneumocystis carinii* pneumonia (PCP) (12 cases) and tuberculosis (TB) (5 pulmonary TB and 1 tuberculous lymphadenitis) were the commonest AIDS-defining diseases. There were 3 cases of oesophageal candidiasis (diagnosed by endoscopy), 2 cases of cerebral toxoplasmosis, 2 cases of HIV encephalopathy, and one case each of isoporiasis, cryptosporidiosis, cytomegalovirus disease, *Mycobacterium avium* complex (MAC) bacteraemia, cryptococcal meningitis and high grade B cell lymphoma. The median CD4 cell count was 17 cells/mm³ (range 4 to 830 cells/mm³). Twenty of the 25 cases had CD4 <100 cells/mm³ and only one patient had a CD4 count of >200 cells/mm³. This particular patient has apical pulmonary TB with a high CD4 cell count of 830 cells/mm³. Table IV shows the common presentations of these 25 patients.

Symptomatic HIV infection: Eight patients (18.6%) had symptomatic HIV infection without clinical AIDS and each had at least one of the following signs and symp-

TABLE II: RACE

Race	HIV population	National census
Chinese	86.1%	77.4%
Malay	4.6%	14.2%
Indian	7.0%	7.2%
Others	2.3%	1.2%

TABLE III: MODES OF TRANSMISSION

Mode of transmission	No.
Heterosexual	37
Homosexual	2
Bisexual	1
Blood transfusion	1
Undetermined	2

TABLE IV: COMMON PRESENTING SIGNS AND SYMPTOMS IN THOSE WHO PRESENTED WITH AIDS

Signs and symptoms	No. (%)
Weight loss	18 (72)
Respiratory symptoms	15 (60)
Oral candidiasis	14 (56)
Fever	8 (32)
Diarrhoea	7 (28)
Neurological symptoms	5 (20)

toms viz. weight loss, oral candidiasis, seborrheic dermatitis, diarrhoea and lethargy. The median CD4 cell count was 211 cells/mm³ (range 20 to 351 cells/mm³). Four patients had CD4 <200 cells/mm³ which would put them in the category of AIDS without an AIDS-defining disease.⁸ (At this time, we continue to only notify patients with clinical AIDS.) For those with weight loss, we were unable to assess whether they would satisfy the criteria for wasting syndrome which is an AIDS-defining illness.⁸

Asymptomatic HIV infection: The remaining 10 (23.3%) cases were asymptomatic for HIV infection at presentation. Only two of the 10 patients requested screening on their own because of their high-risk sexual behaviour. Other cases were detected because of the following reasons: recent sexually-transmitted disease (2), spouse of a patient (1), prostitution (1), medical insurance application (1), reported high-risk sexual behaviour with psoriasis (1), autologous transfusion (1) and unknown (1). CD4 cell count was available for 8 patients. The median CD4 cell count was 464 cells/mm³ (range 39 to 641 cells/mm³). Only one had a CD4 cell count of <200 cells/mm³.

Other clinical data: Other interesting clinical data in these 43 patients were as follows: Six patients (17%) had concomitant chronic disease viz. diabetes mellitus and hypertension, 6 cases had clinical evidence of depression, 1 patient subsequently committed suicide and 4 (9.3%) had history of parasuicide after the diagnosis was made. Eight (23%) patients had adverse reactions to drugs; most commonly due to trimethoprim/sulfamethoxazole. Only 4 patients had history of herpes zoster and 2 patients developed psoriasis.

Natural History: Disease Progression and Survival Patterns

Asymptomatic HIV infection: Of the 10 patients who were asymptomatic; 6 cases remained well, 3 defaulted follow-up, one was contacted and he remains well. One patient with diabetes developed oral candidiasis 7 months after diagnosis but remains well at 4 years 2 months. This patient had also received zidovudine (AZT) monotherapy for 3 years. One patient developed AIDS (oesophageal candidiasis) after 4 years and 2 months and died of pneumonia one year later.

Symptomatic HIV infection: In the symptomatic cohort (8 cases), 4 patients progressed to AIDS (2 HIV encephalopathy, 1 cerebral toxoplasmosis and 1 tuberculosis) within 2 to 5 months and 3 had since died. One patient committed suicide 2 years after diagnosis. Four cases were alive at 7 months to 3 years after initial evaluation. Four patients in this group were placed on AZT monotherapy of whom 3, at the time of writing, are still currently alive.

AIDS at presentation: Of the 25 cases who presented with clinical AIDS, 14 had since died. Five died within 1 month of diagnosis. The median survival was 3 months (range 11 days to 19 months). Of those who died within 3 months of diagnosis, none had PCP. The median survival of younger patients (<50 years old) who presented with AIDS was one year (Leo Y S, personal communication). Of the 11 surviving patients, the duration of follow-up ranged from 1 month to 20 months. Nine patients were on anti-retrovirals: 6 were on AZT monotherapy, 1 on didanosine (ddI) monotherapy, 1 on combination of AZT and ddI and 1 on combination of AZT and saquinavir. Six of these 9 patients are presently alive after a median follow-up period of 4 months.

Mortality: Altogether, 19 patients had died as of June 1996. Table V shows the causes of death. It is noteworthy that none of our patients died of PCP (12 cases).

TABLE V: CAUSES OF DEATH

Cause	NO.
Bacterial pneumonia	7
Septicaemia*	4
HIV encephalopathy	3
Cerebral toxoplasmosis	2
Disseminated <i>M. avium</i> infection	1
Tuberculosis	1
Lymphoma	1
Suicide	1
Acute myocardial infarction	1
Total	19

* Includes 2 patients with pneumonia

Discussion

We report an increasing trend of HIV infection in older and elderly men in Singapore. The reason for this increasing trend was not entirely clear. We found that these individuals were sexually active and for those who were married and not widowed, many had no sexual relations with their respective spouse. For some patients, this could be due a spouse's underlying illness. The booming travel industry has also allowed many of these individuals to seek high-risk sexual activities with commercial sex workers overseas.

Many of these patients had presented late in the course of their infection, more than half of them had AIDS at the

time of diagnosis, thereby accounting for early and high mortality. This poor outcome can be improved by early diagnosis and recognition of the early manifestations of HIV infection in the medical community so that effective interventions can be introduced.⁵ Medical practitioners should consider HIV infection / AIDS in the differential diagnosis of ill elderly patients. Moreover, with the availability of at least 8 different anti-retroviral drugs including protease inhibitors in Singapore, combinations of these drugs may improve the morbidity and mortality rates of our HIV-infected patients.

The median age at presentation of our cohort was 59.2 years. There is evidence that older individuals may progress faster to AIDS from the time of seroconversion.¹⁰⁻¹³ Given that the average life expectancy of Singaporeans is 76.4 years,⁹ there is ample time for individuals with HIV infection to progress to AIDS (average 7 years in adults). This information should erase any prevailing attitude among some older men who persist with high-risk sexual behaviour and who had expressed the view that they may die of natural causes before AIDS developed.

In the West, majority (65%) of HIV infection in older men (>60 years old) were acquired from contaminated blood and homosexual contact, although injecting drug use and heterosexual contact were increasingly being reported.^{3,6} In contrast, nearly all our patients had acquired the infection through unprotected heterosexual contact with commercial sex workers. A study found that older heterosexual men (>50 years) at risk for HIV infection are about one-sixth as likely to use a condom during vaginal/anal intercourse as at-risk adults in their twenties.⁷

The spectrum of AIDS-defining diseases in our cohort is similar to other studies and our overall HIV-infected population.¹⁴ PCP is the most common AIDS-defining disease and usually has a satisfactory outcome in our population. We do note that the small numbers in our study cohort may preclude any definitive conclusions. We did not see an increase of malignancy in our elderly patients, although increasing age was found to be associated with a faster progression to neoplasms in one study.¹⁵ In addition, we did not have any case of Kaposi's sarcoma; this is not surprising as this malignancy is often associated with homosexual men with HIV infection or AIDS.¹⁶ Our study population were mainly heterosexual in orientation.

Mortality in our series was high especially in those with clinical AIDS when compared to the younger HIV-infected patients. Several factors could have accounted for this observation. Many of our patients presented late and there could also be possible delay in diagnosis for some cases. Age and the underusage of anti-retrovirals were other possible reasons. Studies have shown

increasing age to be an independent factor that is associated with a more rapid progression to AIDS and death.¹⁰⁻¹³ In a study by Pezzotti et al,¹³ older patients (>35 years) showed a more rapid progression to AIDS independent of exposure categories, sex, CD4 counts, anti-retroviral and prophylactic treatments.¹³ The reason for this observation is not entirely clear but may be related to an age-related decreasing ability of the thymus to generate new CD4 cells.¹⁶ Ship et al³ found that the proportion of AIDS cases diagnosed in the same month as death rises with age, suggesting that there may be a delay in diagnosing HIV infection / AIDS in the elderly. Diagnosis may be delayed as doctors attribute their manifestations to concurrent medical illnesses or age and fail to recognise a HIV-related disease. As an example, one of our cases who had defaulted follow-up at our clinic, presented and died at another hospital, the cause of death was certified as lung carcinoma with brain metastasis. On reviewing his clinical charts and radiographic films, we think that he very likely had died of cerebral toxoplasmosis and pneumonia. Anti-retroviral combination therapy has been shown to increase survival in patients with AIDS. Majority of the patients were not on anti-retrovirals or potent combination therapy. Experience with these medications is limited in this age group and more data will be required to determine if adverse events like bone marrow suppression and peripheral neuropathy would be more common in the elderly.

Our study also raises important issues on the need to provide effective strategies for prevention of HIV infection in this population. Current preventive educational programmes in the media have focused on family values and monogamy. Health-care providers managing elderly patients should take every opportunity to raise issues on sex as well as educate on safe sex practices. Older patients may be more reticent about their sexual history and we should not assume that they are not at risk for HIV infection; instead a complete sexual history should be routinely sought. Sexual history should date back to about 10 years in view of the long asymptomatic phase of the infection. For those who are married, especially women in Singapore, sexual history may also include a private interview with the spouse if there is suspicion of a sexually-transmitted disease. Different people progress at different rates and the spouse may present with an HIV-related illness earlier. We plan to review the clinical records of "serologically untested" spouses of patients who had died recently to ascertain whether they may have died of an undiagnosed HIV-related illness.

In conclusion, our study shows an increasing proportion of HIV infection / AIDS in our population aged 50 years and above with specific demographic data. The prognosis of the illness in this population is poor and

there is a need for early recognition of this infection. Medical practitioners should have knowledge of the common manifestations of HIV infection and consider the infection in older and elderly individuals. Primary prevention programmes of HIV transmission should also be targeted at this population with focus on sexual transmission and safe sex.

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