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Twenty years of clinical human immunodeficiency virus (HIV) and acquired immunodeficiency syndrome (AIDS) in Hong Kong

香港愛滋病毒感染及愛滋病二十年臨床回顧

Objective. To elucidate the development of human immunodeficiency virus (HIV) clinical care and research in Hong Kong.

Data sources. Articles on clinical HIV and acquired immunodeficiency syndrome (AIDS) published from 1985 to 2004 were identified through four sources: Red Ribbon Centre, Special Preventive Programme, Secretariat of the Scientific Committee on AIDS, and PubMed search. The first three are operated by the Centre for Health Protection, Department of Health, Hong Kong.

Study selection. Key words for the literature search were 'AIDS', 'HIV', and 'Hong Kong'.

Data extraction. Only papers with original local data were included.

Data synthesis. Sixty papers were identified. The contents were catalogued under seven areas: clinical epidemiology, HIV disease course and presentation, specific complications or organ-based manifestations, immunological evaluation and other monitoring, antiretroviral therapy, HIV/AIDS mortality, and HIV in specific groups. Prevalence of HIV has remained low in Hong Kong but new infections continue to occur together with a significant number of late presenters. Three published AIDS patients' series, up to the first 200 reported cases, identified *Pneumocystis carinii* pneumonia as the most common AIDS-defining illness in Hong Kong. *Penicillium marneffei* and *Mycobacterium tuberculosis* were two important specific infections studied most; uniqueness of the former in patients of South-East Asia was evident. Local studies of Kaposi's sarcoma and HIV-associated lymphoma have also been reported. Research on CD4 counts has revealed that it is lower in healthy and HIV-infected Chinese than their western counterparts. Children, pregnant women, and haemophiliac patients infected with HIV are among the specific groups of patients studied. Survival of patients with advanced disease has greatly improved over the years, particularly after the advent of highly active antiretroviral therapy.

Conclusion. The clinical presentation and outcome of HIV/AIDS patients in Hong Kong are a mixture of those of western and developing countries. Research on clinical HIV/AIDS in Hong Kong is not only beneficial to the planning of patient care, but also enables the formulation of treatment guidelines and provides a reference for other countries.

目的：探討香港愛滋病毒臨床治理和研究的發展。

資料來源：搜集 1985 年至 2004 年間發表的有關臨床研究愛滋病毒及愛滋病的文章，包括衞生署衞生防護中心轄下的紅絲帶中心、特別預防計劃、愛滋病科學委員會，以及 PubMed 檢索系統。

研究選擇：以「AIDS」，「HIV」和「Hong Kong」為關鍵詞搜集資料。

資料選取：回顧本地原始數據的文章。

資料綜合：共搜集並檢視了60篇文章，內容可劃分為七個範疇：臨床流行病學、愛滋病毒感染的進程和表徵、特定或器官的併發症、免疫和其他的評估、抗逆轉錄病毒療法、死亡率、以及個別患者組別的情況。結果顯示雖然愛滋病在本港的感染率維持偏低，但仍然有新的感染個案，不少病人在後期才被診斷。從三個系列的研究顯示，首 200 名被呈報的愛滋病港人中，肺囊蟲肺炎是最常見的愛滋病界定疾病。馬氏青霉病菌和微小桿菌屬結核病是本地最具代表性的感染併發症，前者在

Key words:
Acquired immunodeficiency syndrome;
Antiretroviral therapy, highly active;
Epidemiology;
HIV infections;
Sexually transmitted diseases

關鍵詞：
愛滋病；
高效抗逆轉錄病毒療法；
流行病學；
愛滋病毒感染；
性傳播疾病

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東南亞病人的獨特性尤為顯著。卡波齊氏肉瘤和與愛滋病毒相關的淋巴瘤亦有文獻記載。研究顯示健康或感染愛滋病毒的中國人的CD4淋巴細胞數量都比西方人為低。兒童、孕婦和血友病患者皆是不少研究所覆蓋的特定人群。近年受愛滋病毒感染 / 愛滋病人的存活率有顯著改善，情況在出現高效抗逆轉錄病毒療法後尤為明顯。

結論：香港的愛滋病感染/愛滋病人的臨床表徵和結果與西方和發展中國家都各有共通點。有關的臨床研究不但有助計劃對本地病人治理的方案和制訂治療指引，亦可供其地方參考。

Introduction

Human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) was first reported in the United States in 1981.[1] It manifested as profound immunodeficiency with a rapidly fatal course. Since then, rapid scientific advances have greatly improved the prognosis of affected patients.[2]

In Hong Kong, the first patient with AIDS was diagnosed in 1984. The HIV infection remains a relatively uncommon condition but its impact on all sectors of society cannot be underestimated. In the health care setting particularly, the diagnosis and management of HIV/AIDS carries far-reaching clinical implications. Clinical expertise has rapidly evolved, new standards have been established, and lessons have continued to be learned. Hong Kong has strived through a long way in its provision of high-quality HIV care services. In preparing for the challenge of the third decade, we set out to review the literature from Hong Kong to determine the clinical characteristics of HIV/AIDS and the development of clinical care for people living with the infection locally.

Methodology

All retrievable papers that concerned clinical HIV/AIDS in Hong Kong, published between 1985 and 2004 in peer-reviewed journals, were reviewed. Articles were identified through four sources: (1) collection at the Red Ribbon Centre; (2) publication list maintained by Special Preventive Programme; (3) stock-taking exercise conducted by the Secretariat of the Scientific Committee on AIDS in September 2004; and (4) the PubMed search using the key words 'AIDS', 'HIV', and 'Hong Kong'. The first three sources are operated by the Centre for Health Protection, Department of Health, Hong Kong. All published articles in English or Chinese with local data on the subject were included, irrespective of their sources from indexed or non-indexed journals. Review articles and abstracts without original local data were excluded, regardless of author origin. A total of 60 papers were reviewed and their scope classified as follows: (1) clinical epidemiology, (2) HIV disease course and presentation, (3) specific complications or organ-based manifestations, (4) immunological evaluation and other monitoring, (5) antiretroviral therapy, (6) HIV/AIDS mortality, and (7) HIV in specific groups.

HIV in Hong Kong

In 1998, over 1100 HIV-infected patients had been reported, of whom 372 had progressed to AIDS.[3] Haemophiliacs were among the first patients to be infected in mid-1980s. Subsequently most infection arose through sexual contact, with infection in drug users still rare. At the time, there was concern that the apparently low HIV prevalence may signal a pre-epidemic, given the presence of an ongoing risk behaviour, and that this would have a major impact on local AIDS programmes.[3] The lack of an ageing cohort effect on the prevalence of sexually acquired infection in Hong Kong provided further cause for concern.[4] Ongoing new infections, rather than past but longstanding infections, continued to occur as evidenced by a 'flat' median age of 31.5 to 36.0 years among the 1215 heterosexually or homosexually infected patients reported from 1987 to 2000.[4]

A substantial proportion of HIV patients was characterised by late diagnosis. In a study of reported HIV infection from 1984 through 2000,[5] some 24% to 52% of patients fulfilled one or more of the late diagnostic criteria: progression to AIDS within 3 months of HIV diagnosis, CD4 count of lower than 200 /μL at diagnosis of HIV, and HIV diagnosed in hospital. This phenomenon did not seem to improve over a course of 15 years. Late diagnosis of the disease may have been partly due to patients' risk perception. In a survey of 84 Hong Kong Chinese patients who first attended the government HIV clinic in 1995,[6] 70.3% perceived little or no risk of HIV infection before the diagnosis was confirmed. Many were prompted to be tested for HIV only when they presented with a sexually transmitted infection or after they had developed clinical complications.

The advent of molecular technology enabled tracking of the source and spread of HIV. A study of HIV-1 subtypes in patients reported from 1999 to 2001 revealed that B and CRF01_AE were the predominant strains in Hong Kong.[7] When compared with the prevalent subtypes in Mainland China, there did not appear to be an epidemiological link between infection in the two areas. Understandably this was a dynamic situation. A growing diversity of HIV subtypes and the detection of new strains suggested that the epidemic might have started to change its course.

HIV presentation and disease course

The HIV disease is characterised by an acute, or primary, viral infection followed by the establishment of chronic infection. Diagnosis can be made at different stages depending on the manifestations of the infection, health-seeking behaviour of the patient, and awareness of health care providers. The first report of primary HIV infection in

Hong Kong was a patient who presented with classical symptoms of fever, lymphadenopathy, generalised skin rash, and aseptic meningitis in 1996.[8] A heightened awareness could enable early detection of acute infection and improve clinical management and public health responses. Nonetheless HIV continued to be diagnosed in infected patients at a late stage. Several case series of AIDS patients in Hong Kong have been published that illustrate the different clinical presentations.[9-12]

The first case series concerned 22 AIDS patients seen from 1985 to mid-1989.[9] The most frequent presenting symptoms related to respiratory, gastro-intestinal, and neurological involvement. During this early history of the disease, survival was poor: the median survival after AIDS was only 3.5 months. Survival was better in patients with a higher CD4 count and a longer HIV-AIDS interval. Analysis of data from the first 100 AIDS patients reported in Hong Kong up to March 1994 indicated that the overall disease pattern was similar to that in western countries. *Pneumocystis carinii* pneumonia (PCP) was the most common primary AIDS-defining illness (ADI) and occurred in 46% of patients.[10]

When the second 100 AIDS patients in Hong Kong were compared with the first 100, several differences became evident. The second 100 cases were reported over a much shorter period than the first 100: 26 months compared with 122 months.[11] This suggested the occurrence of a rapidly rising number of new infections in the community. The proportions of Caucasians and men who had sex with men (MSM) fell in the second 100 patients. Although PCP remained the most common primary ADI, the incidence of tuberculosis (TB) and *Penicillium marneffei* increased.[11] Opportunistic infections arising as a result of immunosuppression related to HIV were clearly the most common presentation of infected patients. A study of opportunistic infections in Hong Kong patients in the 10 years before 1994 indicated that the disease profile in Chinese patients appeared slightly different from that of non-Chinese (largely Caucasian) patients.[12] In terms of all ADI, TB, cytomegalovirus diseases, and penicilliosis occurred more frequently in Chinese patients whereas PCP, toxoplasmosis, and cryptosporidiosis were more common in non-Chinese population. Herpes zoster and oral candidiasis were the most frequently encountered non-ADI opportunistic infections.[12]

Specific complications or organ-based manifestations

Following the identification of AIDS in Hong Kong, *P marneffei* became recognised as a prominent opportunistic pathogen. The first case of penicilliosis was reported in 1985 in a 53-year-old patient with prolonged pyrexia, unresolved lobar pneumonia, cervical lymphadenopathy, generalised subcutaneous abscesses, and pericardial effusion.[13] Immunological evaluation demonstrated depressed T cell number, reduced T helper count, and reversed T helper/suppressor ratio. The patient went on to develop disseminated cutaneous zoster and *Salmonella* osteomyelitis. In retrospect, this was highly suggestive of an AIDS case although no HIV antibody test result was reported. In Hong Kong, *P marneffei* infection, which is often the presenting disease in HIV-infected patients, has been reported to present as a solitary pulmonary nodule,[14] colitis,[15] or oral ulcers.[16] Nonetheless disseminated penicilliosis remained the most common manifestation, with involvement of multiple organs or systems such as the lymph nodes, liver, lung, intestine, and bone marrow.[17,18]

Examination of bone marrow aspirate for engorged histiocytes with the characteristic round-to-oval intracytoplasmic inclusions that contain purplish dot-like structure and, sometimes, transverse septum proved to be a useful investigation for diagnosing *P marneffei* in AIDS patients.[19,20] Compared with HIV-negative patients, serum antigen titres by a *P marneffei*–specific mannoprotein Mp1p enzyme-linked assay were higher in HIV-positive patients.[21] Their response to antifungal treatment with intravenous amphotericin followed by oral itraconazole was good but death occurred quickly after presentation if therapy was delayed or not started.[17,18] In 1992, because of the associated morbidity and mortality in HIV-infected patients in South-East Asia, *P marneffei* was proposed as an ADI in the region.[22] About 10% of the primary and 5% of subsequent ADI from 1990 to 1997 in Hong Kong were attributed to penicilliosis.[23]

Mycobacterial infections are other important diseases in HIV/AIDS patients in Hong Kong. *Mycobacterium tuberculosis* has become more common since the 1990s.[24] In 1994, *Mycobacterium avium* complex (MAC) was reported the most common MOTT (mycobacterium other than TB) associated with a poorer outcome than TB.[24] In a study of the clinical features of 60 TB/HIV-coinfected patients, 37% had only pulmonary TB, 13% had extrapulmonary disease, and 50% had both pulmonary and extrapulmonary involvement.[25] Nearly 40% had primary TB radiographic patterns such as air-space consolidation at the middle/lower lobes and pleural effusion. Patients with disseminated TB had a significantly lower CD4 count than those with pulmonary involvement alone (mean, 40 /μL vs 102 /μL; P=0.048).[25] In a retrospective review of 5757 TB patients treated in Hong Kong in 1996,[26] six were also confirmed HIV-positive. Extrapulmonary TB (22.3%) was not related to HIV infection in this study.[26]

In a study of patients seen before 1994 at Queen Elizabeth Hospital, cryptococcal meningitis was the most frequent neurological manifestation of AIDS.[27] Extraneural involvement occurred in half of the patients with cryptococcosis and most had multiple sites affected.[28] Like penicilliosis, this major fungus could also be effectively diagnosed by bone marrow examination in the case of systemic infection.[29] Cytomegalovirus retinitis was the

diagnosis in 70% of 10 consecutive patients with visual symptoms referred to the Hong Kong Eye Hospital between 1991 and mid-1993. Retinal detachment was a frequent complication, and occurred in one patient at presentation and four other patients despite ganciclovir or foscarnet therapy.[30]

Oral manifestations of HIV have been systematically studied in Hong Kong patients. Over a period of 1 year, 3-monthly follow-up of 32 patients (94% Chinese) referred to the University of Hong Kong revealed that 24 developed one or more oral pathology.[31] The most common oral lesion was minor aphthous ulceration (27.4%), followed by xerostomia (17.8%), and oral thrush (12.4%). While the disease pattern was similar to that reported overseas, the frequency of oral lesions appeared to be lower.[31] Using an oral rinse method, the most common yeast and Enterobacteriaceae carried in the oral cavity in the same HIV-infected cohort were identified as *Candida albicans* and *Enterobacter cloacae*, respectively.[32]

In addition to opportunistic infections, malignancy is a major opportunistic complication in patients with HIV/AIDS. In an early study of HIV-related Kaposi's sarcoma, all patients had acquired HIV via a sexual route, with the majority being MSM.[33] Skin manifestation alone occurred in all but one patient who also had gastro-intestinal involvement. Death was not uncommon but none was directly related to Kaposi's sarcoma.[32] Lymphoma is the second most common malignancy in HIV infection. Of 10 patients seen at Queen Elizabeth Hospital from 1995 to 2001 with HIV-associated lymphoma at a median CD4 count of 56 /μL, nine had diffuse large B-cell lymphoma and one systemic Burkitt-like lymphoma.[34] The overall survival was poor with conventional chemotherapy. Epstein-Barr virus–associated smooth muscle tumour, a distinctive mesenchymal tumour in immunocompromised subjects, has also been reported among HIV-positive patients in Hong Kong.[35]

Other less common disease manifestations have been reported over the last two decades in HIV/AIDS patients in Hong Kong. HIV-associated nephropathy was diagnosed in a 52-year-old Chinese patient prescribed highly active antiretroviral therapy (HAART) who had an undetectable plasma viral load and a CD4 count of 437 /μL, and who presented with acute renal failure. The patient's condition responded to intravenous pulse methylprednisolone.[36] In a report of nine Chinese patients with stable HIV disease (eight on HAART), hyperthyroidism was the underlying cause for their presentation of weight loss with or without other thyrotoxic symptoms.[37] HIV-associated eosinophilic folliculitis, previously thought to be rare in non-western MSM, was identified (skin biopsy–proven) in three of 451 Chinese patients.[38] One patient was female and two were heterosexuals. Response to treatment with cetirizine, ultraviolet B therapy, itraconazole, and ketoconazole varied from no improvement to marked improvement.

Immunological and other monitoring for HIV disease progression

The CD4/CD8 T-lymphocyte subset test is the single most important immunological marker for the monitoring and evaluation of HIV disease. In a study to establish lymphocyte subpopulation normal values in Chinese adults, the 95% reference ranges of subsets were found to be lower than those of Caucasians. With a median of 670 /μL, the 95% reference range of CD3+ CD4+ lymphocyte count in healthy HIV-negative Chinese adults was 292 /μL to 1366 /μL.[39] For CD4 cell percentage, the mean of 26% was much lower than the corresponding 43% in Caucasian adults, and the 95% reference range was also substantially lower (23-51 vs 28-58).[40] Concomitantly, there was a high percentage of natural killer cells in healthy Chinese adults. In a separate study that looked at natural immunological and clinical disease progression, it also appeared that major opportunistic complications occurred at somewhat lower CD4 levels in Chinese patients.[41] A study that correlated clinical course of events and CD4 changes in a cohort of local patients in the pre-HAART era proposed new CD4 criteria to stage HIV disease in Chinese patients.[42] Under this new classification, a CD4 count of below 100 /μL (6%) and between 100 /μL and 220 /μL (6-12%) in Chinese patients corresponded to below 200 /μL (<14%) and between 200 /μL and 500 /μL (14-28%) in Caucasian patients, respectively according to US Centers for Disease Control and Prevention staging.

Chest X-ray (CXR) screening has been a routine investigation in government HIV clinic. A study that followed 191 HIV-infected patients for 792 person-years with 311 routine CXRs revealed only 22 abnormal results,[43] one of which led to the diagnosis of pulmonary TB. No patient with a normal routine CXR developed TB within the following 2 months. This low yield (0.32%) suggested that routine CXR was not useful in screening for active TB in asymptomatic HIV-infected patients even in a locality where the prevalence of TB is high. In a study of the utility of isoniazid preventive therapy (IPT) for TB, only eight (17%) of 47 patients tested positive at a cut-off of 5 mm to 2 units of purified protein derivative (PPD)–RT23.[44] There was no relation between PPD positivity and CD4 level. The tuberculin test and IPT have since been adopted routinely in HIV services in Hong Kong.

Antiretroviral therapy

Zidovudine monotherapy was the first available anti-HIV treatment and local experience of its use from 1987 to 1993 has been reviewed.[45] Immunological and clinical benefits, albeit modest, were noted among the majority of 89 patients treated. Nonetheless, toxicity was a genuine concern, probably related to the high doses used at the time: two thirds of patients experienced haematological, gastro-intestinal, or other side-effects and nearly 50% stopped treatment because of intolerance.[45] The early results of

combination antiretroviral therapy appeared promising when it first became available in Hong Kong in mid-1996. Treatment response was better in treatment-naïve than treatment-experienced patients, echoing overseas studies.[46] Combination treatment with HAART is the current standard when antiviral treatment is indicated. Triple therapy comprising two nucleoside reverse transcriptase inhibitors plus one protease inhibitor or non-nucleoside reverse transcriptase inhibitor (NNRTI) is the current preferred regimen.

Compliance with therapy is vital to the success of HAART. In Hong Kong, nurses have played a pivotal role in the delivery and monitoring of compliance with HAART. A user-friendly grading table was designed by the Integrated Treatment Centre to assess and grade self-reported HAART compliance based on the number of missed doses since a patient's last clinic visit. It can be readily applied in developing countries.[47] Evaluation in 130 patients attending the Integrated Treatment Centre identified a sensitivity of 85%, specificity of 42%, positive predictive value of 89%, and negative predictive value of 36% in the prediction of virological response using this self-report assessment tool.[47] Unlike overseas findings, full drug compliance was remarkably high: about 80% in HIV-infected Hong Kong Chinese patients.[48,49] Psychosocial factors rather than HIV disease stage and treatment regimen were the more crucial determinants of compliance with treatment. The characteristics of the patient population and the care setting affect compliance with HAART.

Drug toxicity is clearly an issue of concern that may limit the success of advances in HIV treatment. Lipodystrophy is one notable adverse condition that emerges after HAART, especially when protease inhibitor is included in the regimen. When the international medical community started to become concerned about lipodystrophy, doctors in Hong Kong were already assessing the use of indinavir, the first widely used protease inhibitor, and the occurrence of facial lipodystrophy.[50] Seven (24%) of 29 patients who took indinavir for at least 3 months developed facial lipodystrophy, most prominently over the cheek and temporal regions.[51] No other factors were associated with the toxicity in this study.

A high rate (62.5%) of nevirapine rash, the most important limiting side-effect of this NNRTI, has been reported in Chinese patients.[52] Further analysis of a bigger cohort subsequently revealed sex differences in the frequency of rash, with females 1.5 times more likely to develop severe rash than males.[53] Antihistamines were prescribed with success in less than 10% of the patients. All patients who developed nevirapine rash did so within the first month of treatment. This information enables doctors to advise patients before commencing treatment of the possibility of developing a rash and to plan treatment if toxicity occurs.

HIV/AIDS mortality

Opportunistic complications are important causes of death in patients with HIV/AIDS. Among the first 100 AIDS cases in Hong Kong, PCP accounted for one fifth of the 67 deaths recorded.[10] Cryptococcosis and MAC were the next most common causes of death. Although poor, post-AIDS survival had, however, improved gradually from less than 2 months for cases reported between 1985 and 1987, to over 15 months in patients reported between 1990 and 1991. Prognosis further improved in the second 100 patients with AIDS.[10] In addition, TB and septicaemia were more common causes of death than PCP, although this change was not statistically significant.[11]

A dramatic impact of reduced morbidity and mortality at a population level emerged only after the availability of HAART. This was in line with results reported overseas.[2] Progression to death and to AIDS was significantly delayed in a cohort of Hong Kong patients with advanced HIV disease during the era of HAART.[54] In this study of 581 patients with AIDS and/or CD4 count of below 200 /μL seen from 1984 to mid-2003, median survival after AIDS increased from 29.8 months during the pre-HAART era to more than 70 months in the HAART era ($P<0.001$). Compared with patients in the pre-HAART era, the adjusted hazard ratio of death after AIDS was 0.15 (95% confidence interval, 0.08-0.26) for patients in the HAART era.

HIV in specific groups

Infected children form a distinct group of patients with HIV, with most infected by mother-to-child transmission (MTCT). In a retrospective observational study, one (8.3%) of 12 babies born to mothers with known HIV status before delivery became HIV-infected, compared with nine (64.3%) of 14 mothers whose HIV status was diagnosed only after giving birth.[55] A landmark prospective study evaluated the benefit of universal HIV screening of pregnant women with an opt-out approach and found it practicable, feasible, and clinically acceptable.[56] These studies provided support for the introduction of a universal antenatal screening programme for MTCT prevention. In reviewing eight of 11 reported paediatric patients managed at the Queen Mary Hospital as of 2000, most of them fared well and responded to HAART.[57] As with adults, studying maturational changes of lymphocytes in Chinese children also served as a good reference for monitoring HIV-infected children.[58]

Haemophiliacs infected with HIV constitute another unique group of patients with HIV/AIDS. All haemophiliac infections in Hong Kong occurred prior to 1985, before clotting factors were screened for HIV. A retrospective study of 63 such patients in 1994 demonstrated the problems faced: schooling obstacles, employment difficulties, and disturbed social relationships.[59] Although the CD4 count gradually fell and was lower than in their HIV-negative counterparts, disease progression appeared

Table 1. Publication years of clinical HIV/AIDS papers (n=60)

Year	No. of papers
1985	1
1986	0
1987	0
1988	0
1989	1
1990	0
1991	1
1992	2
1993	2
1994	5
1995	1
1996	7
1997	1
1998	10
1999	3
2000	4
2001	7
2002	6
2003	4
2004	5

Table 2. Classification of 60 papers published from 1985 to 2004

Areas*	No. of papers
Clinical epidemiology	5
HIV disease course and presentation	5
Specific complications or organ-based manifestations	27
Immunological evaluation and other monitoring	6
Antiretroviral therapy	10
HIV/AIDS mortality	6
HIV in specific groups	6

* The same paper may be classified under more than one area; HIV denotes human immunodeficiency virus, and AIDS acquired immunodeficiency syndrome

slow in a group of 20 HIV-infected haemophiliacs: by 1996, only two (10%) had developed AIDS.[60] This observation was supported by another study of HIV 'non-progressors' in Hong Kong, which reported that all eight 'non-progressors' of 58 infected people followed for more than 7 years were haemophiliacs.[61] When Hong Kong was hard hit by severe acute respiratory syndrome (SARS) in 2003, an AIDS patient on Kaletra-containing HAART (Kaletra; Abbott, Illinois, US) was admitted to the Princess Margaret Hospital with respiratory symptoms and later diagnosed with coronavirus infection.[62] This was the first AIDS patient to contract SARS.

Discussion

We reviewed the literature that concerned clinical HIV/AIDS in Hong Kong over the last two decades that might shed light on the key developments in clinical care and research in the area. The content and format of this paper is very much influenced by the available publications from Hong Kong. This, together with the wide array of subjects covered by the published papers in the last 20 years, means it was impossible to perform a meta-analysis or critical appraisal of all studies. Instead, a collation, synthesis, and descriptive analysis is reported. This paper may thus not present an absolute picture of the AIDS epidemic in Hong Kong.

As shown in Table 1, the number of papers published in the second decade (48, 1995-2004) vastly exceeded those in the first decade (12, 1985-1994). Many studies were observational and retrospective, and many concerned a single case, or a descriptive analysis of a varying number of patients. Most studies also focused on specific/organ-based complications, followed by antiretroviral therapy (Table 2), and most were generated by service institutions that directly care for patients with HIV/AIDS. Although every effort has been taken to identify all relevant papers, this review is not necessarily exhaustive.

Most of the study findings echoed those of western countries although some were specific and unique to Hong Kong. The profile of AIDS-defining opportunistic infections in Hong Kong was a mixed pattern of presentations seen in western and developing countries, as illustrated by the similar prevalence of PCP and *M tuberculosis* infection. Locally, Kaposi's sarcoma and non-Hodgkin's lymphoma were the most common malignancies. Prognosis for patients with HIV/AIDS improved as the early HIV epidemic evolved, again echoing overseas studies.[63,64] Despite this, a remarkable public health impact of reduced progression to AIDS and death was witnessed only after the local availability of HAART; the extent of this was similar to or even better than that of western countries.[65,66]

There were some specific aspects of the disease where experience in Hong Kong has contributed to the global knowledge base of HIV/AIDS. First, *P marneffei* has been extensively studied, with many reports on the diagnosis, clinical course, management, and epidemiology. Research in endemic areas of South-East Asia[67] but not western countries aided in the care of local AIDS patients and also added to the overall understanding of this infection that mostly occurred in HIV-infected individuals. Second, the study of lymphocyte subpopulation values in healthy as well as HIV-infected Chinese patients was another area of uniqueness for Hong Kong. Both the CD4 count and percentage of CD4 cells in healthy Chinese population were lower[39] than in healthy Caucasians[68] albeit the total lymphocyte counts were very similar for both populations. Although the cause for comparatively low CD4 levels in Chinese population remains unclear, such findings affect the evaluation of the course of HIV and initiation of treatment for opportunistic infections and HIV per se. This provides a particularly useful reference for HIV management in Mainland China and other parts of the world. Third, systematic analysis of treatment experience has provided a rich source of reference for practising clinicians who care for people living with HIV/AIDS. This has enabled treatment guidelines, protocols, and clinical audit systems to be developed.

The scope of HIV management has changed due to scientific advances and improved patient survival. In contrast to conventional HIV-related opportunistic infections, other infections have emerged as increasingly important complications in HIV/AIDS patients. Notable examples are co-infection with hepatitis B and/or hepatitis C.[69,70] They adversely affect morbidity and mortality of co-infected patients and also impact on antiretroviral treatment.[71] Highly active antiretroviral therapy has been in place for nearly a decade, with unprecedented health improvements in treated patients to date. Nonetheless this lifelong treatment demands good drug compliance that is not always achieved by all patients. In addition, long-term toxicity, in particular metabolic abnormalities such as dyslipidaemia and hyperglycaemia and their implications for cardiovascular disease, may be a cause for long-term concern.[72,73]

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