HIV and Noncommunicable Diseases:
The Asian Perspective

Jintanat Ananworanich, MD, PhD*† and Anchalee Avihingsanon, MD, PhD‡§

Abstract: Asia is seeing a rise in noncommunicable diseases in their general population and among people living with HIV. Many Asians have low body weight, which can lead to higher plasma concentrations of antiretrovirals and, as a result, their toxicities. Examples are metabolic complications from protease inhibitors, chronic kidney disease from tenofovir, and hepatotoxicity from nevirapine. Asia has not only the highest burden of hepatitis B viral infection than any other continent but also a predominance of genotypes B and C, the latter associated with higher risk for hepatocellular carcinoma. HIV-associated neurocognitive disorders are equally common among Asians as other populations. Diastolic dysfunction and asymptomatic myocardial ischemia are not infrequent. Non-Hodgkin lymphoma is the most common AIDS-related cancer, whereas Kaposi sarcoma is relatively infrequent. Emerging data show high prevalence of human papillomavirus–associated anal dysplasia in men who have sex with men. Resource-limited countries in Asia suffer from lack of resources for national screening programs of noncommunicable diseases, which, in turn, limits the epidemiologic data that exist to guide the use of national health resources.

Key Words: HIV, Asia, noncommunicable diseases, HIV-associated neurocognitive disorders, non-Hodgkin lymphoma, kidney disease

From the *US Military HIV Research Program, Walter Reed Army Institute of Research, Silver Spring, MD; †Henry M. Jackson Foundation for the Advancement of Military Medicine, Bethesda, MD; ‡HIV-NAT, The Thai Red Cross AIDS Research Center, Bangkok, Thailand; §Division of Allergy and Immunology, Department of Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand.

The views expressed are those of the authors and should not be construed to represent the positions of the US Army or the Department of Defense. Correspondence to: Jintanat Ananworanich, MD, PhD, US Military HIV Research Program, 6720A Rockledge Drive, Suite 400, Bethesda, MD 20817 (e-mail: jananworanich@hivresearch.org).

Copyright © 2014 by Lippincott Williams & Wilkins

INTRODUCTION

More people live in Asia than any other continent. Among its population of 4.3 billion, around 5 million are living with HIV. This number could rise markedly even with a small increase in HIV incidence in highly populated countries like China, India, or Indonesia. Although access to antiretroviral therapy (ART) is improving and the death rate from HIV/AIDS is decreasing, Asia continues to grapple with 270,000 deaths and 350,000 new infections each year and only half of those infected have access to ART.1

Noncommunicable diseases (NCDs) account for half of all deaths reported in the general population in South and Southeast Asia.2,3 Diabetes, coronary heart diseases (CHD), and cancer are being diagnosed at a younger age in these particular regions than in other parts of the world, likely because of unplanned urbanization, smoking, unhealthy diet, physical inactivity, poverty, and alcohol use.4,5 Diabetes quadrupled in the last 30 years in Thailand, Indonesia, and China, whereas the rate barely doubled in the United States.9 Among South Asians, earlier onset of acute myocardial infarction and diabetes was observed.7 Genetic, anthropometric, and biological factors, such as greater accumulation of visceral fat and lower glucose disposal, may underlie South Asians’ propensity for diabetes.8 South and Southeast Asians also seemed to have more unfavorable health outcomes than others at similar waist–hip ratio or lipid levels.2,3,8

This article will focus on some key HIV-related NCD burdens and outcomes among Asians and discuss areas for future research. Although this commentary is on the Asian experience, it focuses on South, East, and Southeast Asia and does not include experiences of Pacific Islanders.

METABOLIC AND BONE DISORDERS

In a 10-year study, diabetes incidence was almost 7 times higher in Taiwanese living with HIV compared with the general population.9,10 A large study among newly infected Chinese found that 20% had hyperglycemia and 10% had diabetes and that these conditions were associated with older age, low CD4 count, and genetic and lifestyle risk factors. Among those receiving ART, prolonged exposure to protease inhibitors and nucleoside analogs also increased the risk.9 Dyslipidemia and lipodystrophy are also common in Thais and Indians, particularly after the use of suboptimal antiretrovirals (ARVs), such as stavudine and indinavir.11,12 In a regional Therapeutics Research, Education, and AIDS Training study with an Asian cohort, 1 in 10 had clinically diagnosed lipodystrophy.13 Plasma concentrations of ARVs were found to be higher among South, Southeast, and East Asians, possibly because of unique genetics and low body weight.14–20 Lowering the dose of atazanavir/ritonavir from 300/100 to 200/100 mg in Thais reduced lipid and bilirubin levels without compromising its antiviral activity.16 It is possible that lower doses of many ARVs would be more appropriate for Asians, and the pharmacokinetics of ARVs should be studied to inform the design of clinical trials comparing low vs. standard ARV doses.

Cohort studies across South, Southeast, and East Asian countries report that at least 25% of people living with HIV experience low bone mass.21–26 Studies among Koreans and
Thais suggested that they may be predisposed to this condition because of their low height and body mass index. Despite most of Asia being in the tropics with year-round sunshine, vitamin D deficiency is highly prevalent in Thais and Nepalese, and causal factors may include diet, pollution, sun protection, ARV, and other comorbidities, such as viral hepatitis.

Future research should focus on identifying the true incidence of these metabolic-related disorders among people with HIV, and the long-term outcomes, to guide the use of national health resources.

**CHRONIC KIDNEY DISEASES**

Emerging cohort data are suggesting worrisome rates of severe chronic kidney diseases of up to 10% among Chinese, Japanese, and Indians living with HIV. Older age and low CD4 count predicted chronic kidney diseases, and the use of nephrotoxic drugs, such as indinavir, seemed to have a long-lasting adverse effect, highlighting the importance of treating earlier and with safer ARVs. Asians may also be prone to tenofovir-related kidney complications. Cohort studies suggest a higher prevalence of proximal tubular dysfunction among East and Southeast Asians than among Westerners, thought to result from high tenofovir plasma concentration, which develops because of their generally low body weight and unique genetics associated with poorer tenofovir renal excretion. Concomitant use of protease inhibitors with tenofovir in second-line regimens further enhances this risk.

Perhaps, the most challenging comorbidity management issue in the region is the assessment of the glomerular filtration rate (GFR). The widely used Cockroft-Gault and modification of diet in renal disease equations significantly underestimate the true GFR in Thais and could lead to premature modifications of ART or unnecessary treatment. Future research should identify the appropriate estimated glomerular filtration rate (eGFR) measure for each Asian population and monitor glomerular and tubular functions, particularly as tenofovir use is widely scaled up.

**HEPATIC DISEASES**

Nearly 75% of the 350 million people worldwide chronically infected with hepatitis B virus (HBV) are from the Southeast Asia and Western Pacific regions. The more virulent HBV genotypes C and B predominate in Southeast and East Asia, in contrast to the more favorable genotype A in Europe and the United States. Genotype C is associated with more rapid liver fibrosis and a higher risk for hepatocellular carcinoma (HCC). Tenofovir given with emtricitabine or lamivudine is extremely effective in lowering the risk for HCC and ultimately preventing death, particularly if treatment is started early.

Worldwide, about 185 million people have chronic hepatitis C virus (HCV) infection, and Central and East Asia are among the most affected regions. This infection predominates in people who inject drugs (PWID), but the incidence is rising among men who have sex with men (MSM) living in large Asian cities. It is not surprising that many PWID and other persons at risk in Vietnam and Cambodia have triple HIV, HBV, and HCV infections, which markedly increase their risk for end-stage liver disease and other comorbidities, such as kidney and bone diseases, in addition to complications from commonly used first-line ART with non-nucleoside analogs. A large study of Vietnamese with HBV examined coinfection rates with HIV and HCV. Among PWID with HBV, 28% also had HIV and 90% had HCV. Among commercial sex workers with HBV, 15% also had HIV and 40% had HCV. In Thailand, high costs and weak infrastructure for diagnosing, genotyping, and treating HCV have led to an almost universal lack of access to HCV management.

Even when viral hepatitis is absent, patients with HIV continue to be at risk for chronic hepatitis. The incidence of chronic hepatitis was 5.4 per 100 person-years in a Thai cohort, and the onset was generally within the first 18 months of ART, occurring more in males and those with higher body mass index.

Nevirapine is commonly used in first-line ART in Asia. However, Chinese may be at a greater risk for nevirapine-related hepatotoxicity because of high plasma concentration of the drug. From 25% to 40% of Indians and Chinese experience hepatotoxicity from nevirapine, which is associated with having a CD4 count above 250 cells per cubic millimeter. This has a direct implication for ART choices in national programs, as a higher CD4 threshold for ART initiation is now recommended.

**NEUROCOGNITION**

Asians are as prone to HIV-associated neurocognitive disease (HAND) as those living in Western countries, with 30%–50% of Chinese and Thais exhibiting some form of HAND; its severity is associated with advanced HIV disease. Although there is information supporting the neurovirulent nature of HIV clade D found in parts of Africa, such an association is less clear with other clades found in Asia (B, C, E), and limited data suggest no clinically relevant differences between these clades. Studies in Thais have informed the field regarding the brain insult that occurs very early in HIV infection and the associations between high proviral DNA burden and HAND (also brain atrophy, inflammation, and injury).

Screening for HAND is challenging in the Asian context. Lack of time and personnel to perform a comprehensive assessment in busy clinics and limited validated tools are major barriers. A Thai study found that adding Trail Making Test A to the international HIV Dementia Scale significantly improved its sensitivity and specificity in identifying HIV-associated dementia but not the less severe forms of HAND. Interestingly, even healthy Thais performed differently from Hawaiians on almost every aspect of the same neuropsychological test, illustrating the need for appropriate controls in HIV studies.

A possible research area for HAND intervention that could be synergistic with Asian cultures, religions, and ways of life is mindfulness or meditation. Mindfulness can reduce...
stress and symptoms of psychiatric conditions in HIV patients. Although its favorable effect on cognitive function is suggested for other neurologic diseases, this has yet to be explored in association with HAND.

**CORONARY HEART DISEASES**

Hypertension, the most important treatable risk factor for CHD, is commonly underdiagnosed in Asians, as it is in other populations. Though its prevalence among Asians is largely unknown, high rates of hypertension have been observed, for example, among Malaysian adults with HIV, whose rate approaches 50%. Although the population of Asians with HIV is aging, the majority is still relatively young; therefore, CHD events are infrequent. Assessing the 10-year risk for CHD may aid in targeting people who need monitoring and preventive therapy. There are some warnings that more CHD cases will be identified in the future. In the Strategies for Management of Antiretroviral Therapy (SMART) study, asymptomatic myocardial ischemia was borderline more common among subjects in Asia than those in North America. In India and China, up to 40% had diastolic dysfunction on echocardiogram, associated with having low CD4. The commonly used Framingham equation overestimated the CHD risk in Thais; so, identifying population-appropriate equations will be important.

**CANCER**

The types of cancer observed in Asians living with HIV are similar to those reported elsewhere. In the Therapeutics Research, Education, and AIDS Training Asia retrospective study of 13 sites across South, Southeast, and East Asian regions, which included about 200 HIV-infected Asians with cancer, two-thirds had AIDS-defining cancers [40% non-Hodgkin lymphoma (NHL), 16% Kaposi sarcoma, and 9% cervical cancer]. The remaining one-third had non–AIDS-defining cancers (5% lung, 5% breast, and 5% HCC). Having a low CD4 count, being older, or not being on ARVs were predictors. Still, not much is known about the true prevalence of cancers among Asians with HIV. A Thai study of around 1500 people with HIV reported a 3% prevalence over 5 years.

Declining rates of NHL after the highly active ART era were observed in a retrospective study from Taiwan. Kaposi sarcoma was infrequent in Korea, likely because of low-circulating Kaposi sarcoma–associated herpesvirus. Another study in Japanese MSM also found a low Kaposi sarcoma–associated herpesvirus seropositivity of 10%. Asians living in hot spots for HBV and HCV are at risk for these infections and for HCC, but little has been reported on the latter. Chronic HBV infection may also increase the risk for other types of cancers, such as NHL, as has been shown in a study from Korea.

Cervical cancer is among the top killers of women with HIV, but the screening rate is generally low, as illustrated by a report from Taiwan. A recent study from India evaluated 4 methods of screening and found that sequential testing with visual inspection with acetic acid followed by visual inspection with Lugol iodine was feasible and had adequate sensitivity and specificity to detect abnormalities confirmed by colposcopy and biopsy. Of around 1100 women with HIV screened, 5% already had cervical intraepithelial neoplasia grades 2 and 3. Among Cambodian female sex workers younger than 30 years living with HIV, 44% had cervical infection with multiple human papillomavirus (HPV) types, and their HPV risk was 6 times higher than their HIV-uninfected peers. Emerging data are identifying anal HPV infection and anal intraepithelial neoplasia (AIN) as important health issues for Asian MSM. A Thai study found that 60% of MSM living with HIV had oncogenic anal HPV infection, and among these MSM, 29% progressed from normal/low-grade AIN to high-grade AIN in 1 year. Abnormal anal pap smear was also observed in 40% of HIV-infected MSM in China. Immunization against HPV is not yet the standard of care in most Asian countries, and its high price renders it out of reach to most Asians living with HIV.

**CONCLUSIONS**

Knowledge of HIV/NCD disease burdens and related characteristics among Asians is important not only for patient care in Asia but also for providers in other parts of the world who are increasingly caring for immigrants from Asia. Not surprisingly, screening programs found high rates of HBV and HCV infections among Vietnamese immigrants in the United States and the Netherlands. End-stage renal diseases from diabetes were also more common among South Asian immigrants.

For clinicians in these resource-rich settings, active screening and management of conditions Asians face are likely achievable given the available resources. For those who care for Asians living with HIV in resource-limited settings, there is an unfortunate theme of limited access for managing all types of NCDs. A concerted effort is needed to prioritize research to understand the magnitude of NCDs among people living with HIV and determine how best to target diagnosis and treatment for those most at risk.

**ACKNOWLEDGMENT**

The authors thank Ms Piraporn June Ohata for her help in preparing the manuscript.

**REFERENCES**


