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Growing challenges for HIV programmes in Asia: Clinic population trends, 2003–2013

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Abstract

The scale-up of antiretroviral therapy (ART) has led to a substantial change in the clinical population of HIV-positive patients receiving care. We describe the temporal trends in the demographic and clinical characteristics of HIV-positive patients initiating ART in 2003–13 within an Asian regional cohort. All HIV-positive adult patients that initiated ART between 2003 and 2013 were included. We summarized ART regimen use, age, CD4 cell count, HIV viral load, and HIV-related laboratory monitoring rates during follow-up by calendar year. A total of 16 962 patients were included in the analysis. Patients in active follow-up increased from 695 patients at four sites in 2003 to 11,137 patients at eight sites in 2013. The proportion of patients receiving their second or third ART regimen increased over time (5% in 2003 to 29% in 2013) along with patients aged ≥ 50 years (8% in 2003 to 18% in 2013). Concurrently, CD4 monitoring has remained stable in recent years, whereas HIV viral load monitoring, although varied among the sites, is increasing. There have been substantial changes in the clinical and demographic characteristics of HIV-positive patients receiving ART in Asia. HIV programmes will need to anticipate the clinical care needs for their aging populations, expanded viral load monitoring, and the eventual increase in second and third ART regimens that will lead to higher costs and more complex drug procurement needs.

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Competing Interests

The authors do not have any competing interests to declare.

Authors' contributions

NLD and ML contributed to the concept development. KN, PSL, OTN, KVN, TPM, DDC, MPL and JYC contributed data for the analysis. NLD performed the statistical analysis and wrote the first draft of the manuscript. All authors commented on the draft manuscript and approved the final manuscript.

Keywords

Asia; HIV; characteristics; clinical; ART; demographics

Introduction

The massive scale-up of antiretroviral therapy (ART) for HIV-positive individuals has allowed for more people than ever to receive ART in the Asia and Pacific region, with an estimated 2.1 million adults receiving ART and treatment coverage at 41% in 2015 (UNAIDS, 2016). Since ART expansion, there have been many changes to the WHO treatment guidelines to achieve better patient outcomes, including earlier ART initiation, more tolerable and convenient first-line ART regimens, and a greater emphasis on adherence counselling and support services (World Health Organisation, 2013). Improved care and greater access to ART in recent years has been accompanied with reductions in mortality as well as increased life expectancies for HIV-positive patients (Antiretroviral Therapy Cohort, 2008; De La Mata et al., 2016; Teeraananchai, Kerr, Amin, Ruxrungtham, & Law, 2016).

Evaluating how this population has changed over time is useful in assessing the progress in HIV programmes, particularly in the context of changing guidelines, and to allow for better planning of future needs. ART treatment coverage in Asia is still lower relative to other regions and continued ART scale-up will place considerable pressure upon HIV programmes to increase their capacity (World Health Organisation, 2013). In order to maintain the quality of care provided, monitoring previous trends and identifying potential pitfalls in HIV programmes is required to ensure health care systems do not weaken.

There are few large cohorts in the Asia Pacific region capable of describing demographic and clinical population changes over time (Loo et al., 2012). Our study objective was to utilize patient data from a regional cohort to evaluate and describe time trends in the demographic and clinical characteristics of HIV-positive patients initiating ART in Asia between 2003 and 2013.

Methods

Data collection and Participants

The TREAT Asia HIV Observational Database (TAHOD) is a cohort that collects prospective data on a subset of adult HIV-positive patients that attend 20 clinical sites in the Asia-Pacific region. A sub-study of TAHOD, the TREAT Asia HIV Observational Database Low Intensity Transfer (TAHOD-LITE) collects retrospective data on all adult HIV-positive patients receiving care in 8 of the 20 participating clinical sites, with one site each in Cambodia, Hong Kong SAR, India, Indonesia, Singapore, and South Korea, and two sites in Vietnam. A more detailed description of TAHOD-LITE can be found elsewhere (De La Mata et al., 2016). Briefly, routinely collected patient data were anonymized at the site before being electronically transferred for data management at the Kirby Institute, UNSW Australia. Patient data included demographics, hepatitis serology, HIV-related laboratory results and ART history.

Ethical approvals for TAHOD-LITE were obtained from local institutional review boards (IRBs) for each participating site, the University of New South Wales, and the coordinating center at TREAT Asia/amfAR. Written informed consent is not obtained unless required by the site-specific IRBs.

This analysis included HIV-positive patients who were aged ≥ 18 years and had initiated ART with three or more antiretroviral (ARV) drugs between 01 January 2003 and 31 December 2013.

Statistical analyses

First-line ART was defined as the first combination regimen with three or more ARV drugs. Second ART was defined as a subsequent regimen to the first-line ART, undertaken for ≥ 14 days, which either had at least one ARV drug class change or two or more ARV drug changes within a class. Similarly, the third ART was defined as a subsequent regimen to the second ART, undertaken for ≥ 14 days, which either had at least one ARV drug class change or two or more ARV drug changes within a class.

Patient follow-up was from first-line ART initiation to the most recent clinic visit or 01 January 2014, whichever occurred earliest. Only HIV-related laboratory measurements, including CD4 cell count and HIV viral load, during follow-up were included. Pre-ART measurements were considered as the result closest to, and within 6 months prior to, ART initiation. If there were multiple measurements within a given calendar year, then the average value of all the tests within the year was taken. Hepatitis B (HBV) surface antigen and hepatitis C (HCV) antibody results were considered as ever positive, otherwise negative if a test was ever previously conducted, and not tested if never tested.

We descriptively analysed the data using absolute patient numbers and proportions. Absolute patient numbers were considered as the total number of patients who had either initiated an ART or were in active follow-up from ART initiation, in the given calendar year. Simple proportions were calculated by dividing the number of patients within a particular category by the patient total for the given calendar year. We summarized the ART regimen type, age, CD4 cell count, HIV viral load, HBV, and HCV results for each calendar year from 2003 to 2013, across all sites.

Results

A total of 16 962 patients aged over 18 years had initiated a first-line ART between 1 January 2003 and 31 December 2013. Of these patients, 11 137 were in active follow-up in 2013. Overall, the number of patients receiving care increased from 695 in four sites to 11,137 in eight sites (Table 1). The proportion of males and patients with heterosexual HIV exposure decreased from 80% and 90% in 2003 to 67% and 76% in 2013, respectively. Across all the sites over time, the ART regimen use in the clinical patient population differed (Figure 1A). In 2003, there were 660 (95%), 25 (4%) and 10 (1%) patients receiving their first, second and third ART regimens, respectively. In 2013, these numbers increased to 7902 (71%), 2376 (21%) and 859 (8%), respectively. The proportion of patients receiving their

second or third ART increased from 5% in 2003 to 29% in 2013. These trends were also apparent when examining by country (Appendix 1).

The age distribution of the clinical patient population shifted towards an older population where the majority of patients (67%) were aged 36 years or older in 2013 (Figure 1B). The median age increased from 35 years (interquartile range, IQR: 30–40) in 2003 to 40 years (IQR: 34–46) in 2013 (Table 1). The proportion of patients <30 and 30–35 both decreased from 22% and 36% in 2003 to 10% and 23% in 2013, respectively. Whereas the proportion of patients aged 50 years or above increased from 8% in 2003 to 18% in 2013.

There was a significant increase in the distribution of the current CD4 cell count (Figure 2A). The median current CD4 cell count went from 137 (IQR: 61–216) in 2003 to 400 (IQR: 244–568) in 2013 (Table 1). The proportion of patients with a current CD4 count of 100 cells/ μ L or less decreased from 35% in 2003 to 7% in 2013. While the proportion of patients with a current CD4 count greater than 350 cells/ μ L increased from 5% in 2003 to 52% in 2013. In addition, the proportion of patients without a current CD4 count decreased from 22% in 2004 to 10% in 2013 (Figure 2A).

Although, the proportion of patients not tested for HIV viral load decreased by 22% from 2003 to 2013, over half the patients (52%) did not have an HIV viral load assessment in 2013 (Figure 2B). The median current HIV viral load decreased from 750,000 (IQR: 23,000–191,350) in 2003 to 40 (IQR: 20–150) in 2013 (Table 1). The proportion of patients with a current HIV viral load of 400 copies/mL or less increased from 2% in 2003 to 38% in 2013. The proportion of patients with an HIV viral load greater than 1000 copies/mL decreased from 23% in 2003 to 10% in 2013 (Figure 2B).

The CD4 testing rates across all sites initially increased from 1.1 tests per person-year (py) in 2003 to 2.2 tests/py in 2008, then remained relatively stable until 2012. In 2013, there was a drop in the CD4 testing rate to 1.5 tests/py (Figure 3A). The decline in CD4 testing rates from 2012 to 2013 was also present when stratified by country (Appendix 2). Concurrently, the overall HIV viral load testing rate steadily increased from 0.4 tests/py in 2003 to 1.2 tests/py in 2013. The HIV viral load testing rates were different between the sites, where some sites consistently had testing rates below 1 test/py for the entire follow-up period. However, most countries presented an increasing trend (Appendix 2).

Most of the clinical patient population had received HBV and HCV tests by 2013 (Figure 4A–B). The proportion of patients not tested for HBV decreased from 68% in 2003 to 32% in 2013. The proportion with positive HBV remained relatively stable over time, at 6% in 2013. Similarly, the proportion not tested for HCV decreased from 80% in 2003 to 37% in 2013. The proportion with positive HCV did slightly increase from 2% in 2003 to 7% in 2013.

Discussion

In this study, we found considerable changes in the clinical and demographic characteristics of the 16 962 HIV-positive patients in our cohort who had initiated ART between 2003 and 2013. Over the decade, each of the eight clinical sites had substantial increases in the

number of patients attending for care, initiating ART and in the proportion of patients receiving their second or third ART. The age distribution of our patient population shifted towards an older population, with those aged 50 years or older increasing from 8% in 2003 to 18% in 2013. A majority of patients had a current CD4 count >350 cells/ μ L in 2013 and CD4 monitoring stabilized in recent years to 1.5–2 tests/py. However, HIV viral load monitoring varied between clinical sites and was generally poor overall, with over half the patients (52%) not tested in 2013.

Scale-up of first-line ART has substantially increased the number of HIV-positive people receiving ART within our clinics from 695 patients in 2003 to 11 137 patients in 2013. However, with the extensive use of ART, there is an increased need for access to regimens beyond first-line. In developed countries, there are ample resources to provide optimal patient care, including HIV viral load monitoring, drug resistance testing and alternate ARV drugs, so ART regimens after first treatment failure can be accommodated. In resource-limited settings (RLS), patients have limited options due to drug affordability, minimal laboratory monitoring and ARV drug supply (Duda et al., 2014; Hirsch et al., 2008; Kumarasamy & Krishnan, 2013; Long, Fox, Sanne, & Rosen, 2010). Hence, the rate of switching from the first-line ART to the second ART is lower in resource-limited settings compared to developed countries (Group et al., 2009; Pujades-Rodriguez et al., 2010; Renaud-Thery et al., 2007). Projections in South Africa, assuming targeted HIV viral load monitoring and stable scale up, have estimated that, by 2020, the number of adult patients requiring second ART will likely be at least double that of 2014 (Estill et al., 2016). Similarly, we found a 24% increase in the proportion of patients receiving second or third ART from 2003 to 2013. Clearly, in future years, healthcare systems will need to accommodate for, not only an increased number of patients receiving ART, but also provide access to regimens beyond first-line (Figuerola, Sued, & Cahn, 2014; World Health Organisation, 2007).

There was a 10% increase in the proportion of patients aged 50 years or older between 2003 and 2013. Similar trends in the US have shown an 8% increase in HIV-positive adults aged >50 years from 35% in 2010 to 43% in 2013 and, by 2015, it is expected to rise to greater than 50% (Centers for Disease Control and Prevention (CDC), 2015; Effros et al., 2008). The shift towards an older population of HIV-positive adults was largely a result of improvements in survival due to ART and patient care (Antiretroviral Therapy Cohort, 2008). However, older HIV-positive adults are increasingly at risk of multi-morbidity (Miller et al., 2014; Oni et al., 2015; Rodriguez-Penney et al., 2013), polypharmacy (Edelman et al., 2013; Gleason, Luque, & Shah, 2013), and geriatric conditions, such as frailty (Brown & Qaqish, 2006; Greene et al., 2015). In coming years, healthcare for this population will become increasingly complex as it encompasses not only HIV management but also non-AIDS HIV-related conditions associated with advanced aging (Ball, 2014). As a result, healthcare systems will need to establish strategies that more efficiently integrate HIV and additional care for older adults to ensure their longer term needs are met (High et al., 2012; John, 2016).

Since 2008, the CD4 testing rate was relatively consistent and stable across all sites at 1.5–2.2 tests/py. Concurrently, the current CD4 count markedly improved, where over half the

patients in 2013 had a CD4 count >350 cells/ μ L. In contrast, the HIV viral load testing rate varied among sites, where 5 of 8 sites had 1 test/py and the remaining 3 sites had 1.5 tests/py during follow-up. Over half the patients in 2013 did not have a current HIV viral load. Many ART programmes in RLS have minimal HIV viral load monitoring for patients due to inadequate laboratory equipment and high cost (Boyer et al., 2013; Kumarasamy & Krishnan, 2013). In these settings, HIV viral load testing is targeted rather than routine to confirm treatment failure, but potential delays in treatment switching can increase the risk of disease progression, drug resistance and HIV transmission (Arnedo et al., 2012; Kanapathipillai et al., 2011; Nettles et al., 2005). With the increasing use of regimens beyond first-line, there are strong clinical benefits for routine HIV viral load testing in RLS to prevent unnecessary treatment switching, identify treatment failure early to facilitate switch and avoid accumulation of resistance mutations, and guide adherence interventions (Benator et al., 2015; Bonner, Mezochow, Roberts, Ford, & Cohn, 2013; Keiser et al., 2011; Sigaloff et al., 2011). In future years, efforts should be made to provide HIV viral load testing that is affordable and easier to use for HIV programmes in RLS (Calmy et al., 2007).

There were limitations to our study. First, we used observational data obtained from eight clinical sites in seven countries in Asia, where most countries were represented by only one site. Therefore, our findings reflect the trends in the patient population occurring within our clinical sites, but may not be representative of trends in the country or region. Second, differences between sites should be cautiously interpreted. There were differences in when patients present for care, the level of care that can be provided with available local resources and other unmeasurable confounders. Third, the patient population was also heavily weighted by the Indian site which contributed more patients than the other sites. We did stratify results by site to determine if the trends have been occurring among all or some of the sites. Fourth, there was potential bias introduced from those lost to follow-up (LTFU). Patients LTFU affect our analysis as the demographics and clinical characteristics of these patients over time may have differed. It is also not currently possible in our cohort to distinguish patients genuinely LTFU from those transferred to another site for care. However, the LTFU rate in TAHOD-LITE was relatively low and consistent between the years of ART initiation (2003–05: 2.1 per 100 person-years; 2006–09: 2.9 per 100 person-years; 2010–13: 2.8 per 100 person-years) (De La Mata et al., 2016).

Our analysis has described the trends in the clinical and demographic characteristics of HIV-positive patients receiving ART at eight HIV programmes in Asia. Our findings suggested three important changes have occurred over time. First, there were substantial increases in the number of patients initiating ART and greater proportions receiving second or third ART regimens in recent years. Second, the age distribution of our patient population moved towards an older population. Third, CD4 monitoring has stabilized, where most patients have a CD4 >350 cells/ μ L, yet HIV viral load monitoring is varied among our sites, where over half the patients were not tested in 2013.

These changes have significant implications for the clinical management of patients within our HIV programmes. In future years, HIV programmes will likely need to accommodate for the continual increase in patients receiving ART, provide access to regimens beyond first-line ART, integrate additional care for older adults and increase laboratory monitoring.

Implementing effective strategies will be essential to manage the strain this will place on healthcare systems, which may already be weakened from scale-up.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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(A) ART regimen use during follow-up

(B) Age of patients during follow-up

Figure 1.

Over time, the (A) ART regimen use and (B) Age of patients, across all sites during follow-up from ART initiation.

Figure 2.

Over time, the (A) current CD4 cell count (cells/ μ L) and (B) HIV viral load (copies/mL), across all sites during follow-up from ART initiation.

Figure 3. Testing rates (per person-year) for patients across all sites during follow-up: (A) CD4 cell count and (B) HIV viral load.

(A) Hepatitis B results during follow-up

(B) Hepatitis C results during follow-up

Figure 4.

Hepatitis testing for patients across all sites during follow-up: (A) Hepatitis B and (B) Hepatitis C.

Table 1

Summary of the patient characteristics across all countries.

	2003	2004	2005	2006	2007	2008
Total, n	695	1,502	2,558	3,762	4,912	6,087
Clinical Sites, n	4	5	5	6	6	6
Age (yrs), median [IQR]	35 [30, 40]	35 [31, 40]	36 [31, 41]	36 [31, 42]	37 [32, 43]	37 [32, 44]
Male sex, n (%)	558 (80)	1174 (78)	1883 (74)	2673 (71)	3401 (69)	4207 (69)
Heterosexual HIV exposure, n (%)	626 (90)	1331 (89)	2224 (87)	3269 (87)	4269 (87)	5179 (85)
Current CD4 cell count (cells/ μ L), median [IQR]	137 [61, 216]	154 [72, 270]	188 [94, 320]	220 [124, 362]	240 [138, 386]	274 [164, 424]
Current HIV viral load (copies/mL), median [IQR]	75000 [23000, 191350]	1930 [400, 56554]	674 [150, 55274]	3146 [64, 79800]	400 [40, 5616]	400 [40, 12392]

	2009	2010	2011	2012	2013
Total, n	7,005	8,378	9,804	10,760	11,137
Clinical Sites, n	6	8	8	8	8
Age (yrs), median [IQR]	38 [33, 44]	38 [33, 45]	39 [33, 45]	39 [33, 46]	40 [34, 46]
Male sex, n (%)	4837 (69)	5738 (68)	6608 (67)	7263 (68)	7480 (67)
Heterosexual HIV exposure, n (%)	5881 (84)	6830 (82)	7814 (80)	8359 (78)	8411 (76)
Current CD4 cell count (cells/ μ L), median [IQR]	314 [182, 470]	314 [182, 476]	338 [200, 492]	370 [224, 526]	400 [244, 568]
Current HIV viral load (copies/mL), median [IQR]	250 [40, 5224]	150 [30, 2530]	150 [26, 9892]	44 [20, 1020]	40 [20, 150]