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Comorbidities among HIV-infected injection drug users in Chennai, India

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Abstract

Background & objectives—HIV-infected injection drugs users (IDUs) are known to have high rates of co-infections. A few reports exist on comorbidities among HIV-infected IDUs in India. We carried out a retrospective study to analyse data on comorbidities in India and treatment challenges faced when treating HIV-infected IDUs in India.

Methods—A retrospective chart review of 118 HIV-infected IDUs who accessed care at the YRG Centre for Substance Abuse-Related Research, Chennai, between August 2005 and February 2006 was done. Demographic, laboratory and clinical information was extracted from medical records. Descriptive demographic and clinical characteristics and distributions of comorbidities across CD4 cell count strata were analysed.

Results—All IDUs were male with a median age of 35.5 yr. The majority were married with average monthly income less than INR 3000 per month. The prevalence of hepatitis B and C infections were 11.9 and 94.1 per cent, respectively. Other common co-morbidities included oral candidiasis (43.2%), tuberculosis (33.9%), anaemia (22.9%), lower respiratory tract infections (16.1%), cellulitis (6.8%), herpes zoster (9.3%) and herpes simplex (9.3%). Among participants with CD4+ < 200 cells/μl, the prevalence of TB was 60 per cent.

Interpretation & conclusions—IDUs in Chennai were commonly co-infected with HBV, HCV and tuberculosis, complicating use of antiretroviral and anti-tuberculous therapy. The current regimens available for the management of HIV and TB in India may need to be re-assessed for IDUs given the potential for increased rates of hepatotoxicity.

Keywords

Comorbidities; HCV; HIV; India; injection drug users – tuberculosis

India, with an estimated 5.7 million infections[1] until recently was home to the largest population of HIV- infected persons in the world. In 2006, a community- based surveillance estimated that there were 2.5 million people in India with HIV infection in India[2] - the third highest in the world. Since over 85 per cent of these infections are transmitted heterosexually[3] most research on the management of opportunistic infections (OIs), optimization of HIV care, and prevention interventions has focused on heterosexual

transmission. Injection drug users (IDUs) have commonly been neglected in these efforts in most parts of India except in the northeastern region, where injection drug use drives the HIV epidemic.

India is estimated to have approximately 1.1 million IDUs with HIV prevalence as high as 64 per cent among IDUs in certain cities[4]. While the HIV epidemic among IDUs receives appreciable attention only in the northeastern regions of India, recent reports suggest high prevalence of HIV among IDUs in other cities such as Chennai, Mumbai, Kolkata and Delhi[5]. Chennai, the capital of Tamil Nadu, has approximately 10,000 – 15,000 IDUs[6]. In 2003, Chennai was one of two IDU sentinel surveillance sites to show a significant increase in HIV prevalence from the previous year3. HIV prevalence among IDUs in Chennai ranges from 30 to 40 per cent5,[7,8,] translating to at least 3,000 HIV-infected IDUs in the city of Chennai alone. This indicates that although the epidemic is driven by heterosexual transmission in most parts of India, there is a large and mostly unmet need for medical and psychosocial care for IDUs living with HIV.

A few reports exist on co-morbidities and opportunistic infections among IDUs in India. HIV- infected IDUs have been shown to have high rates of co-infection with hepatitis B virus (HBV) and hepatitis C virus infection (HCV)[9–12]. Early studies identified high rates of tuberculosis, chronic diarrhoea, abscesses and herpes zoster among IDUs in India[9,13,14].

This paper describes the spectrum of co-morbidities among HIV-infected IDUs in Chennai and highlights some of the common treatment challenges faced when providing medical care to this population.

Material & Methods

The YR Gaitonde Centre for Substance Abuse-Related Research (YRGCSAR) was established in north Chennai in November 2004 to estimate the incidence of HIV among IDUs in Chennai, utilizing a cohort study design. YRGCSAR is a branch of the YR Gaitonde Centre for AIDS Research and Education (YRGCARE) located in south Chennai. YRGCARE, a non-profit, non- governmental organization, has provided medical and psychosocial care to over 10,000 HIV-infected individuals since its establishment in 1993. This study was approved by the YRGCARE Institutional Review Board.

All participants testing positive for HIV at screening for the ongoing incidence study were referred to YRGCARE and government hospitals for further medical management, but most patients failed to pursue follow up care. Therefore, a clinic was opened on-site at YRGCSAR, a convenient location for IDUs, in August 2005 to provide HIV- and general medical care to these individuals.

Study population

The sample consisted of the 118 consecutive HIV-positive IDUs who visited the on-site clinic for medical care between August 2005 and February 2006. There were no specific eligibility criteria. All the IDUs who accessed care at the clinic were included in the analysis. A participant’s decision to avail himself of services at the clinic was purely

voluntary. The participants were not offered monetary compensation for clinic visits, but were provided with free medications such as multivitamins tablets, trimethoprim-sulphamethoxazole (TMP-SMX) prophylaxis if absolute CD4+ count was < 300 cells/μl and selected antibiotics. Patients who qualified for antiretroviral therapy (ART) following local guidelines were referred to government ART roll-out centers15 where ART was initiated as per government protocol. Absolute CD4 count measurement was routinely performed for all participants using FACS Count (Beckton Dickinson, USA).

Data analysis

Information on OIs, other co- morbidities, demographics, weight, height, laboratory parameters and treatment regimens was extracted from participants' medical records. These data were stripped of all participant identifiers and were entered into an electronic natural history clinical database at YRGCARE. Regular quality checks are carried out on the data collection/entry processes. Hepatitis C was diagnosed using Murex Anti-HCV kit (Abbott Murex, UK) and HBV was diagnosed by the presence of hepatitis B surface antigen (Hepanostika Uniform II kit, Biomerieux, The Netherland). Tuberculosis (TB) was diagnosed based on radiological, clinical and/or laboratory findings and history. All patients diagnosed with TB were referred to the nearest government directly observed therapy (DOT) center for further management. Gastrointestinal symptoms included diarrhoea and/or vomiting. Cellulitis was defined as localized cutaneous swelling, with fever and tenderness for at least one week. An IDU was classified as having an opportunistic infection (OI) if he was diagnosed with an OI at any visit. For CD4 stratification of co-morbidities, the closest CD4 count performed (+/− 2 months) to the follow up visits was used.

All analyses were performed using SPSS Version 13.0 (Chicago, USA). The prevalence of selected OIs and co-morbidities was stratified by CD4 cell count at presentation, and chi-squared statistic was used to detect differences between strata. $P<0.05$ was considered statistically significant.

Results

Demographics and clinical characteristics

Among the 118 HIV-positive IDUs attending the clinic, the mean age was 35.5 ± 6.25 yr. All patients were male, and most were of Tamil ethnicity (97.5%). Thirty nine per cent of the HIV-infected IDUs were unmarried and single, while 49.2 per cent were married and living with their spouse. The majority of the patients had either primary or no formal education (57.6%). Eighty two per cent worked for daily wages, and 11.9 per cent were unemployed. The demographic data also showed that 92.4 per cent of the HIV-infected IDUs attending the clinic earned less than INR 3000 per month. All patients had injected drugs at least once in the prior six months. The median absolute CD4 count at presentation was 395 cells/μl (range: 34–800), with 12.7 per cent of patients having an absolute CD4 count less than 200 cells/μl.

Co-morbidities

The prevalence of HBV and HCV infection among patients was 11.9 and 94.1 per cent, respectively. Thirteen (11%) patients were infected with HIV, HBV and HCV.

The most common HIV-related conditions were oral candidiasis (43.2%) and pulmonary TB (33.9%). Anaemia was detected in 22.9 per cent of patients. Other common co-morbidities included lower respiratory tract infection (16.1%), papular pruritic eruptions (PPE) (16.1%), herpes zoster (9.3%), herpes simplex (8.5%), gastrointestinal symptoms (8.5%), cellulitis (6.8%), hydrocoele (3.4%) and malaria (3.4%). There was one The median absolute CD4 count at presentation was 395 cells/μl (range: 34–800), with 12.7 per cent of patients having an absolute CD4 count less than 200 cells/μl.

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Oral candidiasis and pulmonary TB were significantly more common in patients with lower CD4+ counts ($P<0.05$). No such differences were observed for other common co-morbidities such as hepatitis B or C virus infection and herpes zoster. Among patients with an AIDS-defining CD4+ cell count of <200 cells/μl (n=15), 66.7 per cent had oral candidiasis and 60 per cent had pulmonary TB. Even among the patients with absolute CD4 counts between 201–350 cells/μl (n=34), occurrence of oral candidiasis infection (55.9%) and pulmonary TB (50%) was high.

Twelve patients in the clinic have been initiated on highly active ART, 11 on a nevirapine-containing regimen, and one on an efavirenz-containing regimen. The most common nucleoside reverse transcriptase inhibitor (NRTI) backbone was stavudine and lamivudine (n=11), with one patient on a zidovudine and lamivudine backbone.

Discussion

These results highlight several issues that require urgent attention for the management of the HIV-infected IDUs. Almost 90 per cent were daily wage earners and the majority earned less than INR 1500 per month, with drug use itself costing up to INR 150 per injection. The low body weight of these patients also indicated poor nutritional levels, which could accelerate the progression of HIV[16] and could also suggest dose modifications. Such economic deprivation, coupled with a lack of health insurance, low levels of education, and ongoing drug use may interfere with optimal adherence to ART[17], thereby compromising the benefits of highly active antiretroviral therapy (HAART)[18].

As almost 50 per cent of the HIV-infected IDUs were married, interventions aimed at preventing transmission of HIV from IDUs to their spouses, as has been shown in the past[19], also need to be addressed. There should also be an emphasis on improving access to voluntary counselling and testing services to the spouses/sexual partners of IDUs.

Co-infection with HBV and/or HCV was a common finding in this cohort. Reports from other regions of India have also identified similar findings. Studies from Manipur estimated the prevalence of HCV to be over 90 per cent[11,12]. A report by Sarkar et al estimated the prevalence of HCV to be 48 per cent among IDUs in the Darjeeling district of West Bengal, but this population also had a relatively lower prevalence of HIV (11.8%) compared to the reports from Manipur[10]. Panda and colleagues[9] estimated the prevalence of HBV to be 20 per cent among street based IDUs in Kolkata in 1998, while a report by Saha and colleagues[11] estimated the prevalence of HBV at 100 per cent among HIV-infected IDUs in Manipur. A plausible explanation to the wide disparity in the rates of co-infection between HCV and HBV could be attributable to the tests used - in HBV, the tests detects the presence of HbsAg, a marker of active infection, while in HCV, the test detects antibodies (anti-HCV). If an antibody test was used for HBV (e.g., anti-HbC), it is likely that all IDUs would test positive.

Co-infection with HCV and HBV complicates the management of HIV and TB. A combination of stavudine, lamivudine and nevirapine is the most commonly used first-line regimen in India due to its low cost (INR 800 per month) and co-formulation. However, studies have found increased levels of nevirapine-induced hepatotoxicity among patients co-infected with HCV or HBV[20,21]. Long-term nevirapine use in co-infected patients has also been shown to accelerate progression to liver cirrhosis[22]. The co- administration of rifampin, an anti-tuberculous drug, and nevirapine can result in lower nevirapine concentrations. Thus, the currently favoured regimens for the management of HIV in India may not be optimal for active or former IDUs, especially for those with HBV and/or HCV co-infection or in those who also abuse alcohol.

High rates of tuberculosis were observed among IDUs in this cohort, especially at absolute CD4 cell counts less than 350 cells/μl. Anti-tuberculous therapy could hamper the efficacy of HAART. Additionally, three of the four drugs commonly used in anti- tuberculous treatment regimens in India, namely rifampin, isoniazid and pyrazinamide, can be hepatotoxic. The extent of hepatotoxicity caused by these drugs in patients infected with HBV and HCV warrants further research and the protocols for management of tuberculosis in India need to be re- evaluated for the IDU population, especially given the high levels of alcohol abuse among them[23].

It may also be worthwhile to investigate the role of earlier initiation of HAART in India to decrease the risk of TB and/or progression of HCV disease. It is also important to note that injection drug use has been linked with poor adherence to medications and higher likelihood of HIV treatment failure[24–27]. Buprenorphine[28] and methadone substitution[24,29,30] have been shown to improve effectiveness of HAART, but the feasibility of such programmes in resource-constrained settings has not been established. Thus, it is of utmost importance to

identify the appropriate modes of delivering HAART as well as anti-tuberculous drugs to IDUs.

Other studies from India[14,31] also found tuberculosis and oral candidiasis to be the most common comorbidities associated with HIV disease. A report from Chennai in 2006 identified TB as a reason for admission in one-third of patients[31] which is similar to the rates among the IDUs reported here. Agarwal and colleagues[14] found a higher rate of pulmonary TB in their cohort of[76] IDUs from Manipur in 1994, possibly due to a longer follow up period and the non availability of HAART at that time.

The IDUs in our cohort also had other co- morbidities that required medical/surgical attention, some of which could be related to their injecting practices. Cellulitis with/without abscesses was a common finding. A majority of these IDUs reported injecting spasmoproxyvon, a combination of dextropropoxyphene and diclofenac that is sold in tablet form over-the-counter, which does not dissolve and is hence injected in powder form. There have also been similar reports of abscesses among IDUs in Kolkata9. Hydrocoeles were also common among the patients at our clinic. Ramaiah and colleagues[32] detected presence of a hydrocoele in 3.8 per cent men in Chennai. Lymphatic filariasis was considered the most common aetiology in this report.

Unfortunately, CD4 strata comparisons were not possible for most infections due to the restricted sample size. Due to economic constraints some diagnoses were not confirmed. The clinic did not have the financial resources to perform bacterial cultures, thus the aetiology of lower respiratory tract infections was not determined. Echocardiograms were also not performed routinely in individuals with abnormal auscultatory findings.

In conclusion, IDUs in Chennai have numerous social and medical issues that complicate their management. High rates of co-infection with HBV, HCV and tuberculosis suggest that new guidelines are urgently needed for the management of HIV and TB, given the potential for hepatotoxicity and drug interactions. IDUs have a multitude of other co- morbidities and health complaints that, for them, may take precedence over their HIV infection. Effective treatment of IDUs requires a comprehensive approach to health care management that incorporates management of HIV infection, co-infecting conditions, symptomatic management, and substance abuse treatment.

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Table

Spectrum of co-morbidities among 118 HIV-infected IDUs availing care at the YR Gaitonde Centre for Substance Abuse-related Research, Chennai, India, 2006

Co-morbidity	n (%)
Hepatitis C virus infection	111 (94.1)
Oral candidiasis	51 (43.2)
Pulmonary TB	40 (33.9)
Anaemia	27 (22.9)
Lower respiratory infection	19 (16.1)
Hepatitis B virus infection	14 (11.9)
Herpes zoster/herpes simplex/gastrointestinal symptoms *	11 (9.3)
Cellulitis (with/without ulcers or abscesses)	8 (6.8)
Others **	6 (5.1)

* each of the conditions listed in this row had the same prevalence;

** others include extrapulmonary TB, tinea infections, papular pruritic infections, malaria, hydrocoeles, hemorrhoids, leg ulcers, endocarditis and inguinal hernia