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Emerging Disparity in HIV/AIDS Disease Progression and Mortality for Men Who Have Sex with Men, Jiangsu Province, China

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Abstract

Few data exist on HIV disease progression and antiretroviral treatment (ART) impact among men who have sex with men (MSM) in China. Using data from the national case reporting system from 2004 to 2010, we describe changes in CD4 cell count before and after ART initiation, disease progression, and mortality among MSM in Jiangsu province compared with other persons living with HIV/AIDS. Median CD4 cell count among MSM at HIV diagnosis was 432 and decreased rapidly in 12 months to below the level of heterosexuals (slope: MSM -38.0 , heterosexuals -15.5 , injection drug users [IDU] -8.0 , blood donors -10.5). Among those initiating ART, median CD4 cell count among MSM was 157, yet the increase in count was slower than for other groups (slope: MSM 26.9 , heterosexuals 31.9 , IDU 29.0 , blood donors 35.0). Progression to AIDS was faster among MSM than heterosexuals and IDU. For the present, the mortality rate was lower for MSM compared with heterosexuals and blood donors; however, against a backdrop of more recent infection (ie, MSM had younger age, and 93.8 % were diagnosed after 2008), findings suggest a survival rate for MSM that will fall behind other groups. Improved medical and psychosocial supportive care is needed for this stigmatized population lest disparities become greater.

Keywords

China; Gay men; Surveillance; Disease progression; Mortality; HIV

Introduction

China's HIV epidemic has recently changed from being focused primarily among injection drug users (IDU) and former blood and plasma donors to being spread primarily through sexual transmission [1–4]. The proportion of reported patients who acquired HIV through sexual contact has increased significantly—from 33.1 % in 2006 to 76.3 % by 2011 [1]. Men who have sex with men (MSM) account for a fast-growing proportion of the HIV epidemic [2], comprising 29.4 % of the estimated 48,000 new infections in 2011, up from 12.2 % in 2007 [3, 4]. In Jiangsu province, in central coastal China, surveys of MSM rarely detected any infection before 2003 yet found an HIV prevalence of 7.1 % by 2009 [5, 6]. A recent cohort study of MSM in Nanjing, Jiangsu's capital, documented an HIV incidence of 5.12 per 100 person-years (p100py) [7]. Moreover, the population size of MSM in China is huge—an estimated 2–5% of adult males, or 10 million persons [8]. The rapidly expanding HIV epidemic among MSM, accompanied by extremely large numbers, could account for the majority of the nation's HIV transmission in coming years.

In response to the HIV epidemic, the Chinese government in 2003 launched the “Four Frees and One Care” policy, including free antiretroviral treatment (ART), free prevention of mother-to-child transmission, free voluntary counseling and testing, free schooling for children orphaned by AIDS, and care for all people living with HIV/AIDS (PLWHA) [9]. By 2009, a total of 81,739 persons had received ART [10]. AIDS mortality decreased from 39.3 p100py in 2002 to 14.2 p100py in 2009, accompanied by a concomitant increase in ART coverage, from 0 to 63.4% of those eligible [11]. However, many persons still die from AIDS. In 2009, AIDS became the country's leading cause of death by infectious diseases, surpassing tuberculosis [12]. Hence, there is urgent need to better understand current disease progression to optimize treatment, especially among the increasingly affected MSM population.

Previous studies on HIV disease progression and mortality in China focused mainly on former blood and plasma donors and IDU, populations whose incidence of new infection peaked in previous decades [13–16]. Few data exist on disease progression and treatment impact among MSM. In this paper, we examine changes in CD4 cell count before and after ART initiation, disease progression, and mortality among HIV-positive MSM in Jiangsu province and compare them with other groups of PLWHA.

Methods

Study Design

We conducted a retrospective cohort study to examine rates of disease progression, from HIV diagnosis and from initiation of ART, using data from the Chinese national case reporting system from 2004 to 2010. The system consists of two databases: (1) a national epidemiology database, which includes individuals reported with an HIV diagnosis but not receiving ART; and (2) a national ART database, including persons who met the national treatment criterion at the time of CD4 cell count < 200 per μ l or WHO stage 3 or 4 [17]. The databases were linked by individuals' national identification numbers and managed by the National Center for AIDS/STD Control and Prevention of the Chinese Center for Disease Control and Prevention (CDC). Each province, autonomous region, and municipality has access to data for its jurisdiction.

Subjects and Measurements

For this analysis, we selected HIV/AIDS patients who were registered as a resident of Jiangsu and reported in the province between January 1, 2004, and December 31, 2010—a period that coincides with ART scale-up. For all newly identified HIV-infected individuals, baseline CD4 cell counts were measured. Among individuals not receiving treatment, a CD4 count was measured once a year if the initial baseline count was >350 cells per μl , and every 6 months if the initial baseline count was <350 cells per μl [18]. Among those on ART, counts were measured at 3, 6, 12, and 18 months to monitor early treatment, and every 6 months thereafter [17].

To describe changes in CD4 cell counts among individuals not receiving ART, we included those whose CD4 cell counts were measured and followed for three consecutive years after initial HIV diagnosis. If an individual's CD4 cell count was measured multiple times during a follow-up year, his/her most recent count during that year was used for analysis. A median count was calculated, based on the cluster of the samples for each year and transmission group, to describe changes in CD4 cell counts over time. To assess the impact of ART, similar methods were used to compare changes in CD4 cell counts among individuals on treatment.

To describe HIV disease progression to AIDS diagnosis, we included individuals who were first confirmed for an HIV non-AIDS diagnosis between 2004 and 2010 then were later clinically assessed for AIDS during these years. Median times from HIV diagnosis to AIDS diagnosis were calculated for each year and transmission group. To assess mortality, we included individuals who were diagnosed with AIDS and subsequently assessed for vital status between 2004 and 2010. Causes of death were categorized by two types: (1) HIV/AIDS-related death and (2) nonrelated death, typically including suicide, overdose, and “other” causes not recorded [19]. We recognize that cause-specific data may be incomplete in the HIV/AIDS case reporting system and in vital statistics records, particularly if not confirmed and reported by physicians in hospitals or by case managers from the CDC at the county and district levels. Therefore, we used all-cause mortality for Kaplan–Meier curves and survival analysis. As for death with HIV but not AIDS, only 29 patients with HIV infection died without ever having a diagnosis of AIDS. We have excluded these from our analysis. Median times from AIDS diagnosis to death were calculated for each year and transmission group.

Statistical Analysis

For each patient, the mean of the difference between baseline and 36-month follow-up CD4 cell count was calculated and analysis of variance (ANOVA) was conducted to detect significant differences between years and transmission groups. A slope to describe the trajectories of changes in CD4 cell counts was calculated using standardized commands in Microsoft Excel software. A scatter diagram was first created, with x (time) as the independent variable and y (CD4 count) as the dependent variable, fitting the points to a straight trend line of $y = ax + b$, with the value in the formula as the reported slope of the line. SPSS 16.0 software was used for other analyses. The Kaplan–Meier method was used to estimate disease progression from the time of HIV diagnosis to onset of AIDS and from onset of AIDS to death (all-cause mortality). P values < 0.05 were considered significant for differences between groups, all two-sided.

Results

From 2004 to 2010, a total of 1,420 MSM, 2,112 heterosexuals, 757 IDU, and 418 blood donor HIV/AIDS patients were reported in Jiangsu (Fig. 1). Of these, 1,116, 1,225, 392, and

327, respectively, were eligible for follow-up by virtue of being registered as residents of the province. The numbers of patients in each group who had four consecutive years of records of CD4 cell counts were 195, 224, 33, and 16, respectively, among those not on ART and 175, 241, 135, and 24, respectively, among those on ART. The overall CD4 cell count follow-up rate of the four groups was 33.2, 38.0, 42.9, and 12.2 %, respectively. Of cases, 381 (34.1 %) MSM, 641 (52.3 %) heterosexuals, 78 (19.9 %) IDU, and 158 (48.3 %) blood donors developed AIDS after HIV diagnosis between 2004 and 2010. Of these, 68, 262, 71, and 145, respectively, were known to have died prior to study end (all-cause mortality). Of these, 35, 125, 15, and 101, respectively, were reported as AIDS-related deaths.

Table 1 shows median CD4 cell counts at baseline, 12, 24, and 36 months for each group, by treatment status. Among those not on ART, baseline counts were 432, 420, 475, and 354 cells per μ l for MSM, heterosexuals, IDU, and blood donors, respectively. At 36 months, median counts decreased by 12.3 % among MSM compared with 8.3 % among heterosexuals, 20.4 % among IDU, and 10.2 % among blood donors ($P = 0.265$ for difference by groups). Among those on ART, baseline median CD4 cell counts were 159, 148, 216, and 137.5 cells per μ l for MSM, heterosexuals, IDU, and blood donors, respectively. At 36 months, the increase in CD4 cell counts was 43.4 % among MSM, compared with 63.5 % among heterosexuals, 43.1 % among IDU, and 82.9 % among blood donors; however, the difference was not statistically significant by ANOVA ($P = 0.673$).

Figures 2 and 3 show the trajectories of changes in CD4 cell counts among each group before ART eligibility (Fig. 2) and after ART initiation (Fig. 3). Among those not on ART, the slopes of the lines for MSM, heterosexuals, IDU, and blood donors were -38.0 , -15.5 , -8.0 , and -10.5 , respectively, showing a relatively more rapid decline of CD4 cell counts among MSM compared with others, especially at the 12-month follow-up. Among those on ART, the slopes of the lines for MSM, heterosexuals, IDU, and blood donors were 26.9, 31.9, 29.0, and 35.0, respectively, indicating a slower increase in CD4 cell counts among MSM compared with others. By 36 months, CD4 cell counts among MSM had dropped to the lowest level of any group.

Figures 4 and 5 show Kaplan–Meier curves for disease progression and mortality. Survival analysis showed that disease progression from HIV to AIDS (Fig. 4) was faster among MSM compared with heterosexuals ($X^2 = 4.98$, $P < 0.050$) and IDU ($X^2 = 163.89$, $P < 0.01$), but slower among blood donors ($X^2 = 116.72$, $P < 0.01$). So far, the mortality rate (Fig. 5) is lower among MSM compared with heterosexuals ($X^2 = 19.73$, $P < 0.01$) and blood donors ($X^2 = 130.91$, $P < 0.01$). However, the vast majority (93.8 %) of cases among MSM were diagnosed after 2008, while most cases among blood donors (64.1 %) and IDU (51.6 %) were diagnosed prior to 2008 (Table 2). Moreover, MSM cases were younger at diagnosis (median age 32 years) compared with blood donors (median age 40 years) after 2008. In the contexts of more recent infection, younger age, and the vast majority being diagnosed in the era of ART availability, the survival experience of MSM with HIV/AIDS should be better than other groups. Yet, by multiple indications of our data, their disease progression appears to be worse.

Discussion

Taken together, our observations may give early warning of an emerging disparity in disease progression and survival of MSM with HIV/AIDS in Jiangsu, China. Our findings show a faster rate of disease progression from HIV to AIDS among MSM compared with heterosexuals, IDU, and blood donors; a faster decline in CD4 cell count among MSM before ART; and a slower increase in CD4 cell count after ART compared with other groups. In contrast, IDU have slower progression to AIDS and higher CD4 cell counts at

diagnosis. This may be due to routine HIV testing upon entry to detoxification centers and methadone clinics, leading to earlier diagnosis and close linkage to care clinics. Overall mortality is currently higher among IDU, possibly due to the contribution of non-AIDS causes of death, particularly overdose [20]. However, projections for future mortality must be interpreted within the context that wide HIV transmission among MSM in China is a recent phenomenon. Most HIV/AIDS cases among MSM have occurred in the last few years, an era with wider availability of ART, whereas most cases among IDU and blood donors occurred many years in the past.

We fear that an explanation for the emerging disparity is the particularly challenging barriers to MSM getting appropriate care and support. It is possible that the worse outcomes for MSM after treatment initiation may be due to weaker social support systems to help with treatment adherence and access to ancillary care. It is also possible that MSM experienced more adverse psychosocial problems that predict poorer prognosis in HIV diseases [21]. Both homosexuality and HIV/AIDS are heavily stigmatized within the Chinese social environment, and many gay and bisexual men are unable to disclose their sexual orientation or HIV-positive status [22–24]. Without social and familial support, many MSM would experience anxiety, self-blame, fear, and helplessness [25], which may compromise the immune system and further catalyze the disease progression. Thus, MSM-friendly psychosocial support and mental health services should be provided, especially during the first months of follow-up, to improve coping with positive status. Other hypotheses for poorer prognosis among MSM are more virulent HIV strains [26] and ART resistance mutations, although the latter does not yet seem to be the case in Jiangsu [27]. Unfortunately, our surveillance data do not have good measures of adherence, quality of care, or stigmatization and discrimination experienced by MSM—areas in need of rigorous studies.

We recognize other limitations as well. Among HIV-positive MSM who were followed by the local health departments, one-third were retained in the management system from 2004 to 2010, lower than for heterosexuals and IDU. The high loss for follow-up shows that retention in care of MSM is problematic. Improved quality of pre- and post-test counseling, nonstigmatizing attitudes toward MSM among health care providers, and well-organized referral services are needed to strengthen linkage and retention in care. We also recognize that the lack of behavioral and psychosocial data as well as measures of quality of care limit our ability to interpret findings. Rigorous studies using locally appropriate measures of these domains should be prioritized.

We are fortunate to have these indicators of faster disease progression and poorer response to treatment as early signals, allowing enough time to act before an opportunity to prevent morbidity and mortality is lost for this group. Of great significance, this disparity appears to be emerging during a period of increased availability of ART. As observed in other places, such as the pre- vs. post-ART era in San Francisco [28, 29], disparities are exacerbated when access to care makes a profound impact on health outcomes. A shift to earlier ART initiation might result in MSM falling relatively further behind, both in individual benefits as well as in relation to the population, by virtue of slowing transmission through viral load suppression [30, 31]. Our data therefore stand as a wake-up call to help ensure that future benefits of early care and treatment are equitably given to all groups affected by HIV in China.

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Fig. 1.
Reported HIV/AIDS cases by risk and disease progression, Jiangsu province, China, 2004–2010

Fig. 2.
Trends in CD4 cell counts by risk before ART eligibility, Jiangsu Province, China, 2004–2010

Fig. 3.
Trends in CD4 cell counts by risk after ART initiation, Jiangsu Province, China, 2004–2010

Fig. 4.
Disease progression from HIV to AIDS by risk, Jiangsu province, China, 2004–2010

Fig. 5.
Disease progression from AIDS to death (all causes) by risk, Jiangsu province, China, 2004–2010

Table 1

Median CD4 cell count by follow-up visit and risk, Jiangsu province, China, 2004–2010

Risk	Baseline		12 months		24 months		36 months	
	Non-ART	ART	Non-ART	ART	Non-ART	ART	Non-ART	ART
MSM	432	159	394	213	394	233	379	228
Heterosexuals	420	148	405.5	184	402	207	385	242
IDU	475	216	467	250	431	261	378	309
Blood and plasma donors	354	137.5	343.5	207.5	332.5	215.5	318	251.5

Table 2

HIV cases and median age at diagnosis, by risk, 2004–2010 and after 2008, Jiangsu province, China

Risk	Total cases 2004–2010	Median age at diagnosis (years)	Cases detected after 2008 (%)	Median age at diagnosis after 2008 (years)
MSM	1,420	32	93.8	32
Heterosexuals	2,112	37	74.8	38
IDU	757	30	48.4	31
Blood and plasma donors	418	38	35.9	40