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Changes in epidemiological and treatment-related characteristics among newly reported HIV/AIDS cases in an urban area in Shanghai, China from 2001 to 2019: A population-based retrospective study

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Abstract: The HIV/AIDS epidemic has changed significantly over the past 40 years. Changes in AIDS intervention strategies over time and across regions may have influenced epidemiological characteristics and intervention strategies. The aim of the current study was to analyze the changes in multi-year epidemiological characteristics of newly reported HIV/AIDS cases in an urban area (the Fengxian District of Shanghai) from 2001 to 2019 based on the national AIDS comprehensive data information system and Shanghai Statistical Yearbook. In total, the average annual incidence of HIV/AIDS was 1.92 per 100,000 persons. The annual incidence fluctuated and tended to increase from 2001 to 2019 $(\chi^2 = 128.38, p < 0.001)$. More male patients were reported compared to female patients, accounting for 82.9%. The proportion of patients over 65 years of age increased from 5% in 2009 to 12% in 2019. The majority of cases involved sexual contact (97.7%), early diagnosis (58.8%), full virologic suppression (72.9%), and early antiretroviral therapy (ART) (44.3%). Migrant patients have significantly increased over the years. There were significant differences between local and migrant patients in terms of the age at diagnosis, transmission route, and baseline CD4 count. The disparity in high-risk temporal clusters was also explored to indicate the delay of an epidemic between local patients and migrant patients. HIV remains at a low endemic level. AIDS prevention and control measures have been highly effective, and especially in virologic suppression of ART and early diagnosis. More efforts should be made to enhance early diagnosis and treatment among key vulnerable groups, including the elderly in the local population and young male migrants, and the scale of HIV/AIDS testing should be expanded to the general population to control HIV transmission.

Keywords: HIV epidemic, Shanghai, epidemiology, time clustering, feature analysis

Introduction

Human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS) has a negative impact on public health and economic development. According to The United Nations Joint Program on HIV/AIDS (UNAIDS), prior to 2022, approximately 39 million people were estimated to be living with HIV globally, and 29.8 million people living with HIV were receiving antiretroviral therapy (ART) globally (*1*). There have been an estimated 1.3 million new HIV infections, marking a 38% decline in people acquiring HIV since 2010, and 630,000 people died from HIVrelated illnesses by 2022 (*1*). Despite extraordinary progress, HIV/AIDS remains a major global public health issue, imposing a serious burden on human life and economic stability (2). UNAIDS set the "95-95-95" treatment targets to end the HIV/AIDS epidemic by 2030 (3). Higher requirements should be implemented in HIV/ AIDS prevention and control. Since the first AIDS case was reported in China in 1985, 60,154 cases and 19,623 deaths were reported in mainland China in 2021 (4). At the end of 2022, there were estimated 1.22 million people living with HIV in China (5). That said, HIV/AIDS has a low level of incidence and prevalence nationwide. HIV is the leading cause of death from national notifiable infectious diseases (except for COVID-19) in China (5).

To prevent the spread of the HIV/AIDS epidemic, China has implemented national policies for HIV/ AIDS control for several decades. Through AIDS

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intervention strategies, China has achieved substantial progress in combating the HIV/AIDS epidemic. The Chinese Government started the national "Four Frees and One Care" policy in 2003. Moreover, the policy has been adjusted by critically evaluating tailored interventions and iterative assessment and improvement of HIV-related services. The Chinese National Free Antiretroviral Treatment Program (NFATP) for individuals with HIV is part of prevention interventions aimed at reducing HIV transmission. ART is an effective measure to control HIV/AIDS transmission and improve the quality of life of HIVinfected people, prolong their survival, and reduce AIDS-related mortality (6-8). Individuals meeting the primary criteria of a CD4 count ≤ 200 cells/ mm³ can utilize the NFATP. While this threshold was revised to ≤ 350 cells/mm³ in 2008 (9). the World Health Organization (WHO) contended that rapid ART imitation is a critical step to reducing HIV transmission in 2015. The eligibility requirement for free ART has been revised and the CD4 count threshold was eliminated in 2016, i.e. implementation of the "Treatment as Prevention" strategy. Baseline CD4 cell counts, the time difference between HIV diagnosis and ART initiation, and the viral load (VL) after ART initiation are core treatment-related indicators linked to HIV early detection, early diagnosis, and early treatment. The baseline CD4 count is associated with severe illness. A low CD4 cell count (< 200 cells/mm³) can indicate late diagnosis. Late diagnosis and ART initiation could lead to an increased risk of negative health outcomes, including opportunistic infections and even death. First VL monitoring is recommended at 6 months after ART initiation under national ART guidelines to evaluate viral suppression. A high VL after ART initiation could reflect failure of virologic suppression and ART treatment. Virologic suppression almost promotes immunologic recovery and reduces the incidence of opportunistic infections and malignancies. Virologic suppression is defined by the WHO as a VL < 1,000 copies/mL. Nevertheless, the threshold could underestimate adverse outcomes. Low-level viremia (LLV) of 50-999 copies/mL could increase the risk of drug resistance. Early detection and ART of HIV infections and viral suppression could avoid negative outcomes and reduce the risk of HIV transmission.

The HIV/AIDS epidemic has changed significantly over the past 40 years, and it has a geographical heterogeneity across China. AIDS intervention strategies have changed over time and across regions. The changes may have affected epidemiological characteristics and intervention strategies. Moreover, an increasing migrant population and aging population in urban areas, and especially in Shanghai, could lead to changes in demographic characteristics and HIV/AIDS transmission patterns. Given the completeness of HIV/ AIDS epidemic data and demographic characteristics, the Fengxian District in Shanghai was chosen as a study site in the current study to explore the multi-year epidemiological and treatment-related characteristics of HIV infections and AIDS patients (HIV/AIDS cases) among different sub-populations and to evaluate changes in transmission patterns and the effectiveness of intervention policies.

Patients and Methods

Study site

The Fengxian District, which includes 11 communities, is situated in the southern part of Shanghai at the junction with the Huangpu River to the north. Located southeast of the Yangtze River Delta, it covers an area of 733.38 square kilometers (Figure 1). It is a picturesque coastal urban area with an obvious geographical location. Fengxian is a typical urban area with a high level of industrialization and a large migrant population (10). As industrialization has accelerated in the area, the migrant population has grown markedly. According to the Shanghai Statistical Yearbook, the migrant population accounts for half of the total population in Fengxian. Because of the consistency between the demographic characteristics of Fengxian and Shanghai overall, well collected data in Fengxian are considered to be representative of Shanghai, facilitating this study.

This study was approved by the Ethics Administration Committee of the Shanghai Municipal Center for Disease and Prevention (ID: KY-2024-33).

Data source

Individual information on newly reported HIV/ AIDS patients with current addresses in the Fengxian District in 2001-2019 were retrieved from the National AIDS Comprehensive Prevention and Control Data Information System, including HIV-infected persons and AIDS patients. Base information on these individuals included sex, age, local address, current address, date of disease onset, date of diagnosis, date of ART initiation, first VL about 6 months after ART initiation, baseline CD4 cell count at diagnosis, and case classification (AIDS or HIV). Yearly aggregated data were calculated based on date of diagnosis. The time range was calculated as the time difference between the date of diagnosis and the date of ART initiation. According to national criteria in different periods, all individuals were divided into 3 groups (2002-2007, 2008-2015, and 2016-2019) based on the year of diagnosis. Population data in the study area were gathered from the Shanghai Statistical Yearbook (http://tjj.sh.gov.cn/tjnj/index.html).

In this study, the VL after about 6 months after ART initiation, baseline CD4 cell count, and time

difference from diagnosis to ART can be considered as comprehensive indicators with which to monitor disease procession and the effectiveness of ART therapy. Timely HIV diagnosis and late HIV diagnosis were defined as a baseline CD4 cell count \geq 200 cells/ mm³ and < 200 cells/mm³ (11). A time from diagnosis to ART within 30 days was considered to be immediate ART, and other times were considered to be delayed ART (12). VL is an indicator with which to evaluate the effectiveness of ART therapy and virologic suppression. Full virologic failure were defined as a VL < 50 copies/ mL, a VL < 1,000 copies/mL, and a VL \geq 1,000 copies/ mL (13).

Statistical analysis

The incidence of HIV infections and AIDS patients (per 100,000 people) among the overall population, locals, and migrants was calculated from 2001 to 2019 at the study site. The time distribution in the incidence of newly reported HIV infections and AIDS patients was described to indicate potential temporal trends. Descriptive statistics were used to summarize the demographic, behavioral, and treatment-related characteristics of local and migrant HIV/AIDS patients. Significant differences were assessed with Pearson's chi-squared test or Kruskal-Wallis test for unordered categorical data and the Cochran-Armitage test for ordinal categorical data. Demographic, behavioral, and treatment-related variables for local and migrant HIV/ AIDS patients over the years were visually depicted to describe the temporal trends in and epidemiological characteristics of HIV/AIDS. The trends in HIV/AIDS cases with respect to different variables during these years was analyzed using the Cochran-Mantel-Haenszel test.

The software SaTScanTM version 10.1 used Kulldorff's retrospective space-time scan statistic based on a discrete Poisson model to explore temporal clusters of HIV infections and AIDS patients during the study period and to identify potential patterns of disease among local and migrant patients (14). The maximum temporal size of the clusters was set at 20% for the study period, and the number of Monte Carlo simulations was set at 999. The analysis generates 3 model parameters, including log-likelihood ratios (LLRs), p values, and risk ratios (RRs). A cluster with the maximum LLR represents the most likely cluster. The p value for the LLR parameter can be estimated via Monte Carlo simulations to indicate statistically significant clusters if the p value < 0.05. The RR is the estimated risk within the cluster divided by the risk outside the cluster (14).

The study was conducted using the software R version 4.2.3 for data collection and analysis. A p value < 0.05 was considered a statistically significant difference.

Results

Demographic characteristics

A total of 388 people with HIV/AIDS were reported in the area from 2001 to 2019, accounting for 41.2% of AIDS patients in Fengxian. The first case was reported in 2001. Figure 1 shows the geographical distribution of the Fengxian District and annual incidence of HIV infections and AIDS patients among the total population, locals, and migrants. The average annual incidence of HIV/AIDS was 1.92 per 100,000 persons (range: 0-4.34 per 100,000 persons). The annual incidence of HIV/AIDS among locals and migrants was 0-5.91 per 100,000 persons and 0-3.64 per 100,000 persons, respectively, with an average annual incidence of 2.75 per 100,000 persons and 0.995 per 100,000 persons. In total, annual incidence fluctuated and tended to increase from 2001 to 2019 ($\chi^2 = 128.38$, p < 0.001).

Among the migrant population, the incidence of HIV/AIDS remained at low levels before 2006. The annual incidence of HIV/AIDS increased steadily from 2006 to 2013, and the annual incidence fluctuated and increased from 2014 to 2019 ($\chi^2 = 36,67, p < 0.001$). The trends in incidence among migrants were similar to those in the total population ($\chi^2 = 120.71, p < 0.001$) (Figure 1).

The characteristics of HIV/AIDS cases among locals and migrants are shown in Table 1. Among all reported HIV/AIDS patients, HIV/AIDS cases among migrants increased over the years ($\chi^2 = 11.59, p < 0.001$), accounting for 25.5%. Fifty-nine-point-nine percent of local patients and 52.5% of migrant patients were diagnosed in 2008-2015 and 2016-2019, respectively. More male patients were reported compared to female patients, with a male-to-female ratio of 4.88:1. There were no significant differences between or temporal trends in local and migrant patients in terms of sex. In terms of age distribution, the median age (IQR) was 43 (31-54) years. Patients 25-65 years of age comprised 82.7% of cases. There were significant differences and temporal trends in the age distribution of local and migrant patients (p < 0.001). The majority of local and migrant patients were 45-65 years and 25-45 years, respectively. The proportion of patients over 65 years of age have increased from 5% in 2009 to 12% in 2019. In addition to the increase in local patients over 65 years of age ($\chi^2 = 6.55$, p < 0.05), the proportion of migrant patients ages 25-45 years increased from 17% in 2007 to 24% in 2019 ($\chi^2 = 8.72$, p < 0.05). There were no obvious trends in the diagnosis of patients 18-25 years of age (10.1%) (Table 1 and Figure 2).

The level of education of patients was mainly primary school and below, accounting for 56.2% (58.1% for local patients and 50.5% for migrant patients). The proportion of migrant patients whose level of education was primary school or below declined over



Figure 1. Geographical distribution of Fengxian District in Shanghai and temporal trends in newly reported HIV/AIDS cases among locals and migrants in the area from 2001 to 2019. (A) The geographical distribution of Fengxian District, Shanghai; (B) The annual incidence rates per 100,000 persons reported by years among local (green line), migrant (blue line) population and total population (red line) from 2001 to 2019; (C) The bar plot of HIV/AIDS local and migrant patients. Line plot shows temporal changes in the proportion of local patients.

the years ($\chi^2 = 5.02$, p < 0.05). Married or cohabiting patients comprised 53.4% of HIV/AIDS patients, and the proportion increased over the years ($\chi^2 = 16.59$, p < 0.001). There were no significant differences in the distribution of marital status among local and migrant patients. The dominant transmission route has been sexual contact over the years (heterosexual contact for local patients and male-to-male sexual contact (MSM) for migrant patients). Fifty-seven-point-five percent of patients were infected via heterosexual contact and 40.2% were infected via MSM (Figure 2). The proportion of patients infected via heterosexual contact ($\chi^2 = 16.59$, p < 0.001) or who were married or cohabiting ($\chi^2 = 17.21$, p < 0.001) tended to increase over the years. The proportion of HIV/AIDS attributed to heterosexual contact as a transmission route increased from 50% in 2007 to 76% in 2019.

Treatment-related characteristics

The median (IQR) baseline CD4 count was 239 (103, 370) cells/mm³, and 82% of people with HIV had a CD4 count between 200 and 500 cells/mm³. Fortyone-point-two percent of patients were diagnosed late. There were significant differences in the CD4 cell count of local and migrant patients (p < 0.001). More local patients (44.3%) were diagnosed late than migrant patients (32.3%). Seventy-two-point-nine percent had full virologic suppression, 10.1% had LLV, and 3.1% had a VL \geq 1000 copies/mL. The majority of those with no VL test were reported from 2013-2015 (57.4%). The time difference between diagnosis and initiation of ART was within 30 days for 44.3%. The median time to ART initiation decreased from 68 months in 2001 to 12 days in 2019. Patients in whom ART was initiated early increased over the years, and especially after 2016. The proportion of patients with LLV ($\chi^2 = 9.06$, p < 0.01), a late diagnosis ($\chi^2 = 6.42$, p < 0.05), and in whom ART was initiated within 30 days ($\chi^2 = 96.59$, p < 0.001) tended to increase over the years. More details are shown in Table 1 and Figure 3.

Temporal cluster analysis

Two significant temporal clusters were found during the study period. The most likely cluster of local patients was from March 2012 to November 2015. RR was 2.27. There were 2.27 times more local patients diagnosed in March 2012-November 2015 than in other years. Moreover, there were 2.78 times more migrant patients diagnosed in August 2016-December 2019 than in other years. More details are shown in Table 2.

Discussion

HIV/AIDS remain a major public health concern in China. With an increasing migrant population and aging population in urban areas, epidemiologic characteristics

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> 365 73 (18.8) 55 (19.0) 18 (18.2)	< 365	15 (3.9)	9 (3.1)	6 (6 1)	
12/10/01	> 365	73 (18.8)	55 (19.0)	18 (18.2)	

Table 1. Characteristics of newly reported HIV/AIDS cases among local and migrants from 2001 to 2019 in the study area

*Other transmission routes included injection drug use (IDUs) and blood (plasma) donation.

and intervention strategies for HIV have varied across regions. This study explored changes in the epidemiological patterns of HIV/AIDS and detected the high-risk periods in an urban area of Shanghai. Results indicated that the average annual incidence was 1.92 per 100,000 persons, which is far lower than the incidence in China overall. HIV/AIDS still remains at low endemic levels in Shanghai. The increase in incidence over 20 years might be related to improvements in the HIV testing capacity, standardization of the AIDS prevention and control network and improvement of the national AIDS report system, and expansion of the scale of HIV testing (15).

This study found that 83.0% of patients were male. This could be due to the increasing number of MSM. MSM are the highest-risk sub-population for HIV/AIDS infections and are causing an increasing public health burden in China (*16*). Eighty-two-pointseven percent of patients were 25-65 years of age. The proportion of patients 25-45 years of age and over 65 years of age has significantly increased over the years. The young and middle-aged more actively engage in sexual behavior. Neglect of the sexual demand among the elderly population by society and the lack



Figure 2. Time distribution of HIV/AIDS cases among local and migrants based on demographic and behavioral variables in 2001-2019. The first column shows the cumulative proportion plot of all HIV/AIDS cases with variables. The second column shows the number of HIV/AIDS cases among local and migrants with variables. (A) The annual cases and proportions of HIV infections and AIDS patients by sex. The line plot shows temporal changes in the proportion of male patients; (B) The annual cases and proportions of HIV infections and AIDS patients by age-group; (C) The annual cases and proportions of HIV infections and AIDS patients by marital status. The line plot shows temporal changes in the proportion of cases by age-group; (C) The annual cases and proportions of HIV infections and AIDS patients by transmission route. The line plot represents the proportion of cases *via* heterosexual contact.

of knowledge of HIV/AIDS can lead to unsafe and unprotected sex, thus increasing the risk of acquiring HIV/AIDS (17,18). More efforts should be made to improve active surveillance and HIV prevention education for the accurate and effective prevention and control of HIV among the elderly, and especially those in the local population.

HIV/AIDS patients who have received a high level of education and who are married or cohabiting have increased in recent years. School-based HIV/ AIDS education and premarital HIV/AIDS counselling should enhance education on HIV/AIDS intervention to provide information to young people and couples getting married. The dominant transmission route has been sexual contact over the years. Heterosexual contact (57.5%) and MSM (40.2%) were the main transmission routes at the study site over the years. The increase in heterosexual contact among local patients (60.9%) indicates the expansion of the HIV/ AIDS epidemic from high-risk groups to the general population (19). Based on the high-risk population, intervention strategies for the general population should be enhanced. Moreover, the proportion of MSM may be underestimated due to fear of social discrimination (20).

VL, the CD4 cell count, and the time difference between diagnosis and ART initiation in HIV-infected individuals can provide information on the effectiveness and achievement of AIDS prevention, control, and treatment. VL and the CD4 cell count can indicate HIV/AIDS progression and thus the extent of early diagnosis. Early diagnosis and early treatment helps to avoid opportunistic infections and antiretroviral resistance (21,22). The rate of full viral suppression among HIV/AIDS patients receiving treatment for at least 6 months was 72.9%, 10.1% had LLV, and 3.1% had a VL \geq 1,000 copies/mL. Late diagnosis was 41.2% and tended to increase; that proportion was higher than in the rest of mainland China (19). Moreover, 67.9% of the elderly (over 65 years of age) were diagnosed late. Late diagnosis is a serious problem. One cohort study found that initiation of ART within 30 days of diagnosis was associated with a 63% reduction in mortality at a 1-year follow-up (12). Rapid ART can decrease HIV/AIDS mortality and opportunistic infections. The median time to ART initiation decreased from 68 months in 2001 to 12 days in 2019. These findings could be due to the expansion of intervention and medical care and the subsequent optimization of treatment. Moreover, a lack of knowledge of HIV/ AIDS or access to medical services could be related to late diagnosis and treatment (23). Furthermore, HIVrelated stigma and discrimination surrounding HIV/ AIDS is still a severe challenge for achieving the goal of ending the HIV epidemic (24). Public health and



Figure 3. Time distribution of HIV/AIDS cases among local and migrants based on treatment-related variables in 2001-2019. The first column shows the cumulative proportion plot of all HIV/AIDS cases with variables. The second column shows the number of HIV/AIDS cases among local and migrants with variables. (A) The annual cases and proportions of HIV infections and AIDS patients by viral load. The line plot shows temporal changes in the proportion of cases of full viral suppression (VL < 50 copies/mL); (B) The annual cases and proportions of HIV infections and AIDS patients by baseline CD4 cell count. The line plot shows temporal changes in the proportions of HIV infections and proportions of HIV infections and AIDS patients by baseline CD4 cell count. The line plot shows temporal changes in the proportion of late diagnosis (CD4 count < 200 cells/mm³); (C) The annual cases and proportions of HIV infections and AIDS patients by duration from diagnosis to ART initiation. The line plot shows temporal changes in the proportion of early ART initiation (duration < 30 days).

Table 2. Results of temporal cluster analysis of HIV/AIDS cases among local and migrants from 2001 to 2019

Clusters	Years	Reported cases	Expected cases	RR	LLR	p value
Locals	2012/3-2015/11	107	59.4	2.27	20.69	0.001
Migrants	2016/8-2019/12	50	26.04	2.86	13.12	0.001

medical departments should enhance health education to eliminate all discrimination against HIV-positive patients and facilitate their treatment to promote early diagnosis and treatment (25-27). In addition, HIV testing is the key to the early diagnosis of HIV/AIDS (23,28).

HIV/AIDS cases among migrants increased over the years ($\chi^2 = 11.59$, p < 0.001), accounting for 25.5%. Moreover, migrant patients were reported to be younger than local patients. The dominate transmission route was MSM. Population migration can hamper the identification and management of cases. Migrants have different a health status than locals (29-31). Population migration increases the opportunities for human contact and promotes the spread of HIV as urbanization proceeds. A low level of risk awareness of HIV infection and engaging in high-risk sexual behavior place migrants at higher risk for HIV (32-34). The current results revealed that the HIV/AIDS epidemic among migrants may be still be high. Temporal cluster analysis explored the peak in local patients in 2012-2015 and migrant patients in 2016-2019. The disparity in temporal clusters of local and migrant patients indicates the delay of the HIV/AIDS epidemic in migrants. These findings suggest that more interventions and education should be provided to young male migrants.

This study had several limitations. First, it was a county-level cross-sectional study on newly reported HIV/AIDS data. In this study, the Fengxian District was considered to be representative of Shanghai, but the reported number of cases was relatively few. Considering the low prevalence in Shanghai and similar demographic characteristics, the epidemiological patterns in the Fengxian District may reflect those in Shanghai. The study only qualitatively analyzed the potential epidemiological patterns of HIV/AIDS. Influencing factors could be explored in a further study. Moreover, age-specific populations could not be identified, leading to lack of age-adjusted incidence.

Finally, this study found that the dominant transmission route has been heterosexual contact. HIV transmission routes rely on self-reports and could be misclassified as a result of stigma and discrimination. To effectively and efficiently identify high-risk groups, molecular epidemiological methods could be used to explore transmission routes.

In conclusion, HIV/AIDS prevention and control measures have achieved substantial progress at the study site. Nevertheless, there are still several emerging challenges. To tackle future challenges of the AIDS epidemic and further advance progress towards achieving the goal of curbing AIDS, the next stage of HIV/AIDS prevention and control should be focused on these key high-risk populations. HIV screening services and the surveillance network should be enhanced for these high-risk populations (migrants and elderly in the local population) to promote early diagnosis, interventional policies and strategies should be tailored, and prevention and control programs should be implemented for sub-populations, and especially the elderly population and MSM population, as well as the general population. Health surveillance and management of the migrant population should be enhanced.

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