Epidemiological, virological and serological features of COVID-19 cases in people living with HIV in Wuhan City: A population-based cohort study

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Summary of the article: In this population-based cohort study, PLWH aged ≥50 years and those with cART discontinuation were at increased risk for COVID-19. High HIV viral load (≥20 copies/ml) might prolong the disease course and decrease the SARS-CoV-2-specific antibody level against COVID-19.

ABSTRACT

Background. We aimed to describe the epidemiological, virological and serological features of coronavirus disease 2019 (COVID-19) cases in people living with HIV (PLWH).

Methods. This population-based cohort study identified all COVID-19 cases among the whole PLWH in Wuhan city, China, by April 16, 2020. The epidemiological, virological and serological features were analyzed based on the demographic data, temporal profile of nucleic acid test for SARS-CoV-2 during the disease, and SARS-CoV-2-specific IgM and IgG after recovery.

Results. From January 1 to April 16, 2020, 35 of 6001 PLWH have experienced COVID-19, with the cumulative incidence of COVID-19 to be 0.58% (95%CI: 0.42%-0.81%). Among the COVID-19 cases, 15 (42.86%) had severe illness, with 2 deaths. The incidence, case-severity and case-fatality of COVID-19 in PLWH were comparable to that in the entire population in Wuhan. 197 persons had cART discontinuation, of whom 4 persons experienced COVID-19. Risk factors for COVID-19 were age ≥50 years old and cART discontinuation. The median duration of SARS-CoV-2 viral shedding among confirmed COVID-19 cases in PLWH was 30 (IQR: 20-46) days. Cases with high HIV viral load (≥20 copies/ml) had lower IgM and IgG levels than those with low HIV viral load (<20 copies/ml) (median S/CO for IgM, 0.03 vs. 0.11, $P<0.001$; median S/CO for IgG, 10.16 vs. 17.04, $P=0.069$).

Conclusions. Efforts need to maintain the persistent supply of antiretroviral treatment to elderly PLWH aged 50 years or above during the COVID-19 epidemic. The coinfection of HIV and SARS-CoV-2 might change the progression and prognosis of COVID-19 patients in PLWH.

Keywords: HIV; COVID-19; SARS-CoV-2; epidemiology; antibody

Introduction

Coronavirus disease 2019 (COVID-19) is an emerging infectious disease, caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which was first reported in the latterly December 2019 in Wuhan, China[1]. According to the WHO status report, more than 16 million COVID-19 cases have been reported worldwide until July 30[2]. COVID-19 has emerged as a great challenge to global public health. Since no vaccine and effective drugs are available against this infectious disease, non-pharmaceutical interventions were implemented to slow the spread and flatten the epidemic curve of COVID-19[3]. Although governments and communities have been dedicated to maintaining HIV service provision for people living with HIV (PLWH), antiretroviral treatment for PLWH may be hindered by the COVID-19 epidemic[4].

Considering the large number of PLWH, it is urgent to evaluate whether the incidence of COVID-19 in PLWH differs from that in the general population. Cases with coinfection of SARS-CoV-2 and HIV have been reported in several countries[5-7]. But only one study calculated the COVID-19 incidence in PLWH based on HIV patients in a single hospital[8]. The population-based incidence of COVID-19 in PLWH needs to assess this population at risk of SARS-CoV-2 infection comprehensively. Previous studies have found that PLWH with low CD4 cell count, high HIV viral load and not taking antiretroviral treatment have an increased risk of other respiratory infections[9]. However, limited data were available for the risk of SARS-CoV-2 infection in PLWH. Several studies have demonstrated the antibody response to SARS-CoV-2 infection in the general population[10, 11], which may inform vaccine intervention in the future. Nevertheless, there is no information currently on the antibody against SARS-CoV-2 infection in PLWH. Guidance has been proposed by US Department of Health and Human Services and EACS European AIDS Clinical Society to

provide information about the proper response to COVID-19 in PLWH[12, 13]. But guidance like these needs more evidence to refine their recommendation.

In the present study, we performed a population-based cohort study to calculate the cumulative incidence of COVID-19 in PLWH from January 1 to April 16, 2020 in Wuhan city, China, and compared it with the entire population of Wuhan. Furthermore, we described the virological and serological features of COVID-19 cases in PLWH.

Methods

Study setting and participants

All individuals in Wuhan who were tested positive for HIV have been reported to Wuhan Center for Disease Control (CDC) through the China National HIV/AIDS Comprehensive Response Information Management System (CRIMS)[14]. According to CRIMS requirement, a standardized form was used to collect HIV-positive persons' information, including basic demographic characteristics (gender, date of birth, education level), mode of HIV acquisition and baseline CD4 cell count and HIV viral load. The local CDC or designated hospital staff followed up them every year for their CD4 cell count and HIV viral load at least once[15]. HIV-positive persons who met the Chinese national treatment criteria were referred to the China National Free Antiretroviral Treatment Programme (NFATP) to receive combination antiretroviral therapy (cART)[16]. On December 31, 2019, 6001 PLWH resided in Wuhan city had been included in CRIMS.

COVID-19 case identification and definitions

COVID-19 has been listed as a Class B infectious disease on January 20, 2020 in China[17]. All COVID-19 cases must be reported to the National Notifiable Infectious Disease Report System (NNIDRS) within 2 hours after diagnosed[18]. All COVID-19 cases

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reported to NNIDRS in Wuhan have been rechecked and verified on April 16, 2020[19]. Therefore, the COVID-19 cases in PLWH were identified by linking the individual information from these two systems in Wuhan using the unique ID Number on April 17, 2020. According to the national guideline, COVID-19 cases were categorized into confirmed cases, clinically diagnosed cases, suspected cases, and asymptomatic cases. And the severity status of COVID-19 cases was categorized as mild, moderate, severe, or critical. The details could be found elsewhere[3, 20]. In this study, COVID-19 cases with severe or critical illness were classified into severe cases group. Otherwise, they were classified into non-severe cases group.

cART hindered status identification during the COVID-19 epidemic

Among the 6001 PLWH, 474 (7.90%) persons were not on cART before Dec 31, 2019. Of the 5527 persons on cART, 4504 (81.49%) persons had obtained antiretroviral drugs during January 1-March 8, 2020, according to the records in the treatment database of CRIMS. An additional telephone survey was conducted among the remaining 1023 PLWH during April 17-19, 2020 to verify whether the COVID-19 epidemic hindered their cART continuation. Of the 530 PLWH interviewed successfully, 31 persons reported having cART interruption. For the other 493 PLWH unreachable, we inferred that 166 persons had cART interruption based on the last record of getting antiretroviral drugs before January 23, 2020 in CRIMS. cART discontinuation was defined as failing to take antiretroviral drugs for at least 14 days during the COVID-19 epidemic in Wuhan according to Prosperi MC's study [21]. Otherwise, cART interruption less than two weeks was considered as cART continuation. Eventually, we classified the cART hindered status of the 6001 PLWH into 3 groups: no cART, cART continuation and cART discontinuation.

Data collection

Demographic characteristics included gender, date of birth, education level, duration of HIV infection, mode of HIV acquisition, cART regimens and treatment status, CD4 cell count and HIV viral load at last routine medical visit within the previous 12 months were obtained from CRIMS. For COVID-19 cases, information including date of onset, date of diagnosis, date of death (if applicable) and case type and clinical severity were extracted from NNIDRS. We also collected temporal profiles of RT-PCR results for testing SARS-CoV-2 in each confirmed case. In addition, we obtained the COVID-19 incidence among the general population by the street where the PLWH's living address located to indicate their chance of infection by SARS-CoV-2. If the COVID-19 incidence among the general population for the street was ≤0.66% (median level of the COVID-19 incidence among all the streets in Wuhan), PLWH located in this street were classified as having low chance, otherwise, they were deemed to have high chance.

Serum IgM and IgG levels against SARS-CoV-2 testing

Serum samples were taken from each alive COVID-19 cases in PLWH on May 18, 2020. SARS-CoV-2-specific IgM and IgG were detected by Magnetic Chemiluminescence Enzyme Immunoassay using commercial kits following the manufacturer's instructions, which have been described elsewhere[10, 22]. The antibody level was expressed as the chemiluminescence signal value divided by the cutoff value (S/CO). IgM or IgG was defined as positive if the S/CO value was higher than 1.0; otherwise, it was regarded to be negative.

Statistical analysis

The COVID-19 incidence was estimated assuming a Poisson distribution and described for the entire PLWH population and subgroups. We used Poisson regression to estimate incidence rate ratios (IRRs) to compare the COVID-19 incidence in subgroups of PLWH. Univariate and multivariate modified Poisson regressions with robust variance were used to evaluate the relationship between characteristics of PLWH with the COVID-19 occurrence[23]. Besides, we imputed the missing data on the basis of multivariable imputation and performed sensitivity analyses retaining all PLWH to explore the risk factors of COVID-19 among PLWH.

We used the direct method to calculate the COVID-19 incidence standardized by age and gender for PLWH and to compare the difference in COVID-19 occurrence between PLWH and the general population in Wuhan. We derived standardization weight from the age and gender distribution of the general population of Wuhan in 2018. A similar method was used to calculate case-severity and case-fatality standardized by age and gender for PLWH, with the number of COVID-19 cases in different age groups obtained from the previous study as a standard[3]. All analyses were conducted using SAS statistical software version 9.4 (SAS Institute Inc) and R Project version 3.6.1 (http://cran.r-project.org). A two-sided *p* value of <0.05 was considered statistically significant.

Ethics

This study was reviewed and approved by the institutional review board of the Wuhan CDC (WHCDCIRB-K-2020001).

Results

Characteristics of PLWH in Wuhan

From January 1 to April 16, 2020, 35 (0.58%) PLWH had experienced COVID-19, including 22 (62.86%) confirmed cases, 11 (31.43%) clinical cases and 2 (5.71%) asymptomatic cases. The median age of PLWH (52, IQR: 36-57 years) for COVID-19 cases was higher than that for non-COVID-19 cases (37, IQR: 29-52 years, P=0.004). Most (92.10% or 5527) of PLWH were on cART at the end of 2019, of whom 197 (3.56%) persons had cART discontinuation, with 4 persons having COVID-19. There was no significant difference in COVID-19 occurrence between PLWH taking different cART regimens (all P>0.05). 5897 (98.27%) and 5004 (83.39%) PLWH have been documented with CD4 cell count and HIV viral load at last routine medical visit, with similar distribution between non-COVID-19 cases and COVID-19 cases (P=0.860 and 0.798) (Table 1). The basic characteristics between the 22 confirmed cases and 11 clinically diagnosed cases were similar (all P>0.05) (Supplementary Table 1).

Incidence of COVID-19 in PLWH

The cumulative incidence of COVID-19 was 0.58% (95%CI: 0.42%-0.81%). There is no significant difference between the COVID-19 incidence for males (0.61%, 95%CI: 0.43%-0.86%) and females (0.35%, 95%CI: 0.09%-1.39%, P=0.444). COVID-19 incidence among PLWH aged ≥50 years was 1.18%, which was higher than that of PLWH below 50 years (0.35%), with IRR to be 3.37 (95%CI: 1.73-6.57, P<0.001). The COVID-19 incidence were 0.52% (95%CI: 0.36-0.76), 2.20% (95%CI: 0.82%-5.86%) and 0.63% (95%CI: 0.20%-1.96%) in PLWH with cART continuation, PLWH with cART discontinuation, and PLWH without cART, respectively (Figure 1).

According to the report from Health Commission of Hubei Province on April 16, 2020, 50333 (0.46%) persons had reported with COVID-19, with 3869 deaths[19]. The COVID-19 incidence in the general population of Wuhan was 0.45% (95%CI: 0.45%-0.46%). Compared to the general population in Wuhan, PLWH did not have an increased risk for COVID-19, with the standardized incidence rate to be 0.38% (95%CI: 0.24%-0.53%). Of the 35 PLWH with COVID-19, 15 (42.86%) cases had severe illness and 2 (5.71%) cases developed to death. No significant differences of basic characteristics were observed between non-severe COVID-19 cases and severe COVID-19 cases in PLWH (all *P*>0.05) (Supplementary Table 2). The standardized rates of case-severity and case-fatality of COVID-19 in PLWH were also similar to that in the entire population in Wuhan (Table 2).

Risk factors for COVID-19 in PLWH

We included the 5004 (83.39%) persons with available data for HIV viral load to analyze the risk factors for COVID-19 in PLWH, with 984 (16.49%) and 3 (8.57%) PLWH exclude from non-COVID-19 and COVID-19 cases groups (Supplementary Figure 1). The multivariate Poisson regression analysis showed positive associations between COVID-19 occurrence and older age and cART discontinuation after adjusting for other variables (Table 3). Compared to PLWH aged below 50 years with cART continuation, PLWH aged 50 years or above with cART discontinuation were at sharply increased risk for COVID-19 (adjusted IRR=16.86, 95%CI: 4.71-60.26) (Table 4). The sensitivity analyses results using multivariable imputation of missing data were consistent with the above analyses retaining only patients with complete data (Supplementary Table 3 and 4).

Temporal profile of RT-PCR results in confirmed COVID-19 cases in PLWH

The temporal profile of RT-PCR results in 22 confirmed COVID-19 cases in PLWH was shown in Figure 2. These cases have been tested for SARS-CoV-2 infection with RT-PCR test for 1 to 12 times. Nineteen of 22 (86.36%) confirmed cases had at least two consecutive negative RT-PCR results for SARS-CoV-2. The duration of viral shedding was defined as the interval from symptoms onset to the primary sample date among the consecutive negative results. The duration of viral shedding of these COVID-19 cases in PLWH varied from 17 to 77 days with a median of 30 (IQR: 20-46) days. Among the two cases with cART discontinuation, the duration of viral shedding was 21 and 77 days, respectively. For the 15 cases with cART continuation, the median duration of viral shedding was 30 (IQR: 20-44) days. The median duration of viral shedding was 25 (IQR: 20-34) days and 32.5 (IQR: 21-46) days in cases with HIV infection ≤3 years and those with HIV infection>3 years, respectively (Supplementary Table 5). None of the 21 alive confirmed cased turned positive for COVID-19 after recovery over a median of 75 (IQR: 50-79.5) days since discharge.

Serological test results for COVID-19 cases in PLWH

Serum samples were collected from 28 of 33 (84.85%) recovered COVID-19 patients in PLWH on May 18, 2020 for testing the level of specific IgM and IgG antibodies against SARS-CoV-2. The IgM level was lower in cases with high HIV viral load (≥20 copies/ml) at last routine medical visit than cases with low HIV viral load (<20 copies/ml) (median S/CO: 0.03 vs. 0.11, *P*<0.001). And the IgG level was also lower in cases with high HIV viral load, despite marginally significant (median S/CO 10.16 vs. 17.04, *P*=0.069) (Figure 3). The IgG level was 20.73 (IQR: 10.16-34.23) in severe cases and 9.61 (IQR: 0.89-16.10) in non-severe cases, respectively (Supplementary Table 6). Only one (3.57%) confirmed case with critical illness was tested positive for IgM with a value of 1.47. 22 (78.57%) were tested positive for

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IgG, including 1 in 3 (33.33%) cases without cART, 18 in 21 (85.71%) cases with cART continuation, 3 of 4 (75.00%) cases with cART discontinuation (Supplementary Table 7).

Discussion

In this cohort study, we reported the COVID-19 incidence among PLWH in Wuhan during the COVID-19 epidemic. The incidence, case-severity and case-fatality of COVID-19 in PLWH were comparable to that in the entire population in Wuhan. The COVID-19 incidence among PLWH aged 50 years or above was twice higher, compared to PLWH below 50 years. The median duration of viral shedding was 30 days for confirmed COVID-19 cases in PLWH. Higher antibody levels were observed in cases with high HIV viral load than those with low HIV viral load.

Although several studies recently reported the COVID-19 cases in PLWH in hospitals, there are few population-based studies having focused on COVID-19 of PLWH. Our study showed that PLWH have similar risk of COVID-19 compared to that in the general population during COVID-19 epidemic. The incidence of COVID-19 among PLWH (0.58%) in Wuhan was lower than that in HIV-infected individuals (1.8%) in Madrid [8]. It may be one of the reasons that PLWH in Wuhan (mean age 40.7 years) were much younger than HIV-infected individuals in Madrid (mean age 53.5 years), since old age was found to be positively associated with COVID-19 in PLWH[24]. In spite of the different incidence, the age and case type were similar in the 35 COVID-19 cases (Wuhan, median age 52 years old, 63% confirmed cases) and 51 COVID-19 cases (Madrid, mean age 53.3 years old, 68% confirmed cases) from these two studies. The case-fatality of COVID-19 in PLWH varied 4%-28.6% in different studies[25-28], further systematic studies are needed to clarify the disparity.

Maintaining antiretroviral therapy during the COVID-19 epidemic is urgent for the health of PLWH, especially in elderly person. Out study firstly suggested that PLWH aged over 50 years with cART discontinuation had over ten times risk of SARS-CoV-2 infection than young PLWH with ART continuation. Similar findings from studies on the coinfection of HIV and tuberculosis demonstrated that antiretroviral therapy for HIV-positive adults could lower the incidence and mortality of people having coinfection of HIV and tuberculosis[29, 30]. Our findings provide the evidence to support the suggestion from NHH Interim Guidance for COVID-19 and Persons with HIV that the elderly persons with HIV are at the highest risk of COVID-19[12]. Although the supply of antiretroviral drugs against HIV had been disrupted during the "lockdown period" in Wuhan, most of PLWH in Wuhan had antiretroviral drugs supply with the help of the CDC staffs and volunteers from the community based organizations (CBOs) during the COVID-19 epidemic. However, designed hospitals for HIV care services have been closed, which means PLWH may have not proper antiretroviral therapy without any timely examination. The challenge would have been the toughest if the COVID-19 epidemic duration lasts over three months. Therefore, it is critical to make a response policy and strategy to provide a timely ART treatment for PLWH during the COVID-19 epidemic.

Our findings suggested that coinfection of HIV and SARS-CoV-2 may change the development and prognosis of COVID-19 in PLWH. The median interval from symptom onset to viral clearance of confirmed COVID-19 cases in PLWH was 30 days in this study, which was longer than that of COVID-19 cases without HIV infection (20 days)[31]. This indicates that COVID-19 cases in PLWH may have delayed viral clearance for SARS-CoV-2 because of immunosuppression, although clinical improvement of COVID-19 in PLWH was not worse than that of individuals without HIV infection as described in the present study and other published studies[25, 32]. Furthermore, our study found that the level of HIV viral load

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influenced the antibody level against SARS-CoV-2. It suggested that HIV infection may affect the process of immune response to SARS-CoV-2 infection and might be associated with SARS-CoV-2 persistence and adverse outcomes. A recent research on the immunologic characteristics of COVID-19 in PLWH also shows that people with prolonged duration of HIV infection remain at risk for severe manifestation of COVID-19[28]. Therefore, more concerns are needed for people having coinfection of HIV and SARS-CoV-2.

A major strength of the present study is is the population based design focused on epidemiological, virological and serological features of COVID-19 in a large PLWH population, but there are still some limitations needed to be addressed. First, the COVID-19 cases were identified by nucleic acid test, which might have missed individuals with asymptomatic infections in the population**[10]**. Further serological tests in all PLWH are needed to identify the previous infection status of SARS-CoV-2 and the disease spectrum of COVID-19 in this population. Second, the risk of SARS-CoV-2 infection in PLWH also depended on the contact chance with COVID-19 patients. Although the possible contact chance to COVID-19 by the incidence of COVID-19 among the general population was assessed by the street where PLWH's living address located, such classification was a rough estimation. Third, the voluntary HIV screening test was hindered by community isolation and clinic closure during the COVID-19 epidemic. The potential new HIV infections have not been included in the present study. Considering the social distance measures, the number of newly infected HIV cases may be limited. Fourth, since hospitals designated for HIV care had been closed during the "lockdown" period, the exact levels for CD4 cell count and HIV viral load were unknown without necessary tests. The role of CD4 cell count and HIV viral load for COVID-19 risk in PLWH needs to be evaluated in the future prospective studies. In spite of these limitations, our study provides the profile of PLWH having COVID-19 in

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Wuhan. Further studies are needed to follow and case for the health of PLWH during the COVID-19 epidemic around the world.

Conclusions

In conclusion, PLWH aged over 50 years and having cART discontinuation had high risk for COVID-19 in Wuhan. Coinfection of HIV and SARS-CoV-2 may change the progression and prognosis of COVID-19 in PLWH. Future studies are needed to clarify the mechanisms underlying the interaction between HIV infection and SARS-CoV-2 pathogenesis.

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NOTES

Contributors

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Disclaimer

The views expressed in this study are those of the authors and do not represent the official position of Wuhan Center for Disease Control and Prevention.

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Conflicts of interest

All authors declare that they have no conflicts of interest.

Reference

1. Zhu N, Zhang D, Wang W, *et al.* A Novel Coronavirus from Patients with Pneumonia in China, 2019. N Engl J Med **2020**;382:727-733.
2. Organization WH. Coronavirus disease 2019 (COVID-19) Situation Report – 192. 2020 [cited 2020 July 17]Available from: https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200730-covid-19-sitrep-192.pdf?sfvrsn=5e52901f_4
3. Pan A, Liu L, Wang C, *et al.* Association of Public Health Interventions With the Epidemiology of the COVID-19 Outbreak in Wuhan, China. Jama **2020**
4. Jiang H, Zhou Y, Tang W. Maintaining HIV care during the COVID-19 pandemic. Lancet HIV **2020**
5. Zhu F, Cao Y, Xu S, Zhou M. Co-infection of SARS-CoV-2 and HIV in a patient in Wuhan city, China. J Med Virol **2020**
6. Blanco JL, Ambrosioni J, Garcia F, *et al.* COVID-19 in patients with HIV: clinical case series. Lancet HIV **2020**;7:e314-e316.
7. Altuntas Aydin O, Kumbasar Karaosmanoglu H, Kart Yasar K. HIV/SARS-CoV-2 co-infected patients in Istanbul, Turkey. J Med Virol **2020**
8. Vizcarra P, Perez-Elias MJ, Quereda C, *et al.* Description of COVID-19 in HIV-infected individuals: a single-centre, prospective cohort. Lancet HIV **2020**
9. Young J, Psichogiou M, Meyer L, *et al.* CD4 cell count and the risk of AIDS or death in HIV-Infected adults on combination antiretroviral therapy with a suppressed viral load: a longitudinal cohort study from COHERE. PLoS Med **2012**;9:e1001194.
10. Long QX, Liu BZ, Deng HJ, *et al.* Antibody responses to SARS-CoV-2 in patients with COVID-19. Nat Med **2020**
11. Phipps WS, SoRelle JA, Li QZ, *et al.* SARS-CoV-2 Antibody Responses Do Not Predict COVID-19 Disease Severity. Am J Clin Pathol **2020**
12. Services. UDoHaH. Interim guidance for COVID-19 and persons with HIV. 2020 [cited 2020 July 31]Available from: https://aidsinfo.nih.gov/guidelines/html/8/covid-19-and-persons-with-hiv--interimguidance-/554/interim-guidance-for-covid-19-and-persons-with-hiv
13. Society EEAC. BHIVA, DAIG, EACS, GESIDA & Polish Scientific AIDS Society Statement on risk of COVID-19 for people living with HIV (PLWH). 2020 [cited 2020 July 31]Available from: https://www.eacsociety.org/home/covid-19-and-hiv.html
14. Mao Y, Wu Z, Poundstone K, *et al.* Development of a unified web-based national HIV/AIDS information system in China. Int J Epidemiol **2010**;39 Suppl 2:ii79-89.
15. Jia Z, Mao Y, Zhang F, *et al.* Antiretroviral therapy to prevent HIV transmission in serodiscordant couples in China (2003–11): a national observational cohort study. The Lancet **2013**;382:1195-1203.
16. Zhang F, Dou Z, Ma Y, *et al.* Effect of earlier initiation of antiretroviral treatment and increased treatment coverage on HIV-related mortality in China: a national observational cohort study. Lancet Infect Dis **2011**;11:516-524.
17. China. NHCotPsRo. Announcement on the pneumonia infected with noval coroavirus. 2020 [cited 2020 April 21]Available from: http://www.nhc.gov.cn/jkj/s7916/202001/44a3b8245e8049d2837a4f27529cd386.shtml
18. China. NHCotPsRo. The prevention and control programmes for the pneumonia infected with coronavirus（ fifth Edition ）. 2020 [cited 2020 April 21]Available from: http://www.nhc.gov.cn/jkj/s3577/202002/a5d6f7b8c48c451c87dba14889b30147.shtml
19. Province HCoH. Statement on the revision of the COVID-19 epidemic in Hubei Province on April 16, 2020. 2020 [cited 2020 July 31]Available from: http://wjw.hubei.gov.cn/bmdt/ztzl/fkxxgzbdgrfyyq/xxfb/202004/t20200418_2234426.shtml
20. China. NHCotPsRo. The diagnosis and treatment programmes for the pneumonia infected with coronavirus（ fifth Edition ）. 2020 [cited 2020 April 25]Available from: http://www.nhc.gov.cn/yzygj/s7653p/202002/3b09b894ac9b4204a79db5b8912d4440.shtml
21. Prosperi MC, Fabbiani M, Fanti I, *et al.* Predictors of first-line antiretroviral therapy discontinuation due to drug-related adverse events in HIV-infected patients: a retrospective cohort study. BMC Infect Dis **2012**;12:296.

22. Long QX, Tang XJ, Shi QL*, et al.* Clinical and immunological assessment of asymptomatic SARS-CoV-2 infections. Nat Med **2020**

23. Spiegelman D, Hertzmark E. Easy SAS calculations for risk or prevalence ratios and differences. Am J Epidemiol **2005**;162:199-200.

24. Del Amo J, Polo R, Moreno S*, et al.* Incidence and Severity of COVID-19 in HIV-Positive Persons Receiving Antiretroviral Therapy: A Cohort Study. Ann Intern Med **2020**

25. Shalev N, Scherer M, LaSota ED*, et al.* Clinical characteristics and outcomes in people living with HIV hospitalized for COVID-19. Clin Infect Dis **2020**

26. Karmen-Tuohy S, Carlucci PM, Zervou FN*, et al.* Outcomes among HIV-positive patients hospitalized with COVID-19. J Acquir Immune Defic Syndr **2020**

27. Maggiolo F, Zoboli F, Arosio M*, et al.* SARS-CoV-2 infection in persons living with HIV: a single center prospective cohort. J Med Virol **2020**

28. Ho HE, Peluso MJ, Margus C*, et al.* Clinical outcomes and immunologic characteristics of Covid-19 in people with HIV. J Infect Dis **2020**

29. Uthman OA, Okwundu C, Gbenga K*, et al.* Optimal Timing of Antiretroviral Therapy Initiation for HIV-Infected Adults With Newly Diagnosed Pulmonary Tuberculosis: A Systematic Review and Meta-analysis. Ann Intern Med **2015**;163:32-39.

30. Worodria W, Ssempijja V, Hanrahan C*, et al.* Opportunistic diseases diminish the clinical benefit of immediate antiretroviral therapy in HIV-tuberculosis co-infected adults with low CD4+ cell counts. Aids **2018**;32:2141-2149.

31. Zhou F, Yu T, Du R*, et al.* Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet **2020**;395:1054-1062.

32. Sigel K, Swartz T, Golden E*, et al.* Covid-19 and People with HIV Infection: Outcomes for Hospitalized Patients in New York City. Clin Infect Dis **2020**

Table 1. Characteristics of the 6001 PLWH.

Characteristics	All cases (N=6001)	Non-COVID-19 cases (N=5966)	COVID-19 cases (N=35)	P
Age on Jan 1, 2020, years, median (IQR)	37 (29-52)	37 (29-52)	52 (36-57)	0.002
Age group on Jan 1, 2020, years				
<50	4300/6001 (71.65)	4285/5966 (71.82)	15/35 (42.86)	<0.001
≥50	1701/6001 (28.35)	1681/5966 (28.18)	20/35 (57.14)	
Gender				
Male	5427/6001 (90.43)	5394/5966 (90.41)	33/35 (94.29)	0.404
Female	574/6001 (9.57)	572/5966 (9.59)	2/35 (5.71)	
Education				
Senior middle school and below	1550/6000 (25.83)	1543/5965 (25.87)	7/35 (20.00)	0.572

Junior high school	1634/6000 (27.23)	1622/5965 (27.19)	12/35 (34.29)	
College and above	2816/6000 (46.93)	2800/5965 (46.94)	16/35 (45.71)	
Mode of HIV acquisition				
MSM	3953/5988 (65.91)	3933/5963 (67.96)	20/35 (57.14)	0.598
Sex (heterosexual)	1939/5988 (32.33)	1924/5963 (32.27)	15/35 (42.86)	
Intravenous drug use	76/5988 (1.27)	76/5963 (1.27)	0/35 (0.00)	
Blood transfusion	21/5988 (0.35)	21/5963 (0.35)	0/35 (0.00)	
Mother to child	9/5988 (0.15)	9/5963 (0.15)	0/35 (0.00)	
cART treatment				
Yes	5527/6001 (92.10)	5495/5966 (92.11)	32/35 (91.43)	0.883
No	474/6001 (7.90)	471/5966 (7.89)	3/35 (8.57)	
cART hindered status				
No cART treatment	474/6001 (7.90)	471/5966 (7.89)	3/35 (8.57)	0.077
cART continuation	5345/6001 (89.07)	5317/5966 (89.12)	28/35 (80.00)	

cART discontinuation	182/6001 (3.03)	178/5966 (2.98)	4/35 (11.43)	
NRTIs treatment				
No treatment	474/5933 (7.91)	471/5958 (7.91)	3/35 (8.57)	0.984
Without NRTIs in cART	1/5933 (0.02)	1/5958 (0.02)	0/35 (0.00)	
With NRTIs in cART	5518/5993 (92.07)	5486/5958 (92.08)	32/35 (91.43)	
NNRTIs treatment				
No treatment	474/5933 (7.91)	471/5958 (7.91)	3/35 (8.57)	0.496
Without NNRTIs in cART	691/5933 (11.53)	689/5958 (11.56)	2/35 (5.71)	
With NNRTIs in cART	4828/5993 (80.56)	4798/5958 (80.53)	30/35 (80.53)	
PIs treatment				
No treatment	474/5933 (7.91)	471/5958 (7.91)	3/35 (8.57)	0.465
Without PIs in cART	5054/5933 (84.33)	5023/5958 (84.31)	31/35 (88.57)	
With PIs in cART	465/5993 (7.76)	464/5958 (7.79)	1/35 (2.86)	
IIs treatment				
No treatment	474/5933 (7.91)	471/5958 (7.91)	3/35 (8.57)	0.925

Without IIs in cART	5277/5933 (88.05)	5246/5958 (88.05)	31/35 (88.57)	
With IIs in cART	242/5993 (4.04)	241/5958 (4.04)	1/35 (2.86)	
CD4 cell count at last follow-up time, cells/μL				
<50	91/5897 (1.54)	90/5863 (1.54)	1/35 (2.94)	0.860
50-199	522/5897 (8.85)	518/5863 (8.84)	4/35 (11.76)	
200-499	2657/5897 (45.06)	2643/5863 (45.08)	14/35 (41.18)	
≥500	2627/5897 (44.55)	2612/5863 (44.55)	15/35 (44.12)	
HIV viral load at last follow-up time, copies/ml				
<20	3334/5004 (66.63)	3312/4972 (66.61)	22/32 (68.75)	0.798
≥20	1670/5004 (33.37)	1660/4972 (33.39)	10/32 (31.25)	
Duration of HIV infection, years				
≤3	3198/6001 (53.29)	3185/5966 (53.39)	13/35 (37.14)	0.055
>3	2803/6001 (46.71)	2781/5966 (46.61)	22/35 (62.86)	
Incidence rate of COVID-19 by the street where the PLWH's living address located				

≤0.66%	3143/6001 (52.37)	3129/5966 (52.45)	14/35 (40.00)	0.145
>0.66%	2858/6001 (47.63)	2837/5966 (47.55)	21/35 (60.00)	

PLWH: people living with human immunodeficiency virus; MSM: men who have sex with men; IQR: inter quartile range; cART: combination antiretroviral therapy. NRTIs: Nucleoside reverse transcriptase inhibitors; NNRTIs: Non-Nucleoside reverse transcriptase inhibitors; PIs: Protease Inhibitors; in this study, only Lopinavir/Ritonavir (LPV/r) was in this category of antiretroviral; IIs: Integrase Inhibitors.

Table 2. Comparison of COVID-19 between PLWH and the general population in Wuhan.

	PLWH in Wuhan	General population in Wuhan*
Total number of observations	6001	1.1 million
COVID-19 cases	35	50333
Severe cases of COVID-19	15	NA
Death of COVID-19	2	3869
Incidence of COVID-19(%)	0.58 (0.42-0.81)	0.45 (0.45-0.46)
Standardized incidence rate (%)	0.38 (0.24-0.53)	0.45
Case-severity of COVID-19 (%)	42.86 (25.84-71.09)	22.09 (21.58-22.60)[$]
Standardized case-severity of COVID-19 (%)	30.84 (7.51-54.16)[#]	22.09[$]
Case-fatality rate of COVID-19 (%)	5.71 (1.43-22.85)	7.69 (7.45-7.93)
Standardized case-fatality rate of COVID-19 (%)	3.68 (0-9.19)[#]	7.74

PLWH: people living with human immunodeficiency virus

*according to the report from Wuhan Municipal Health Commission on April 16, 2020 (http://wjw.wuhan.gov.cn/front/web/showDetail/2020041710528).

[$] Estimated based on the data from the published study[3].

[#] Estimated based with the number of COVID-19 cases in different age and gender groups obtained from the published study as a standard[3].

Table 3. The effect of basic characteristics on the risk of COVID-19 in PLWH.

Characteristics	Incidence rate (%)	Unadjusted Model		Adjusted Model*	
		IRR (95% CI)	*p*	IRR (95%CI)	*p*
Age group on Jan 1, 2020, years					
<50	0.36 (0.21-0.62)	1.00		1.00	
≥50	1.35 (0.86-2.11)	3.72 (1.85-7.53)	<0.001	3.74 (1.62-8.66)	0.002
Gender					
Male	0.69 (0.48-0.98)	1.00		1.00	
Female	0.20 (0.03-1.44)	0.30 (0.04-2.16)	0.229	0.20 (0.03-1.48)	0.113
Mode of HIV acquisition					
Non-MSM	0.86 (0.51-1.45)	1.00		1.00	
MSM	0.53 (0.34-0.85)	0.62 (0.31-1.25)	0.181	0.76 (0.34-1.70)	0.512
cART hindered status					
cART continuation	0.57 (0.39-0.83)	1.00		1.00	
cART discontinuation	2.35 (0.88-6.27)	4.15 (1.47-11.74)	0.007	3.80 (1.43-23.61)	0.016
No cART treatment	1.49 (0.21-10.60)	2.64 (0.36-19.11)	0.338	3.25 (0.45-10.07)	0.246
CD4 cell count at last follow-up time, cells/μL					

≥500	0.56 (0.33-0.95)	1.00		1.00	
<500	0.71 (0.45-1.13)	1.27 (0.63-2.54)	0.508	1.05 (0.52-2.12)	0.899
HIV viral load at last follow-up time, copies/ml					
<20	0.66 (0.43-1.00)	1.00		1.00	
≥20	0.60 (0.32-1.11)	0.91 (0.43-1.91)	0.798	0.84 (0.39-1.82)	0.661
Duration of HIV infection, years					
≤3	0.47 (0.26-0.85)	1.00		1.00	
>3	0.79 (0.52-1.21)	1.69 (0.82-3.50)	0.157	1.59 (0.74-3.42)	0.238
Incidence rate of COVID-19 by the street where the PLWH's living address located					
≤0.66%	0.49 (0.29-0.85)	1.00		1.00	
>0.66%	0.80 (0.51-1.25)	1.62 (0.80-3.27)	0.181	1.43 (0.69-2.95)	0.333

PLWH: people living with human immunodeficiency virus; MSM: men who have sex with men; cART: combination antiretroviral therapy; IRR, incidence rate ratio. IRRs and P values were from Poisson regression models. *Each association was mutually adjusted for the other characteristics in the table.

Table 4. The combined effect of age and cART hinder status on the risk of COVID-19 in PLWH with cART treatment.

Age, years	cART hinder status	Incidence rate (%)	Adjusted Model*	
			IRR (95%CI)	*p*
<50	cART continuation	0.32 (0.18-0.58)	1.00	
<50	cART discontinuation	0.82 (0.12-0.58)	2.45 (0.33-18.34)	0.382
≥50	cART continuation	1.18 (0.72-1.93)	3.60 (1.45-8.92)	0.006
≥50	cART discontinuation	6.25 (2.02-19.38)	16.86 (4.71-60.26)	<0.001

* adjusted for gender, mode of HIV acquisition, CD4 cell count, HIV viral load, duration of HIV infection and incidence of COVID-19 by the street where the PLWH's living address located

Figure Legends

Figure 1. Incidence (with 95% confidence intervals) of COVID-19 in the 6001 PLWH, stratified by gender, age and cART hindered status.

COVID-19: coronavirus disease 2019; PLWH: people living with human immunodeficiency virus; cART: combination antiretroviral therapy; IRR, incidence rate ratio. cART hindered status=1: cART continuation during the COVID-19 epidemic; cART hindered status=2: cART discontinuation during the COVID-19 epidemic; cART hindered status=3: no cART treatment. Error bars indicate 95%CIs.

Figure 2. Diagnosis and treatment course in the 22 confirmed COVID-19 cases.

*The interval between symptom onset to discharge of Case 21 is 111 days, which has not been shown entirely in the figure.

Figure 3. Level of antibodies against SARS-CoV-2 among 28 COVID-19 cases in PLWH with different cART hindered status.

The boxplots indicate medians (middle line) and third and first quartiles (boxes), while the whiskers indicate 1.5× the interquartile range (IQR) above and below the box.
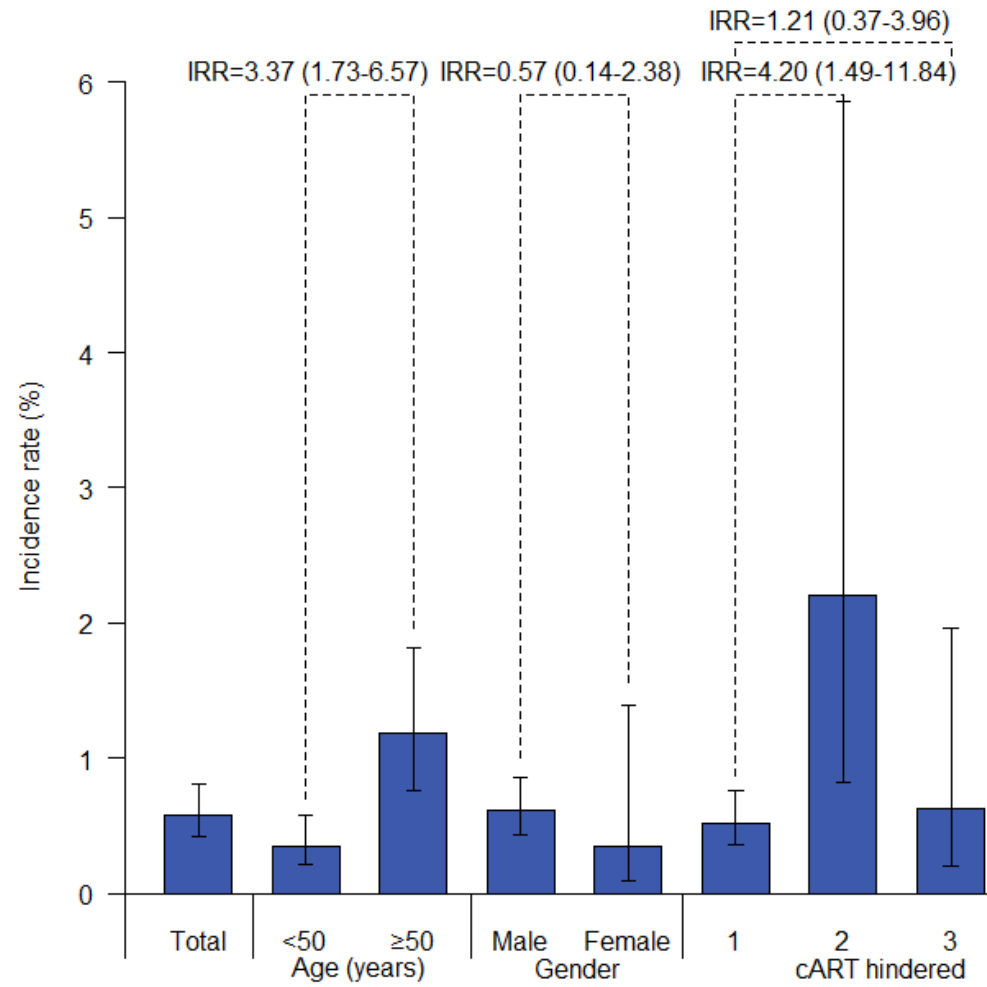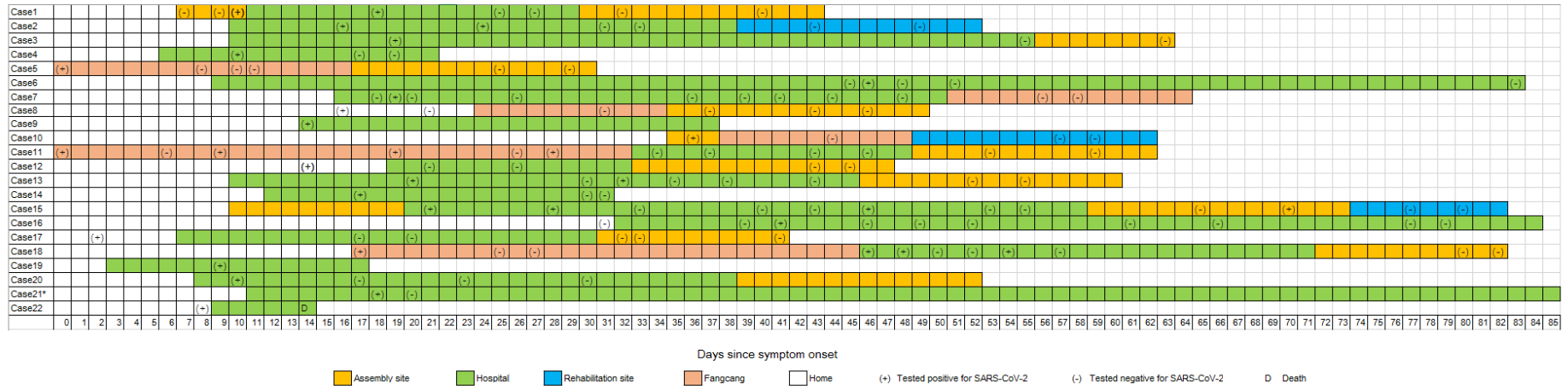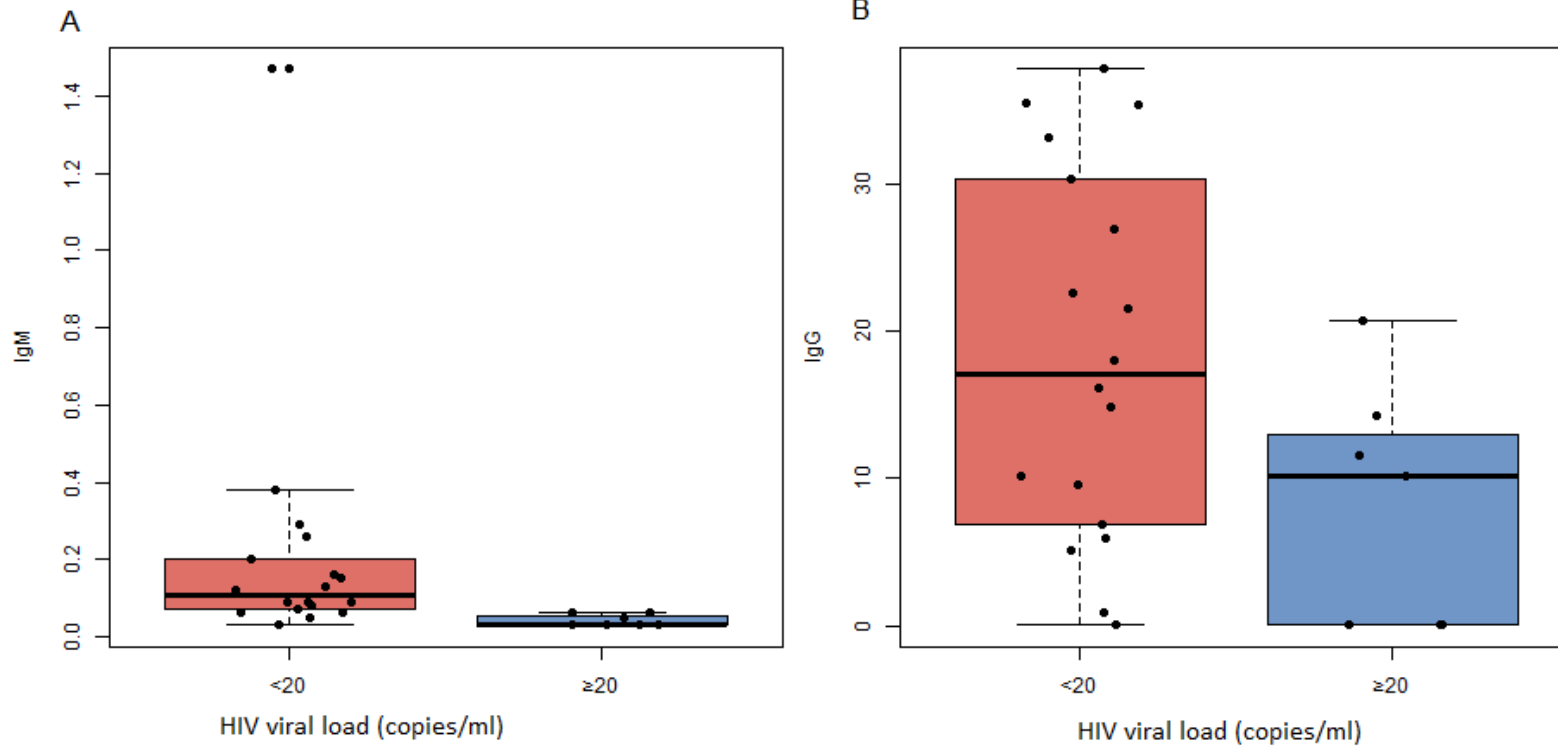
Figure 1

Figure 2

Days since symptom onset

Assembly site Hospital Rehabilitation site Fangcang Home (+) Tested positive for SARS-CoV-2 (-) Tested negative for SARS-CoV-2 D Death