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# A cross-section study of the relationship between lifestyles and severity of COVID-19 symptoms in people living with HIV

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SARS-CoV-2 and its subvariants continue to spread globally. People living with HIV (PLWH), who have weakened immune systems, have heightened concerns about the virus. Thus, the relationship between COVID-19 and HIV remains unclear, and the risks of COVID-19 for PLWH have yet to be fully understood. The study conducted a retrospective cross-sectional survey on the Wenjuanxing platform to identify lifestyle risk factors and epidemic phenotypes associated with the severity of COVID-19 in PLWH. All respondents were over 18 years old and were receiving antiretroviral therapy. The survey included questions about their health status during the COVID-19 illness, and questions about basic sociodemographic information, lifestyle factors, and HIV treatment history. This study included 984 HIV patients with a mean age of 54.44 ± 14.4 years. Among the participants, 635 (64.53%) were male. A total of 33 (3.35%) respondents were unvaccinated, while 951 (96.65%) had received at least one vaccine dose, with 868 (88.21%) participants having received three or more vaccine doses. The association between the severity of COVID-19 symptoms and CD4 count (p = 0.652) and HIV viral load (p = 0.916) was found to be statistically insignificant. In reduced multivariate logistic model, passive smoking increased the risk of severe COVID-19 symptoms compared with non-smokers (odds ratios [OR] 1.66; 95% confidence interval [CI] 1.11-2.48). Mild (OR 2.23; 95% CI 1.55-3.24) and moderate/severe anxiety (OR 5.22; 95% CI 2.36-13.28) were also positively associated with severe COVID-19 symptoms compared to individuals with no anxiety. Comorbidity (OR 1.5; 95% CI 1.04-2.17) demonstrated a significant association with severe COVID-19 symptoms. Moderate/severe anxiety was significantly associated with a higher hospital admission rate (OR 2.62; 95% CI 1.27-5.37) compared to those without anxiety. Patients who consumed whole grains more than three times per week had a lower risk of hospital admission (OR 0.61; 95% CI 0.41-0.89). However, both anxiety and wholegrain intake were nonsignificant for hospitalization rates in individuals who tested positive for COVID-19 through real-time PCR or antigen test. In full multivariate logistic model for SARS-CoV-2 infection of hospitality, CD4 count (> 500 cells/mm3) (OR 0.64; 95% CI 0.41-0.99) and the CD4 count (200-500 cells/mm<sup>3</sup>) (OR 0.68; 95% CI 0.45-1.04) were significantly associated with hospital admission rates compared to CD4 count (< 200 cells/mm<sup>3</sup>), but the results were inconsistent in the reduced logistic models and analysis of Group B. This study indicates that anxiety is positively associated with worsened COVID-19 symptoms and higher hospitalization rates, suggesting a significant link between anxiety and the severity of COVID-19. However, the study did not find evidence of a correlation between CD4 count, HIV viral load, and the severity of COVID-19 or hospitalization rates.

Keywords COVID-19 symptoms, People living with HIV, Anxiety, Hospitaliztion rates

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In 2019, COVID-19 emerged in Wuhan, China, spreading rapidly worldwide and becoming a pandemic. As of now, it continues to be classified as an epidemic<sup>1</sup>. Notably, individuals at higher risk of severe COVID-19 include those, who have developed obesity, diabetes, hypertension, cardiovascular disease, chronic kidney disease, and chronic lung disease<sup>2–7</sup>. However, the relationship between HIV and COVID-19 remains uncertain. It is unclear whether individuals living with HIV(PLWH) experience more severe symptoms than others. Several studies have indicated that patients with both HIV and COVID-19 tend to have worse outcomes, particularly those with CD4 T lymphocyte (CD4) cell counts < 200 cells/mm<sup>38–10</sup>. However, many of these studies were conducted before the widespread adoption of COVID-19 vaccines. Additionally, individuals with advanced HIV may respond less effectively to vaccines<sup>11-13</sup>. Some research suggests that PLWH have higher rates of severe illness, hospitalization, and death compared to the general population<sup>8-10,14-18</sup>, while other studies found no significant differences in severity or mortality<sup>19-25</sup>. On the contrary, early case series of individuals with COVID-19 in Europe and the United States found no significant differences in clinical outcomes between PLWH and the general population<sup>19-26</sup>. Two factors may aid in the treatment of COVID-19: immunosuppressants can help mitigate cytokine storms and antiretroviral drugs have been shown to be effective against coronaviruses<sup>27–29</sup>. Furthermore, previous studies indicate that the pandemic has led to increased levels of psychological distress, including anxiety, depression, and stress<sup>30–33</sup>. Simultaneously, studies indicate that anxiety is a common comorbidity among PLWH<sup>34-36</sup>. However, few studies have focused on the relationship between the severity of COVID-19 and anxiety. Symptoms of Generalized Anxiety Disorder(GAD) are closely associated with higher levels of impairment compared to other anxiety disorders 37,38. Individuals with GAD experience significant functional impairment, which is a strong predictor of overall distress<sup>39,40</sup>. This functional impairment can manifest in various aspects of daily life, such as work, social interactions, and personal care. Studies have shown that GAD symptoms can exacerbate the psychological distress experienced during the COVID-19 pandemic, leading to increased levels of anxiety and depression 30-36. There may be a link between anxiety and the severity of COVID-19, as individuals with higher levels of anxiety may have a more difficult time coping with the stressors associated with the pandemic<sup>30–33</sup>

It is not clear whether there is a definitive connection between the progression of HIV and the severity of COVID-19. This research aims to investigate the relationships between the progression of HIV, lifestyle factors and COVID-19 severity in PLWH.

#### Methods

The study was conducted from April to May 2023 to gather data on PLWH who were infected with SARS-CoV-2 between November 2022 and April 2023. All methods used in this study were approved by the Three Gorges Medical College Ethics Committee (approval No.SXYZ-H-2306-0004), and the research adhered to ethical guidelines from the relevant research ethics committees. Participants were assessed for COVID-19 symptoms using a questionnaire specifically developed for this study, which was distributed via the Wenjuanxing platform (URL: <a href="https://www.wjx.cn/vm/QaVBYIF.aspx">https://www.wjx.cn/vm/QaVBYIF.aspx</a>). The individuals diagnosed with HIV infection were from Panzhihua City, Sichuan Province, as well as Bisan and Jiangjing Districts in Chongqing. All respondents were over 18 years old and were receiving antiretroviral therapy. CD4 counts, HIV viral load, tuberculosis infection, and chronic non-infectious diseases were investigated according to medical records.

The respondents were divided into two groups. Group A included individuals with a confirmed SARS-CoV-2 infection (verified through a real-time PCR or antigen test), those who exhibited symptoms of the SARS-CoV-2 infection, and those who self-reported a SARS-CoV-2 infection; Group B included only those individuals with a confirmed SARS-CoV-2 infection through a real-time PCR or antigen test. The questionnaire gathered basic sociodemographic information such as age, gender, weight, and height from individuals who either had a confirmed COVID-19 infection or exhibited symptoms of the infection. The severity of the symptoms was assessed across three dimensions: fever, the severity of other symptoms(including cough, sore throat, headache, fatigue, muscle weakness, runny nose, chills, loss of smell, loss of appetite, loss of taste, diarrhea, nausea, vomiting, and various rashes), and the progression of the COVID-19 infection. A temperature below 38 °C was classified as mild, a temperature between 38 and 39 °C was classified as moderate, and a temperature above 39 °C was classified as severe. Each symptom was rated on a scale of 0–4, with a total symptom score of below 28 considered mild, a score between 28 and 52 considered moderate, and a score above 52 classified as severe. The duration of the COVID-19 infection was categorized as mild if it lasted fewer than 7 days, moderate if it lasted between 7 and 14 days, and severe if it persisted for more than 14 days.

The Pittsburgh Sleep Quality Index (PSQI) was utilized to assess sleep quality and disturbances through a self-assessment over the course of 1 month<sup>41</sup>. PSQI scores range from 0 to 21,with the following interpretations: scores of 0–10 reflect good sleep quality, scores of 11–15 signify moderate sleep quality, and scores above 15 indicate poor sleep quality. To evaluate anxiety symptoms, the researchers utilized the Generalized Anxiety Disorder Scale (GAD-7). The severity of symptoms was classified using specific cutoff points. GAD-7 scores of 0–4 suggest the absence of anxiety, scores of 5–9 indicate mild anxiety symptoms, scores of 10–14 represent moderate anxiety symptoms, and scores of 15–21 denote severe anxiety symptoms<sup>42–44</sup>. Additionally, the study assesses the dietary habits of the participants and asks several questions to gather pertinent information:

- 1. How many times per week do you eat breakfast?
- 2. Do you pay attention to the proper combination of meat and vegetables in each day of your diet?
- 3. How often do you include whole grains in your diet?
- 4. What kind of beverages do you usually drink? And do you prefer water or other types of drinks?

#### Statistical analysis

Statistical analysis is conducted using R version 4.3.0 software (URL: https://www.r-project.org/). Categorical variables are described using absolute and relative frequencies expressed as percentages. To examine the relationship between categorical variables, chi-square tests are employed. Quantitative variables that follow a normal distribution, as determined by the Shapiro-Wilk test, are presented as means ± standard deviation. In contrast, variables that do not follow a normal distribution are represented as median values along with their interquartile ranges. For comparisons between two groups with normally distributed data, the Student's T-test is utilized. However, the non-parametric Mann-Whitney U test will be employed for comparisons between two independent groups with non-normally distributed quantitative variables. The significant independent variable identified in univariable analysis will be included in multivariable analyses. A multiple logistic regression model will be built to evaluate the dependent variable reflecting the severity of COVID-19 infection. Basic demographic factors (such as age, gender, and BMI) will be included in the full model as potential confounders. Moreover, the factors with a significant relationship identified in univariable analyses will also be included in the full model. The full model of Group B include the same variable as Group A. Both forward and backward stepwise methods will be used to screen the independent variables affecting the severity of COVID-19 infection symptoms. The Akaike Information Criterion(AIC) will be used to select the best-fitting models. The initial model will include one predictor variable. At each step, the AIC value will be calculated for the current model. If adding or removing a predictor variable results in a lower AIC, that variable will be adjusted accordingly. This process will continues until no further changes can reduce the AIC further, at which point the selection process will end.

All risk factors in Group A will be assessed using a multiple logistic regression model. Additionally, these risk factors will be examined in Group B to validate the findings and ensure the robustness of the results. In each scenario, a p-value less than 0.05 will be deemed statistically significant. All missing data will be excluded from the analysis.

#### Results

#### Demographics

This study comprised two groups of HIV patients. Group A included 984 (The details in Fig. 1) HIV patients with a mean age of  $54.44 \pm 14.4$  years (IQR 46-66). The majority, 635 (64.53%) were male. Regarding Vaccination status, 33 (3.35%) patients (3.35%) were unvaccinated, while 951 (96.65%) had received at least one vaccine dose, with 868 patients (88.21%) having received three or more vaccine doses. Group B consisted of 306 patients. (The details in Fig. 1) Overall, 291 (29.57%) patients were hospitalized. Additionally, 93(9.45%) did not take any medication. Moreover, 779 (79.17%) participants reported no other chronic non-infectious co-morbidities. The mean Body Mass Index (BMI) for all participants was  $22.73\pm 2.88$  (IQR 20.94-24.44). In terms of the impact of vaccination on the severity of COVID-19, no significant association was found (p>0.999). However, the presence of other chronic non-infectious comorbidities was significantly associated with an increased prevalence of severe symptoms (p=0.005). Further analysis revealed that the severity of COVID-19 symptoms was not significantly related to factors such as CD4 count (p=0.652), HIV viral load (p=0.916) (Defined as high if  $\geq 10,000$  copies/ml, and mild if < 10,000 copies/ml), or tuberculosis infection (p=1) (Table 1).

#### Potential related factors

The study constructed a multivariable logistic model using significant independent variables identified in the univariable analysis. In the model for analyzing the risk of severe COVID-19, variables that showed significant results in the univariable analysis were included. These variables included smoking status, living environment, treatment method, breakfast intake, presence of comorbidities, anxiety levels, and sleep quality. It was shown that participants who experienced passive smoking, resided in rural areas, and had comorbidities were associated with a 1.63-fold (95% CI 1.09-2.46), 1.93-fold (95% CI 1.41-2.65), and 1.47 fold (95% CI 1.01-2.15) increase in the risk of the severe COVID-19, respectively. Additionally, moderate or severe anxiety was positively associated with severe COVID-19 by 4.85 (95% CI 2.18-12.42) fold. Individuals who engage in self-medication (OR 2.39; 95% CI 1.46-33.98), those who visit the hospital (OR 5.46; 95% CI 3.16-9.59), and those who eat breakfast 2 to 5 days per week (OR 1.94; 95% CI 1.12-3.36) are more likely to experience severe COVID-19 symptoms. Among the potential risk-associated factors in the reduced logistic models with both stepwise methods, the results found that rural residence(OR 1.886; 95% CI 1.38-2.51), passive smoking (OR 1.66; 95% CI 1.11-2.48), comorbidity (OR 1.5; 95% CI 1.04-2.17) and mild (OR 2.23; 95% CI 1.55-3.24) and moderate/serve anxiety (OR 5.22; 95% CI 2.36-13.28) were significantly associated with the severe COVID-19. Individuals who engaged in self-medication (OR 2.37; 95% CI 1.46-3.92), visited the hospital (OR 5.45; 95% CI 3.19-9.50), or consumed breakfast only 2-5 days per week (OR 1.99; 95% CI 1.16-3.43) were more likely to experience severe COVID-19 symptoms. Similar results were observed in Group B (Table 2).

The study also evaluated the association between lifestyle factors and hospital admission risks in PLWH. The multivariable logistic regression model included variables that were identified as significant in the univariable analysis, such as wholegrain intake, residence, CD4 count, comorbidity, anxiety, and sleep quality. The full multiple logistic models showed that the CD4 count (>500 cells/mm³) (OR 0.64; 95% CI 0.41–0.99) and the CD4 count (200–500 cells/mm³) (OR 0.68; 95% CI 0.45–1.04) were significantly associated with hospital admission rates when compared to CD4 counts (<200 cells/mm³), However, the relationship was inconsistent in the reduced logistic models and analyses for Group B. In contrast, several factors were found to have significant associations: being over the age of 65 (OR 1.38; 95% CI 1.00–1.89), having mild anxiety (OR 1.47; 95% CI 1.04–2.06), having moderate/severe anxiety (OR 2.11; 95% CI 1.14–3.85), and residing in a rural area (OR 1.67; 95% CI 1.25–2.24) were associated with an increased likelihood. Conversely, consuming whole grains more than three times a week was associated with a decreased likelihood (OR 0.60; 95% CI 0.41–0.89). The results of reduced logistic models with both stepwise methods indicated that elderly respondents are more likely to be

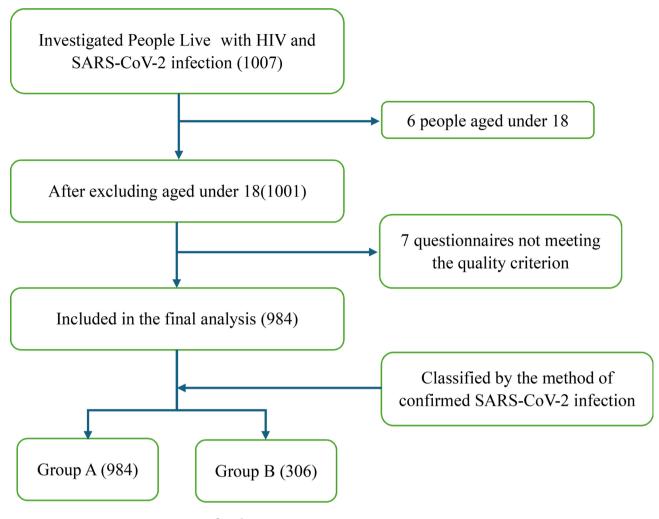


Fig. 1. Participant flow diagram.

hospitalized by 1.44 fold (95% CI 1.06–1.96), eating wholegrain cereal more than 3 times per week is associated with a 0.61 fold reduction(95% CI 0.41–0.89) in hospitalization risk , and residents in rural areas are more likely to be hospitalized by 1.70 fold (95% CI 1.28–2.26). Additionally, moderate or severe anxiety was associated with a 2.62 fold (95% CI 1.27–5.37) increase in hospitalization risk. In the analysis of Group B, most of the factors are not statistically significant besides age (OR 1.8; 95% CI 1.03–3.17) and residence (OR 1.79; 95% CI 1.08–2.98) (Table 3).

#### Discussion

The researchers conducted a multicenter, cross-sectional retrospective study to explore the association between lifestyle factors (such as demographic characteristics, sleep quality, healthy diet, and anxiety) and health outcomes in PLWH. Specifically, this study investigated the relationship between these lifestyle factors and CD4 counts, HIV viral load, tuberculosis infection, comorbidities, specifically chronic non-infectious diseases, and severe COVID-19 symptoms in PLWH. All participants in the study were receiving antiretroviral therapy.

The multivariable analysis identified several factors associated with severe COVID-19 symptoms in PLWH. These factors include exposure to passive smoking, place of residence, comorbidities, and degree of anxiety. The study findings indicate that people over 65 years old, residing in rural areas, and experiencing moderate/severe anxiety are associated with an increased rate of hospitalization due to COVID-19 infection in PLWH. In contrast, consuming wholegrain cereal more than three times a week decreases this rate. It is important to note that the associations with rural residency, passive smoking and anxiety were consistently observed in individuals with confirmed COVID-19 infections through real-time PCR or antigen testing.

There is no significant association between severe symptoms or hospitalization and CD4 counts and HIV viral load in PLWH according to multivariable analyses. Immunosuppressants can help mitigate cytokine storms and antiretroviral drugs are effective against coronaviruses, which may be one of the reasons<sup>27–29</sup>. However, univariable analysis revealed that PLWH with CD4 counts above 500 exhibited lower rates of hospitalization (Table 1). A systematic review comprising 25 published studies showed no increased risk of incident SARS-CoV-2 infection or disease progression for individuals with HIV who are receiving antiretroviral therapy and are virally suppressed, compared to HIV-negative individuals<sup>45</sup>. In contrast, another meta-analysis concluded that

|                            |                  | COVID-19 sympto             |               |         |  |
|----------------------------|------------------|-----------------------------|---------------|---------|--|
| Variables                  | Total (n/median) | Mild or moderate            | Severe        | P       |  |
| Sex                        |                  |                             |               |         |  |
| Males                      | 635              | 243 (38.3%)                 | 392 (61.73%)  |         |  |
| Females                    | 349              | 141 (40.4%)                 | 208 (59.60%)  | 0.557   |  |
| Age                        |                  | (,                          | ,             |         |  |
| 18-65                      | 697              | 279 (40.03%)                | 418 (59.97%)  |         |  |
| >65                        | 287              | 105 (36.59%)                | 182 (63.41%)  | 0.35    |  |
| BMI                        | l                |                             | , ,           |         |  |
| <18.5                      | 55               | 17 (30.91%)                 | 38 (69.09%)   |         |  |
| 18.5-23.9                  | 626              | 249 (39.78%)                | 377 (60.22%)  | 0.434   |  |
| ≥24                        | 303              | 118 (38.94%)                | 185 (61.06%)  |         |  |
| Smoking                    |                  | ()                          | (,-)          |         |  |
| Never smoke                | 347              | 163 (46.97%)                | 184 (53.03%)  |         |  |
| Passive smoking            | 206              | 61 (29.61%)                 | 145 (70.39%)  | -       |  |
| Ever smoke                 | 90               | 36 (40%)                    | 54 (60%)      | 0.0002  |  |
| Smoking                    | 341              | 119 (34.9%)                 | 222 (65.1%)   | -       |  |
|                            | 341              | 119 (34.9%)                 | 222 (03.1%)   |         |  |
| Habitation                 | 514              | 249 (49 259/)               | 266 (51 750/) |         |  |
| City                       | 514              | 248 (48.25%)                | 266 (51.75%)  | < 0.000 |  |
| Rural                      | 470              | 136 (28.94%)                | 334 (71.06%)  |         |  |
| Vaccination                | T                | Ι                           |               |         |  |
| Vaccinated                 | 951              | 371 (39.01%)                | 580 (60.99%)  | 1       |  |
| Unvaccinated               | 33               | 13 (39.39%)                 | 20 (60.61%)   |         |  |
| Treatment method           |                  | 1                           | ı             |         |  |
| Do Noting                  | 93               | 62 (66.67%)                 | 31 (33.33%)   |         |  |
| Self-take medicine         | 600              | 256 (42.67%)                | 344 (57.33%)  | < 0.000 |  |
| Go to hospital             | 291              | 66 (22.68%)                 | 225 (77.32%)  |         |  |
| Breakfast intake per week  |                  |                             |               |         |  |
| Less than 2 days           | 115              | 53 (46.09%)                 | 62 (53.91%)   |         |  |
| 2 to 5 days                | 235              | 52 (22.13%)                 | 183 (77.87%)  | < 0.000 |  |
| More than 5 days           | 634              | 279 (44.01%)                | 355 (55.99%)  | 1       |  |
| Three meals a day          |                  |                             |               | •       |  |
| Yes                        | 94               | 351 (39.44%)                | 539 (60.56%)  | 0.450   |  |
| No                         | 890              | 33 (35.11%)                 | 61 (64.89%)   | 0.479   |  |
| Wholegrain intake          |                  |                             | l.            |         |  |
| Barely                     | 195              | 77 (39.49%)                 | 118 (60.51%)  |         |  |
| Less than 2 times per week | 413              | 157 (38.01%)                | 256 (61.99%)  | 0.855   |  |
| More than 3 times per week | 376              | 150 (39.89%)                | 226 (60.11%   | 1       |  |
| Beverage                   |                  |                             |               |         |  |
| Purity water               | 705              | 112 (40.14%)                | 167 (59.86%)  |         |  |
| Another beverage           | 279              | 272 (38.58%)                | 433 (61.42%)  | 0.704   |  |
| Comorbidity                | 277              | 272 (00.0070)               | 100 (01.1270) |         |  |
| No                         | 779              | 322 (41.34%)                | 457 (58.66%)  |         |  |
| Yes                        | 205              | 62 (30.24%)                 | 143 (69.76%)  | 0.005   |  |
| CD4 count                  | 203              | 02 (30.2470)                | 143 (09.7070) |         |  |
|                            | 124              | 57 (42 540/)                | 77 (57 460)   |         |  |
| <200                       | 134              | 57 (42.54%)                 | 77 (57.46%)   | 0.550   |  |
| 200-500                    | 498              | 190 (38.15%)                | 308 (61.85%)  | 0.652   |  |
| >500                       | 352              | 137 (38.92%)                | 215 (61.08%)  |         |  |
| Anxiety                    | T                | T .                         |               |         |  |
| Noun                       | 856              | 360 (42.06%)                | 496 (57.94%)  |         |  |
| Mild                       | 95               | 20 (21.05%)                 | 75 (78.95%)   | < 0.000 |  |
| Moderate/Severe            | 33               | 4 (12.12%)                  | 29 (87.88%)   |         |  |
| Sleep quality              |                  |                             |               |         |  |
| VC1.1                      | 41               | 12 (29.27%)                 | 29 (70.73%)   |         |  |
| Mild                       |                  | /                           | 220 (50 240() | < 0.000 |  |
| Mild<br>Moderate           | 327              | 97 (29.66%)                 | 230 (70.34%)  | < 0.000 |  |
|                            | 327<br>616       | 97 (29.66%)<br>275 (44.64%) | 341 (55.36%)  | < 0.000 |  |

|                         |                  | COVID-19 sympto  |              |       |  |
|-------------------------|------------------|------------------|--------------|-------|--|
| Variables               | Total (n/median) | Mild or moderate | Severe       | P     |  |
| High(≥10,000 copies/ml) |                  | 5 (35.71%)       | 9 (64.29%)   | 0.916 |  |
| Mild(<10,000 copies/ml) |                  | 245 (40.77%)     | 356 (59.23%) | 0.916 |  |
| Tuberculosis            |                  |                  |              |       |  |
| Free of infection       |                  | 332 (38.47%)     | 531 (61.53%) |       |  |
| Have been cured         |                  | 1 (25%)          | 3 (75%)      | 1     |  |
| On the treatment        |                  | 1 (33.33%)       | 2 (66.67%)   | ]     |  |

**Table 1**. Baseline characteristics of the study population.

there is an increased risk of hospitalization, severe disease, and death among PLWH who contract COVID-19<sup>46</sup>. Additionally, Dandachi et al.'s<sup>14</sup> research found that a lower CD4 count (<200 cells/mm³) was associated with poorer outcomes, including higher hospitalization rates, lower ICU-free survival, and decreased overall survival. Dandachi et al.'s severe outcomes were defined as a composite of intensive care admission, invasive mechanical ventilation, or death. The role of HIV infection as a predictor for the onset and progression of COVID-19 remains unclear <sup>9,16,47-51</sup>. Furthermore, Khadija Khan et al.<sup>52</sup> demonstrated that vaccination in PLWH with well-controlled HIV is not inferior to vaccination in HIV-negative participants, regardless of previous SARS-CoV-2 infection. The findings regarding tuberculosis infection and COVID-19 severity are inconclusive and do not align with previous studies <sup>8,53</sup>. This discrepancy may be due to the very small sample size, as only three patients were infected with tuberculosis, which is insufficient to draw reliable conclusions. While CD4 counts, viral load, and tuberculosis infection are all important factors influencing COVID-19 severity, their impact can vary significantly based on sample sizes and study populations. Sample size and statistical power limitations can introduce variability in the findings, necessitating careful interpretation of results across different studies. Establishing the relationship between COVID-19 infection and HIV-related factors requires a large sample size and follow-up studies.

The results of previous studies indicate that a comorbidity burden is associated with increased rates of severe COVID-19<sup>54,55</sup>. Several previous reviews have reached a similar conclusion<sup>56-58</sup>. For instance, Dandachi et al.'s<sup>14</sup> results show that more comorbidities are associated with poor outcomes of COVID-19. Our findings indicate that exposure to secondhand smoke is associated with severe cases of COVID-19, but no such correlation has been found among smokers. Our findings indicate that living in rural areas increases the likelihood of severe COVID-19 cases compared to living in urban areas. Regarding hospitalization rates, individuals aged 65 and above are more likely to be hospitalized, which is consistent with previous studies. Furthermore, people residing in rural areas exhibit higher hospitalization rates. Conversely, consuming wholegrain foods more than three times a week has been shown to reduce hospitalization rates of PLWH compared to those who do not consume whole grains regularly. Jagielski et al.<sup>59</sup> suggest that wholegrain cereal can effectively reduce the risk of COVID-19 in nonobese healthy physically active young people with normal immune function.

This study shows that anxiety may exacerbate COVID-19 symptoms and raise hospitalization rates. Anxiety may be a potential risk factor for the severity of COVID-19. The role of anxiety in COVID-19 severity is multifaceted and has been extensively studied across various populations and contexts. Anxiety, as a psychological response to the perceived threat posed by COVID-19, can significantly influence both the mental health outcomes and the physiological course of the disease. Much research has indicated that the COVID-19 pandemic, COVID-19 infection, and related quarantine measures will persist in elevating the severe symptom load of depression and anxiety 60,61. Evidence suggests that anxiety during the pandemic is associated with longterm mental health outcomes such as PTSD and depression<sup>62</sup>. Research suggests that anxiety can impair the immune system, making individuals more susceptible to infections. Such stress-related conditions are associated with decreased natural immunity, particularly affecting cellular immunity<sup>63–65</sup>. Therefore, anxiety may aggravate the symptoms of COVID-19. Pérez-López et al.66 also highlighted that anxiety is significantly associated with long-term COVID-19 symptoms. GAD-7 is a widely used tool for assessing anxiety symptoms over the past two weeks, but it has limitations. Specifically, it may reflect the consequences of COVID-19 rather than predisposing factors of the COVID-19 severity. Future studies could consider alternative methods to assess baseline anxiety, such as incorporating longer-term assessments or using different scales that capture broader psychological impacts, including stress and trauma responses, which might better account for the complex effects of anxiety levels on COVID-19 severity.

It is important to acknowledge the limitations of the findings of this study. Firstly, the study was unable to assess changes in sleep disorders and anxiety before and after COVID-19 infection, which means the study cannot establish a causal relationship. Additionally, collecting data on all ailments during a specific period may lead to the overestimation or underestimation of the frequency of individual symptoms. Moreover, the diagnosis of COVID-19 was self-reported, which could result in confusion with other similar illnesses, such as the flu. Similarly, self-reported symptoms and exercise levels may lead to discrepancies between reported values and actual conditions. Notably, the variable related to smoking yielded an unexpected result, showing that individuals who never smoked experienced more severe COVID-19 symptoms and a longer duration of the illness. This discrepancy may be due to the fact that non-smokers are predominantly women, while most smokers are men in China. Thus, gender emerges as a factor that influences the outcomes.

| Variable                     | Group A (n=984)       |        |            |         |          |       | GroupB (n = 306) |             |           |          |  |  |
|------------------------------|-----------------------|--------|------------|---------|----------|-------|------------------|-------------|-----------|----------|--|--|
|                              | В                     | OR     | 95%CI      | Z       | P        | В     | OR               | 95%CI       | Z         | P        |  |  |
| Intercept                    | -0.72                 | 0.49   | 0.19-1.3   | -1.465  | 0.143    | -0.95 | 0.39             | 0.05-3.8    | -0.888    | 0.375    |  |  |
| Sex (female)*                | -0.19                 | 0.82   | 0.58-1.18  | -1.07   | 0.284    | -0.03 | 0.97             | 0.42-2.22   | -0.081    | 0.935    |  |  |
| Age(>65) *                   | -0.11                 | 0.89   | 0.64-1.25  | -0.673  | 0.501    | 0.18  | 1.2              | 0.48-3.11   | 0.385     | 0.7      |  |  |
| BMI                          |                       |        |            |         |          |       |                  |             |           |          |  |  |
| 18.5-24                      | 1.00 (reference)      |        |            |         |          |       |                  |             |           |          |  |  |
| <18.5                        | 0.29                  | 1.34   | 0.71-2.6   | 0.886   | 0.376    | 1.62  | 5.04             | 0.79-100.4  | 1.435     | 0.151    |  |  |
| >24                          | -0.03                 | 0.97   | 0.71-1.33  | -0.189  | 0.85     | -0.42 | 0.65             | 0.31-1.38   | -1.123    | 0.261    |  |  |
| Smoking                      |                       |        |            |         |          |       |                  |             |           |          |  |  |
| Never smoking                | 1.00 (reference)      |        |            |         |          |       |                  |             |           |          |  |  |
| Passive smoking              | 0.49                  | 1.63   | 1.09-2.46  | 2.372   | 0.018    | 1.32  | 3.73             | 1.51-9.91   | 2.763     | 0.006    |  |  |
| Ever smoking                 | -0.18                 | 0.84   | 0.48-1.47  | -0.628  | 0.53     | 2.11  | 8.25             | 1.33-162.28 | 1.893     | 0.058    |  |  |
| Smoking                      | -0.06                 | 0.94   | 0.63-1.41  | -0.278  | 0.781    | 0.79  | 2.19             | 0.94-5.19   | 1.813     | 0.07     |  |  |
| Have breakfast in a w        | 1                     |        |            | 1 3.273 | 1        |       |                  | 1           | 1 -10 -10 | 1 -1     |  |  |
| Less than 2 days             | 1.00 (reference)      |        |            |         |          |       |                  |             |           |          |  |  |
| 2 to 5 days                  | 0.66                  | 1.94   | 1.12-3.36  | 2.369   | 0.018    | -0.04 | 0.96             | 0.29-3.12   | -0.068    | 0.946    |  |  |
| More than 5 days             | -0.27                 | 0.76   | 0.49-1.19  | -1.187  | 0.235    | -0.34 | 0.71             | 0.26-1.82   | -0.7      | 0.484    |  |  |
| Habitation in rural*         | 0.66                  | 1.93   | 1.41-2.65  | 4.1     | < 0.0001 | 0.77  | 2.15             | 1-4.76      | 1.941     | 0.464    |  |  |
| Treatment method             | 0.00                  | 1.93   | 1.41-2.03  | 4.1     | < 0.0001 | 0.77  | 2.13             | 1-4.70      | 1.941     | 0.032    |  |  |
|                              | 1.00 (nofements)      |        |            |         | I        |       |                  |             | 1         |          |  |  |
| Do Noting Self-take medicine | 1.00 (reference)      | 2.20   | 1.46.2.00  | 2.410   | 0.001    | 1.20  | 2.61             | 1.10.11.50  | 2 222     | 0.026    |  |  |
|                              | 0.87                  | 2.39   | 1.46-3.98  | 3.419   | 0.001    | 1.28  | 3.61             | 1.19-11.58  | 2.233     | 0.026    |  |  |
| Go to hospital               | 1.7                   | 5.46   | 3.16-9.59  | 6.011   | < 0.0001 | 2.78  | 16.13            | 4.61-61.54  | 4.236     | < 0.0001 |  |  |
| Sleep quality                | T                     |        |            |         | 1        |       |                  | 1           |           |          |  |  |
| Mild                         | 1.00 (reference)      |        |            |         |          |       |                  |             |           |          |  |  |
| Moderate                     | -0.25                 | 0.78   | 0.34-1.68  | -0.617  | 0.537    | -0.21 | 0.81             | 0.1-4.35    | -0.233    | 0.816    |  |  |
| Good                         | -0.41                 | 0.67   | 0.3-1.4    | -1.035  | 0.301    | -0.63 | 0.53             | 0.07-2.68   | -0.705    | 0.481    |  |  |
| Comorbidity                  | 0.39                  | 1.47   | 1.01-2.15  | 2.007   | 0.045    | 0.17  | 1.18             | 0.52-2.81   | 0.39      | 0.696    |  |  |
| Anxiety                      |                       |        |            |         |          |       |                  |             |           |          |  |  |
| None                         | 1.00 (reference)      |        |            |         |          |       |                  |             |           |          |  |  |
| Mild                         | 0.78                  | 2.19   | 1.51-3.19  | 4.117   | < 0.0001 | 1.22  | 3.4              | 1.54-8.1    | 2.905     | 0.004    |  |  |
| Moderate/Severe              | 1.58                  | 4.85   | 2.18-12.42 | 3.604   | < 0.0001 | 1.77  | 5.9              | 1.36-42.49  | 2.105     | 0.035    |  |  |
| Reduced both stepwis         | se logistic regressio | n anal | ysis model |         |          |       |                  |             |           |          |  |  |
| Intercept                    | -1.19                 | 0.31   | 0.16-0.56  | -3.784  | < 0.0001 | -1.42 | 0.24             | 0.08-0.69   | -2.559    | 0.01     |  |  |
| Have breakfast in a w        | eek                   |        |            | •       |          |       |                  |             |           | •        |  |  |
| Less than 2 days             | 1.00 (reference)      |        |            |         |          |       |                  |             |           |          |  |  |
| 2 to 5 days                  | 0.69                  | 1.99   | 1.16-3.43  | 2.507   | 0.012    | -     | -                | -           | -         | -        |  |  |
| More than 5 days             | -0.29                 | 0.75   | 0.48-1.17  | -1.264  | 0.206    | -     | -                | -           | -         | -        |  |  |
| Smoking                      | l.                    |        |            | 1       | I.       |       |                  | Į.          |           | 1        |  |  |
| Never smoking                | 1.00 (reference)      |        |            |         |          |       |                  |             |           |          |  |  |
| Passive smoking              | 0.51                  | 1.66   | 1.11-2.48  | 2.467   | 0.014    | 1.32  | 3.74             | 1.58-9.58   | 2.895     | 0.004    |  |  |
| Ever smoking                 | -0.11                 | 0.9    | 0.53-1.51  | -0.412  | 0.681    | 2.23  | 9.34             | 1.68-176.03 | 2.08      | 0.038    |  |  |
| Smoking                      | 0.06                  | 1.06   | 0.75-1.5   | 0.332   | 0.74     | 0.78  | 2.18             | 1.07-4.53   | 2.116     | 0.034    |  |  |
| Habitation in rural*         | 0.62                  | 1.86   | 1.38-2.51  | 4.038   | < 0.0001 | 0.67  | 1.96             | 1.01-3.89   | 1.956     | 0.049    |  |  |
| Treatment method             | I .                   |        | 1          |         | 1        |       |                  | I.          |           |          |  |  |
| Do Nothing                   |                       |        |            | -       |          |       |                  |             |           | -        |  |  |
| Self-take medicine           | 0.86                  | 2.37   | 1.46-3.92  | 3.426   | 0.001    | 1.04  | 2.82             | 1.01-8.09   | 1.969     | 0.049    |  |  |
| Go to hospital               | 1.7                   | 5.45   | 3.19-9.5   | 6.095   | < 0.0001 | 2.52  | 12.41            | 3.88-42.7   | 4.147     | < 0.0001 |  |  |
| Comorbidity*                 | 0.4                   | 1.5    | 1.04-2.17  | 2.176   | 0.03     | -     | -                | -           | -         | -        |  |  |
| Anxiety                      |                       | 1      | 01 2.17    |         | 1 3.00   |       | <u> </u>         | <u> </u>    |           |          |  |  |
| None                         | 1.00 (reference)      |        |            |         |          |       |                  |             |           |          |  |  |
| Mild                         | 0.8                   | 2 22   | 1 55 2 24  | 1 29    | < 0.0001 | 1 24  | 3 16             | 164 700     | 3 120     | 0.002    |  |  |
|                              |                       | 2.23   | 1.55-3.24  | 4.28    | < 0.0001 | 1.24  | 3.46             | 1.64-7.88   | 3.129     | 0.002    |  |  |
| Moderate/severe              | 1.65                  | 5.22   | 2.36-13.28 | 3.799   | < 0.0001 | 1.99  | 7.35             | 1.87-49.89  | 2.492     | 0.013    |  |  |

**Table 2**. Full and reduced both stepwise logistic regression analysis models assessing the impact of risk factors on the severity of COVID-19. B, Unstandardized regression coefficient; OR, odds ratio; CI: Confidence Interval; -, Not available. \*Variable reference value, Sex: male, Age: 18–64, Habitation: city, Comorbidity: no non-ifection chronic disease.

| Variable                   | Group A (n = 984) |      |           |          |          | GroupB (n = 306) |      |            |        |       |
|----------------------------|-------------------|------|-----------|----------|----------|------------------|------|------------|--------|-------|
|                            | В                 | OR   | 95%CI     | Z        | P        | В                | OR   | 95%CI      | Z      | P     |
| Full model                 |                   |      |           |          |          |                  |      | •          | •      |       |
| Intercept                  | -1.27             | 0.28 | 0.11-0.67 | -2.774   | 0.006    | -1.61            | 0.2  | 0.03-1.06  | -1.755 | 0.079 |
| Sex (female)*              | -0.24             | 0.79 | 0.58-1.06 | -1.54    | 0.124    | -0.46            | 0.63 | 0.36-1.09  | -1.622 | 0.105 |
| Age (>65)*                 | 0.32              | 1.38 | 1-1.89    | 1.995    | 0.046    | 0.53             | 1.7  | 0.93-3.1   | 1.728  | 0.084 |
| BMI                        |                   |      |           |          |          |                  |      |            |        |       |
| 18.5-24                    | 1.00 (reference)  |      |           |          |          |                  |      |            |        |       |
| <18.5                      | 0.29              | 1.34 | 0.71-2.44 | 0.94     | 0.347    | 0.36             | 1.44 | 0.48-4.09  | 0.673  | 0.501 |
| >24                        | 0.26              | 1.29 | 0.94-1.76 | 1.611    | 0.107    | 0.39             | 1.48 | 0.85-2.59  | 1.384  | 0.166 |
| Wholegrain intake          |                   |      |           |          | 1        |                  |      |            | 1      |       |
| Barely                     | 1.00 (reference)  |      |           |          |          | 1.00 (reference) |      |            |        |       |
| Less than 2 times per week | -0.28             | 0.75 | 0.52-1.1  | -1.485   | 0.137    | -0.37            | 0.69 | 0.35-1.36  | -1.075 | 0.283 |
| More than 3 times per week | -0.51             | 0.6  | 0.41-0.89 | -2.572   | 0.01     | -0.03            | 0.97 | 0.49-1.91  | -0.083 | 0.934 |
| Residence in rural*        | 0.51              | 1.67 | 1.25-2.24 | 3.453    | 0.001    | 0.57             | 1.76 | 1.04-3     | 2.103  | 0.036 |
| CD4 count                  | I                 |      | I         |          | 1        | ı                | 1    |            |        |       |
| <200                       | 1.00 (reference)  |      |           |          |          | 1.00 (reference) |      |            |        |       |
| 200-500                    | -0.38             | 0.68 | 0.45-1.04 | -1.811   | 0.07     | -0.72            | 0.49 | 0.21-1.1   | -1.732 | 0.083 |
| >500                       | -0.45             | 0.64 | 0.41-0.99 | -2.024   | 0.043    | -0.41            | 0.66 | 0.28-1.54  | -0.96  | 0.337 |
| Comorbidity*               | 0.11              | 1.11 | 0.78-1.58 | 0.581    | 0.561    | -0.21            | 0.81 | 0.45-1.45  | -0.709 | 0.479 |
| Sleep quality              |                   |      | l         |          |          | 1                |      |            |        |       |
| Mild                       | 1.00 (reference)  |      |           |          |          |                  |      |            |        |       |
| Moderate                   | 0.69              | 2    | 0.95-4.51 | 1.76     | 0.078    | 1.27             | 3.57 | 0.81-25.54 | 1.51   | 0.131 |
| Good                       | 0.47              | 1.6  | 0.77-3.62 | 1.209    | 0.227    | 1.4              | 4.04 | 0.93-28.68 | 1.671  | 0.095 |
| Anxiety                    | l                 |      |           |          |          | 1                |      |            |        |       |
| None                       | 1.00 (reference)  |      |           |          |          |                  |      |            |        | T     |
| Mild                       | 0.38              | 1.47 | 1.04-2.06 | 2.2      | 0.028    | 0.32             | 1.38 | 0.79-2.4   | 1.134  | 0.257 |
| Moderate/serve             | 0.75              | 2.11 | 1.14-3.85 | 2.413    | 0.016    | 0.75             | 2.13 | 0.91-5.02  | 1.74   | 0.082 |
| Reduced both stepwise mode |                   |      | 1         |          | 1 -11-11 | 1                |      | 1          | 1      |       |
| Intercept                  | -0.99             | 0.37 | 0.26-0.52 | -5.683   | < 0.001  | -1.88            | 0.15 | 0.02-0.73  | -2.149 | 0.032 |
| Age (>65)                  | 0.37              | 1.44 | 1.06-1.96 | 2.364    | 0.018    | 0.59             | 1.8  | 1.03-3.17  | 2.059  | 0.04  |
| Wholegrain intake          | 1                 | 1    |           |          |          | 1                | 1    | 1          |        | 1     |
| Barely                     | 1.00 (reference)  |      |           |          |          |                  |      |            |        | T     |
| Less than 2 times per week | -0.29             | 0.75 | 0.52-1.09 | -1.527   | 0.127    | _                | _    | _          | _      | _     |
| More than 3 times per week | -0.5              | 0.61 | 0.41-0.89 | -2.588   | 0.010    | _                | -    | _          | _      | _     |
| Residence in rural*        | 0.53              | 1.70 | 1.28-2.26 | 3.624    | < 0.001  | 0.58             | 1.79 | 1.08-2.98  | 2.244  | 0.025 |
| CD4 count                  | 0.33              | 1.70 | 1.20-2.20 | 3.024    | \ 0.001  | 0.30             | 1.75 | 1.00-2.50  | 2.244  | 0.023 |
| CD4 count                  | 1.00 (reference)  |      |           |          |          |                  |      |            |        |       |
|                            | -                 | _    | _         | _        |          | -0.76            | 0.47 | 0.21-1.04  | -1.858 | 0.063 |
|                            | _                 | _    | _         | _        |          | -0.42            | 0.47 | 0.29-1.5   | -0.992 | 0.321 |
| Sleep quality              | _                 |      |           |          |          | 0.42             | 0.00 | 0.29-1.3   | -0.332 | 0.341 |
| Mild                       | 1.00 (reference)  |      |           |          |          |                  |      |            |        | I     |
| Moderate                   | 1.00 (reference)  | _    | _         | <u> </u> |          | 1.23             | 3.41 | 0.79-23.95 | 1.478  | 0.139 |
| Good                       |                   | -    |           | -        |          | -0.76            | 0.47 | 0.79-23.93 | -1.858 | 0.139 |
| Anxiety                    | -                 |      | -         | -        |          | -0.76            | 0.4/ | 0.21-1.04  | -1.838 | 0.063 |
| <u> </u>                   | 1.00 (voference)  | T    |           |          |          |                  | I    | Ι          |        | T     |
| None                       | 1.00 (reference)  | 1.20 | 0.74 1.00 | 0.757    | 0.440    | 0.21             | 1.26 | 0.70, 3.33 | 1 117  | 0.261 |
| Mild<br>Madanata/aamaa     | 0.18              | 1.20 | 0.74-1.89 | 0.757    | 0.449    | 0.31             | 1.36 | 0.79-2.32  | 1.117  | 0.264 |
| Moderate/serve             | 0.96              | 2.62 | 1.27-5.37 | 2.649    | 0.008    | 0.79             | 2.19 | 0.98-4.97  | 1.907  | 0.057 |

**Table 3.** Full and reduced both stepwise logistic regression analysis models assessing the impact of hospitalization risk factors on COVID-19. B, unstandardized regression coefficient; OR, odds ratio; CI: Confidence Interval; -, Not available. \*Variable reference value, Sex: male, Age: 18–64, Habitation: city, Comorbidity: no non-ifection chronic disease.

#### Conclusion

This study discovered that anxiety is positively related to the severity of COVID-19 infections and hospitalization rates among PLWH. It also revealed that exposure to passive smoke and pre-existing medical conditions may exacerbate the severity of COVID-19 infections. On the other hand, individuals who consumed wholegrain

cereals had a lower rate of hospitalization. Notably, older people (aged 65 or older) with HIV had a higher hospitalization rate. Finally, the study found no evidence of a correlation between CD4 counts and HIV viral load, and the severity of COVID-19 or hospitalization rates.

#### Data availability

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request. Requests for data access can be directed to kangjiming@cqtgmc.edu.cn.

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#### **Author contributions**

Wanyuan Xia and Jiming Kang—development of assumptions and research methods, questionnaire design, collecting source materials and carrying out research, statistical analysis of research results, preparation of the text of the study, interpretation of obtained results, review and editing; Daikun Zheng, Wu Linbing, Tang Zhi and Ye Qiong—preparation of the text of the study, data collection, review and editing; Wu Linbing and Yuqiang Zhang—statistical analysis of research results, interpretation of the obtained results; Qiong Y, Chongli Leng and Ping Bao—data collection, revise the manuscript. Mingyue Fan and Min Liu—interpretation of obtained results, review, and editing; All authors reviewed the manuscript.

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#### **Declarations**

#### Competing interests

The authors declare no competing interests.

#### **Ethics** approval

This study was approved by the Three Gorges Medical College Ethics Committee (SXYZ-H-2306-0004). The participants were then given the option to consent by indicating their agreement or disagreement to participate at the end of the information provided. Online voluntary informed consent was obtained from all individual participants included in the study.

#### Additional information

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