Prevalence of anaemia and the associated factors among hospitalised people living with HIV receiving antiretroviral therapy in Southwest China: a cross-sectional study

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ABSTRACT

Objectives To estimate anaemia prevalence and the associated factors among hospitalised people living with HIV (PLHIV) receiving antiretroviral therapy (ART).

Design A cross-sectional study.

Setting PLHIV receiving ART and hospitalised in a specialised hospital for infectious disease in Guizhou Province, Southwest China, between 1 January 2018 and 31 March 2021.

Participants A total of 6959 hospitalised PLHIV aged ≥18 years and receiving ART were included in this study.

Primary and secondary outcome measures Anaemia was diagnosed as a haemoglobin concentration <120 g/L for non-pregnant females and <130 g/L for males. Mild, moderate and severe anaemia were diagnosed as below the gender-specific lower limit of normal but ≥110 g/L, 80–110 g/L and <80 g/L, respectively.

Results The prevalence of anaemia was 27.5%, and that of mild, moderate and severe anaemia was 9.2%, 12.2% and 6.1%, respectively. Results from multivariate logistic regression showed that females had increased odds of anaemia (adjusted OR aOR=1.60, 95% CI: 1.42 to 1.81) compared with males. Widowed or divorced patients (anaemia: aOR=1.26, 95% CI: 1.08 to 1.47; severe anaemia: aOR=1.52, 95% CI: 1.16 to 1.97) and thrombocytopenia patients (anaemia: aOR=4.25, 95% CI: 3.54 to 5.10; severe anaemia: aOR=4.16, 95% CI: 3.24 to 5.35) had increased odds of anaemia and severe anaemia compared with their counterparts. Hepatitis C was associated with increased odds of severe anaemia (aOR=1.80, 95% CI: 1.11 to 2.92).

Conclusions Anaemia was prevalent among hospitalised PLHIV. Female sex, those widowed or divorced, and thrombocytopenia were associated with increased odds of anaemia, and those widowed or divorced, thrombocytopenia and hepatitis C were associated with increased odds of severe anaemia. Determination of anaemia predictors, early detection and timely management of anaemia are crucial to prevent anaemia progression.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This study included a large sample of hospitalised people living with HIV (PLHIV) receiving antiretroviral therapy as study participants.

⇒ This study did not include data on HIV/AIDS progression, environmental and nutritional factors, socioeconomic status or lifestyle due to the data availability of this study.

⇒ The findings in this study could provide guidance for improving the health status of anaemic PLHIV during hospitalisation.

INTRODUCTION

Globally, an estimated 37.6 million people were living with (PLHIV) in 2020 and 1.5 million people were newly infected.1 Despite a steady but slow decline in the incidence rates of HIV infection over the past two decades, it remains a public health threat.2 HIV leads to progressive immune dysfunction and disrupts the normal haematopoietic system of infected individuals.3 Anaemia is the most common haematological abnormality in PLHIV, with a prevalence ranging from 20% to 84% in different clinical settings.4–7 Anaemia has been reported to be associated with a poor quality of life, progression to AIDS and shorter survival time of PLHIV.8–10

The causes of anaemia among PLHIV are multifactorial. HIV can directly and indirectly impact the survival and functioning of haematopoietic stem/progenitor cells (HSPCs) that reside in the bone marrow.311 In addition, the drugs used for antiretroviral therapy (ART), inflammatory mediators released during HIV infection and coinfections or opportunistic infections could also affect the proliferation and differentiation of HSPCs during...
Progressive depletion of HSPCs or suppression of their function could both result in haematological abnormalities, such as anaemia, thrombocytopenia and neutropenia. Evidence has reported that anaemia and thrombocytopenia are the two most frequent haematological abnormalities in PLHIV, leading to poor quality of life and high death rates. Of note, thrombocytopenia is often asymptomatic in PLHIV, and it may be associated with a variety of bleeding abnormalities, which could possibly lead to an increased risk of anaemia and even aggravate anaemia. However, there are a few studies about the prevalence of anaemia and its association with thrombocytopenia in PLHIV. The results from different study settings have shown the possible risk factors for anaemia in PLHIV, such as sex, age, education, ART status and stage of HIV disease.

Many previous studies about the prevalence and associated factors of anaemia among PLHIV used data from before or early in the ART era before the current treatment initiation guidelines and improvements in HIV care. In addition, most previous studies evaluating the prevalence and associated factors of anaemia among PLHIV were not conducted among hospitalised patients. However, hospitalised PLHIV were more likely to have a CD4 count <200 cells/mm$^3$ or a high stage of HIV disease (clinical stage 3 or 4), which has been reported to be associated with an increased risk of anaemia among PLHIV.

In the last two decades, China has made great achievements in HIV prevention and control strategies. China’s ‘Four Frees and One Care’ policy implemented in 2004 greatly facilitated the implementation of HIV prevention, treatment and care support. The threshold of CD4 T cell count for ART initiation was increased from ≤200 cells/mm$^3$ in 2004 to ≤250 cells/mm$^3$ in 2008 and ≤500 cells/mm$^3$ in 2014, and since 2016, China has entered the era of immediate treatment irrespective of CD4 T cell count. Therefore, this study aimed to estimate the prevalence of anaemia and the associated factors among hospitalised PLHIV receiving ART from a specialised hospital for infectious diseases in Southwest China in the modern HIV treatment era.

### METHODS

#### Study design and participants

This cross-sectional study included all PLHIV receiving ART and hospitalised in a specialised hospital for infectious disease in Guizhou Province, Southwest China, the Fifth People’s Hospital of Guiyang City, between 1 January 2018 and 31 March 2021 (n=7075). This hospital is also the largest infectious disease prevention and treatment hospital in Guizhou, mainly for the treatment of HIV and other infectious diseases. The hospital’s electronic medical records (EMR) system served as the source for all data used in this study. This study used the existing anonymised demographic, routine clinical and therapeutic data of PLHIV recorded by clinicians during hospitalisation from the EMR system. Inpatients with a recorded diagnosis of HIV infection were identified according to any position of the International Classification of Diseases (ICD-10) codes B20-B24. Individuals aged <18 years and pregnant women were excluded from this study (n=116). Finally, this study included 6959 hospitalised PLHIV.

#### Definition of haematological abnormality

Anaemia was diagnosed as a haemoglobin (Hb) concentration <120 g/L in non-pregnant females and <130 g/L in males, as recommended by WHO. The severity of anaemia was graded as ‘mild’ if the Hb was below the gender-specific lower limit of normal but ≥110 g/L, as ‘moderate’ if Hb was <110 g/L but ≥80 g/L and as ‘severe’ if Hb was <80 g/L. In addition, adjustments of anaemia thresholds for people living at altitudes >1000 m were recommended by WHO: thresholds plus 2 g/L for people living at altitudes at 1000–1500 m; plus 5 g/L at 1500–2000 m; plus 8 g/L at 2000–2500 m; plus 13 g/L at 2500–3000 m; plus 19 g/L at 3000–3500 m; plus 27 g/L at 3500–4000 m; 35 g/L at 4000–4500 m and plus 45 g/L at altitudes >4500 m. Thrombocytopenia was defined as a platelet count <100×10^9 cells/L. PLHIV with anaemia or thrombocytopenia were diagnosed according to the threshold values of Hb and platelet count during hospitalisation, respectively.

#### Other covariates

The EMRs collected inpatients’ demographic and health-related characteristics. Age was categorised into three groups: 18–39, 40–59 and ≥60 years. Ethnicity was categorised into Han or minority. Marital status was categorised into three groups: married, unmarried and widowed or divorced. Health-related characteristics included current tuberculosis disease, hepatitis C, cerebrovascular diseases (CBD), hypertension and diabetes, which were diagnosed according to ICD-10 codes listed in online supplemental table 1.

#### Statistical analyses

First, descriptive statistics were used to summarise the distribution of study participants’ demographic and health-related characteristics, with medians (IQR) for continuous variables and frequencies (percentage) for categorical variables. Second, we calculated the proportions of severity of anaemia among all anaemic inpatients and the prevalence of severity of anaemia using the percentage and 95% CI among all PLHIV. Third, we calculated anaemia prevalence by groups of demographic and health-related characteristics and used univariate and multivariate logistic regression methods to analyse the associations of demographic and health-related characteristics with anaemia prevalence. Finally, severe anaemia prevalence for groups of demographic and health-related characteristics was calculated and univariate and multivariate logistic regression methods were used to analyse the associations of demographic and health-related characteristics with severe anaemia prevalence. In multivariate logistic regression models, all the demographic and
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RESULTS
Characteristics of hospitalised PLHIV
Table 1 shows the characteristics of hospitalised PLHIV. Among 6959 PLHIV, the median age was 45 (IQR 34–58) years and 4970 inpatients were female, accounting for 71.4% of the inpatients (table 1). Most of the PLHIV were Han (91.1%). A total of 4271 PLHIV were married (61.4%), and the remaining inpatients were unmarried and widowed or divorced inpatients, with 1721 unmarried inpatients (24.7%) and 967 widowed or divorced inpatients (13.9%). The prevalence of thrombocytopenia, current tuberculosis disease, hepatitis C, CBD, hypertension and diabetes were 7.6%, 11.6%, 2.8%, 7.5%, 9.2% and 5.4%, respectively.

Proportion and prevalence of severity of anaemia among hospitalised PLHIV
There were 1912 PLHIV with anaemia, with 641 inpatients having mild anaemia, 847 inpatients having moderate anaemia and 424 inpatients having severe anaemia, accounting for 44.3%, 33.5% and 22.2%, respectively. The prevalence of mild anaemia, moderate anaemia and severe anaemia were 9.2% (95% CI: 8.5% to 9.9%), 12.2% (95% CI: 11.4% to 12.9%) and 6.1% (95% CI: 5.5% to 6.7%), respectively.

Factors associated with anaemia prevalence among hospitalised PLHIV
Table 2 shows the prevalence and associated factors of anaemia among hospitalised PLHIV. The anaemia prevalence ranged from 26.3% to 28.5% among all age groups of PLHIV. The prevalence of anaemia differed significantly by sex: 24.8% (95% CI: 23.6% to 26.0%) for male inpatients and 34.1% (95% CI: 32.1% to 36.2%) for female inpatients. The prevalence of anaemia was lower among unmarried PLHIV (23.8%, 95% CI: 21.8% to 25.8%) but higher among widowed or divorced inpatients (32.6%, 95% CI: 29.6% to 35.6%) than among married inpatients (27.8%, 95% CI: 26.5% to 29.1%). The prevalence of anaemia was 57.7% (95% CI: 53.5% to 61.9%) among PLHIV with thrombocytopenia and higher than that of those without thrombocytopenia, which is 25.0% (95% CI: 23.9% to 26.1%).

After adjusting for demographic and health-related variables, females had increased odds of anaemia compared with males (aOR=1.60, 95% CI: 1.42 to 1.81). Compared with married PLHIV, widowed or divorced inpatients had increased odds of anaemia (aOR=1.26, 95% CI: 1.08 to 1.47). Inpatients with thrombocytopenia had increased odds of anaemia compared with those without thrombocytopenia (aOR=4.25, 95% CI: 3.54 to 5.10).

Factors associated with severe anaemia prevalence among hospitalised PLHIV
Table 3 shows the prevalence and associated factors of severe anaemia among hospitalised PLHIV. For the different age groups of PLHIV, the prevalence of severe anaemia ranged from 6.0% to 6.3%. Widowed or divorced inpatients had a significantly higher prevalence of severe anaemia than married inpatients. The prevalence of severe anaemia was 18.0% (95% CI: 15.7% to 21.2%) among PLHIV with thrombocytopenia and higher than that of those without thrombocytopenia, which was 5.1% (95% CI: 4.6% to 5.7%). The prevalence of severe anaemia was 10.3% (95% CI: 6.0% to 14.5%) among PLHIV with hepatitis C and significantly higher than that of inpatients without hepatitis C, which was 6.0% (95% CI: 5.4% to 6.5%).

After adjusting for demographic and health-related variables, being widowed or divorced and having thrombocytopenia or hepatitis C were associated with a higher prevalence of severe anaemia. Widowed or divorced inpatients had increased odds of severe anaemia compared with married PLHIV (aOR=1.52, 95% CI: 1.16 to 1.97). Compared with inpatients without thrombocytopenia, those with thrombocytopenia had increased odds of severe anaemia (aOR=4.16, 95% CI: 3.24 to 5.35). Compared
with inpatients without hepatitis C, those with hepatitis C had increased odds of severe anaemia (aOR=1.80, 95% CI: 1.11 to 2.92).

**DISCUSSION**

Anaemia is a commonly encountered haematological abnormality among PLHIV and the pathogenic mechanisms are often multifactorial. In this cross-sectional study, we estimated the prevalence of anaemia and severe anaemia and the possible associated factors among hospitalised PLHIV receiving ART in Southwest China. We found that anaemia was prevalent among hospitalised PLHIV receiving ART, especially among inpatients with thrombocytopenia. We found that females were more likely to have anaemia and widowed or divorced marital status was associated with increased odds of anaemia and severe anaemia among hospitalised PLHIV receiving ART. In addition, thrombocytopenia was associated with...
increased odds of both anaemia and severe anaemia and hepatitis C was associated with increased odds of severe anaemia among hospitalised PLHIV receiving ART.

We found that the overall prevalence of anaemia was 27.5% among hospitalised PLHIV receiving ART in Southwest China in this study. In China, previous studies have reported that the prevalence of anaemia among PLHIV ranged from 9.8% to 55.1% in various regions depending on different geographical-social-economic conditions. Increased odds of both anaemia and severe anaemia and hepatitis C was associated with increased odds of severe anaemia among hospitalised PLHIV receiving ART.

Increased odds of both anaemia and severe anaemia among hospitalised PLHIV receiving ART in Southwest China in this study. In China, previous studies have reported that the prevalence of anaemia among PLHIV ranged from 9.8% to 55.1% in various regions depending on different geographical-social-economic conditions. Similar anaemia prevalence has been reported among hospitalised PLHIV from Ethiopia by Melese et al (23.0%), and Gedefaw et al (23.1%) and the USA by Semba et al (28.1%). However, a much higher prevalence of anaemia was reported in prior research conducted in Hispanics (41.5%), Indonesia (49.6%), Northeastern Nigeria (57.5%), Ethiopia (52.6%), Congo (69%), Ghanaian (63%) and Iran (71%). Moreover, this study revealed that the prevalence of mild, moderate and severe anaemia were 9.2%, 12.2% and 6.1%, respectively. The prevalence of severity

Table 3  Prevalence and associated factors of severe anaemia among hospitalised PLHIV

| Characteristics          | N  | Prevalence (%) (95% CI) | Univariate model | Multivariate model |
|--------------------------|----|------------------------|------------------|-------------------|
|                          |    |                        | cOR (95% CI)     | P value           | aOR (95% CI)* | P value |
| Overall                  | 424| 6.1 (5.5 to 6.7)       | -                | -                | -            | -       |
| Age (years)              |    |                        |                  |                   |              |         |
| 18–39                    | 162| 6.3 (5.4 to 7.2)       | 1.00             | 1.00              |              |         |
| 40–59                    | 165| 6.0 (5.1 to 6.9)       | 0.95 (0.76 to 1.18) | 0.630             | 0.80 (0.62 to 1.03) | 0.079   |
| ≥60                      | 97 | 6.0 (4.8 to 7.2)       | 0.95 (0.74 to 1.25) | 0.712             | 0.86 (0.63 to 1.17) | 0.331   |
| Sex                      |    |                        |                  |                   |              |         |
| Male                     | 291| 5.9 (5.2 to 6.5)       | 1.00             | 1.00              |              |         |
| Female                   | 133| 6.7 (5.6 to 7.8)       | 1.15 (0.93 to 1.42) | 0.190             | 1.13 (0.90 to 1.41) | 0.287   |
| Ethnicity                |    |                        |                  |                   |              |         |
| Han                      | 383| 6.0 (5.5 to 6.6)       | 1.00             | 1.00              |              |         |
| Minority                 | 41 | 6.6 (4.7 to 8.6)       | 1.10 (0.79 to 1.53) | 0.578             | 1.13 (0.80 to 1.58) | 0.496   |
| Marital status           |    |                        |                  |                   |              |         |
| Married                  | 251| 5.9 (5.2 to 6.6)       | 1.00             | 1.00              |              |         |
| Unmarried                | 91 | 5.3 (4.2 to 6.4)       | 1.08 (0.70 to 1.14) | 0.374             | 0.83 (0.63 to 1.10) | 0.201   |
| Widowed/Divorced         | 82 | 8.5 (6.7 to 10.2)      | 1.48 (1.15 to 1.92) | 0.003             | 1.52 (1.16 to 1.97) | 0.002   |
| Thrombocytopenia         |    |                        |                  |                   |              |         |
| No                       | 329| 5.1 (4.6 to 5.7)       | 1.00             | 1.00              |              |         |
| Yes                      | 95 | 18.0 (15.7 to 21.2)    | 4.06 (3.27 to 5.20) | <0.001           | 4.16 (3.24 to 5.35) | <0.001 |
| Current tuberculosis disease |  |                     |                  |                   |              |         |
| No                       | 380| 6.2 (5.6 to 6.8)       | 1.00             | 1.00              |              |         |
| Yes                      | 44 | 5.5 (3.9 to 7.0)       | 0.88 (0.64 to 1.21) | 0.419             | 0.90 (0.65 to 1.25) | 0.523   |
| Hepatitis C              |    |                        |                  |                   |              |         |
| No                       | 404| 6.0 (5.4 to 6.5)       | 1.00             | 1.00              |              |         |
| Yes                      | 20 | 10.3 (6.0 to 14.5)     | 1.80 (1.12 to 2.89) | 0.015             | 1.80 (1.11 to 2.92) | 0.018   |
| CBD                      |    |                        |                  |                   |              |         |
| No                       | 402| 6.2 (5.7 to 6.8)       | 1.00             | 1.00              |              |         |
| Yes                      | 22 | 4.2 (2.5 to 5.9)       | 0.66 (0.42 to 1.02) | 0.061             | 0.65 (0.41 to 1.02) | 0.061   |
| Hypertension             |    |                        |                  |                   |              |         |
| No                       | 386| 6.1 (5.5 to 6.7)       | 1.00             | 1.00              |              |         |
| Yes                      | 38 | 5.9 (4.1 to 7.8)       | 0.97 (0.69 to 1.37) | 0.865             | 1.12 (0.77 to 1.65) | 0.546   |
| Diabetes                 |    |                        |                  |                   |              |         |
| No                       | 400| 6.1 (5.5 to 6.7)       | 1.00             | 1.00              |              |         |
| Yes                      | 24 | 6.4 (3.9 to 8.9)       | 1.06 (0.70 to 1.63) | 0.777             | 1.10 (0.71 to 1.73) | 0.645   |

*Adjusted for age, sex, ethnicity, marital status, thrombocytopenia, tuberculosis, hepatitis C, CBD, hypertension and diabetes. aOR, adjusted OR; CBD, cerebrovascular diseases; CI, confidence interval; cOR, crude OR; PLHIV, people living with HIV.
of anaemia (mild, moderate and severe anaemia) in this study was lower than that of PLHIV in another study from Southeast China. The wide variation in the reported prevalence of anaemia could be explained by different clinical settings, such as sociodemographic differences, progression of HIV/AIDS differences, differences in ART coverage and regimen taking, different definitions of anaemia and inclusion and/or exclusion criteria in recruiting study participants. Thus, research estimating anaemia prevalence among PLHIV remains to be well designed and conducted in the future.

In the current study, we found that increased odds of anaemia were associated with female sex but not older age among hospitalised PLHIV, which was partly similar to previous study findings. In line with our findings, several previous studies reported that females had an increased risk of anaemia among PLHIV. Females living with HIV have an increased risk of anaemia than males living with HIV, which could be largely explained by menstrual blood loss and the drains on iron stores that occur with pregnancy and delivery. This study found no significant association between severe anaemia and sex in all hospitalised PLHIV, which was similar to two previous studies. However, one previous study reported that females had an increased risk of severe anaemia (Hb <8.5 g/L) among PLHIV in Tanzania. In this study, we found no significant association between anaemia and older age among hospitalised PLHIV receiving ART, which was consistent with results from several previous studies. However, several previous studies reported that older PLHIV had an increased risk of anaemia compared with younger patients. The disparity in the association between older age and anaemia among PLHIV could be largely explained by the differences in study participants’ demographic distribution.

For example, this study was conducted among hospitalised PLHIV with a higher proportion of males living with HIV who were less likely to have anaemia than females living with HIV. In addition, we found that widowed or divorced hospitalised PLHIV had an increased risk of anaemia and severe anaemia than married inpatients. The possible explanations for the difference in anaemia prevalence between different marital statuses remain unclear. Future research is warranted to explore the factors associated with increased odds of anaemia among widowed or divorced PLHIV to improve their health status.

Moreover, we found that hospitalised PLHIV with thrombocytopenia were more likely to have anaemia and severe anaemia than those without thrombocytopenia in this study. Anaemia was also associated with thrombocytopenia, perhaps because myelosuppression caused by HIV and chemotherapeutics may affect the production of all cell lineages. In addition, thrombocytopenia has been reported to be associated with a variety of bleeding abnormalities. Evidence has reported that thrombocytopenia could increase bleeding in the mucous membranes, skin, soft tissue, gastrointestinal tract and intracranial sites among PLHIV, leading to an increased risk of adverse sequelae and death. HIV-related thrombocytopenia has been reported to cause excessive bleeding among females during pregnancy. Thus, thrombocytopenia could further increase the risk of anaemia and even aggravate anaemia owing to acute or chronic blood loss among PLHIV. In addition, this study found that hepatitis C was associated with an increased risk of severe anaemia, which could be explained by the significant side effects of therapy for hepatitis C.

This study estimated the prevalence of anaemia and severe anaemia and the possible associated factors in a large sample of hospitalised PLHIV receiving ART. The majority of the study participants in this study were middle-aged and older hospitalised PLHIV, which were representative and reflected the health status of hospitalised PLHIV well and could provide guidance for improving the health status of anaemic PLHIV. However, some limitations in our study should be mentioned. First, we did not include data on HIV/AIDS progression due to the data availability of this study, such as the routes of HIV infection, CD4+ T count, WHO clinical stage, time of ART and ART regimens, to analyse their effect on anaemia. Second, several factors possibly associated with Hb levels were not included in this study, such as environmental and nutritional factors, socioeconomic status and lifestyle. Third, data on contraceptive measures, menstrual conditions and reproductive conditions among females were not included due to data availability. Finally, this study did not include inpatients without HIV as a control group. Although there were several limitations mentioned above, our results study could also reflect the anaemic status of hospitalised PLHIV.

In conclusion, anaemia was prevalent among hospitalised PLHIV receiving ART in Southwest China, with a prevalence of 27.5% for anaemia and 6.1% for severe anaemia, which was much higher among inpatients with thrombocytopenia. Clinicians should pay more attention to anaemia among hospitalised PLHIV with thrombocytopenia. Policies, strategies and programmes should be considered to identify the predictors of anaemia among PLHIV to reduce the burden of anaemia among patients receiving ART. Early detection and timely management of anaemia are crucial to prevent anaemia progression.

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Contributors ML and GC conceptualised the design of the study, developed the statistical analysis plan, carried out data analysis and drafted the initial manuscript. HL, YL, XX, YF, JH, SS, SL and MZ led data collection, managed data and reviewed the drafts of the manuscripts. JL, YW, YW, MD, WJ and JY were involved in the conceptualisation and design of the study, ML critically revised the manuscript and acted as a guarantor for the study. All authors revised and approved the final manuscript.

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