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Incidence and risk factors regarding atherosclerotic cardiovascular disease in middle-aged and elderly people with HIV treated in Chongqing, China

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Abstract

Background Atherosclerotic cardiovascular disease (ASCVD) has become an increasingly common cause of death among people living with HIV (PLHIV) receiving successful antiretroviral therapy (ART). In Chongqing, approximately half of the PLHIV were middle-aged or elderly, and their diets were mainly high in salt, spices and oil; however, there is still a lack of relevant research on the risk factors and whether the disease burden of ASCVD is greater in these areas. This study was to investigate the risk of ASCVD in middle-aged and elderly PLHIV receiving ART and analyze the factors influencing high risk.

Methods A cross-sectional study was conducted at Chongqing Public Health Medical Center. Questionnaire surveys, physical examinations and laboratory examinations were used to collect information from PLHIV aged ≥ 45 years. Pooled cohort equations (PCEs) were used to calculate the 10-year ASCVD risk and analyze the influencing factors. The 10-year ASCVD risk score was used to define patients in the low-risk subgroup (< 7.5%) and high-risk subgroup (≥ 7.5%), and the risk factors were compared between the two groups.

Results In total, 463 PLHIV (median age 55.0 years, male 68.5%) were included, and the median duration of ART was 45.0 (15.0, 70.3) months. Of the 463 PLHIV, 13 (2.8%) had a known history of ASCVD. In the present study, 153 PLHIV (33.0%) were classified into the high-risk group, and 310 PLHIV (67.0%) were classified into the low-risk group. Compared with the low-risk group, the high-risk group was more likely to be female, older age, live in urban areas, be unemployed, have poor sleep quality, have higher low-density lipoprotein cholesterol (LDL-c), have higher total cholesterol (TC), and have diabetes and hypertension; however, coffee consumption was associated with a low risk of ASCVD. In addition, there were no differences in HIV viral load, CD4 + T-cell count, or duration on ART, or ART regimes between the two groups. According to multiple logistic regression, older age [odds ratio (OR) = 62.469, 95% CI 27.456, 142.134], female sex [OR = 9.635, 95% CI 4.384, 21.179], higher LDL-c levels [OR = 1.018, 95% CI 1.000, 1.036], accompanied hypertension [OR = 8.642, 95% CI 3.373, 22.143] and diabetes [OR = 10.806, 95% CI 3.787, 30.834] were found to be independent risk factors for the 10-year risk of ASCVD.

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Conclusions The overall 10-year ASCVD risk is great for middle-aged and elderly PLHIV in Chongqing, China. The risk factors for the 10-year risk of ASCVD were older age, female sex, elevated LDL-c level, and coexisting hypertension and diabetes.

Keywords HIV, ASCVD, Risk, Age, Sex

Introduction

Antiretroviral therapy (ART) has tremendously improved the survival of people living with HIV (PLHIV) and provided a nearly normal lifespan [1]. However, this improvement in longevity has resulted in an increase in the number of PLHIV living in middle-aged and older age groups; this trend is global and common in China [2]. There is a shift in the prevalence of HIV-associated disorders from opportunistic infection manifestations to other complex comorbid disorders, such as atherosclerotic cardiovascular disease (ASCVD), metabolic syndrome (MetS) and non-HIV-associated cancers [3, 4]. In particular, ASCVD is a common cause of morbidity and mortality among PLHIV, and compared with the general population, PLHIV are twice as likely to develop ASCVD [5]. The causes of the increased ASCVD risk observed among PLHIV include traditional risk factors such as aging, increased smoking rates, dyslipidemia, insulin resistance, and deposition of body fat [6]. and nontraditional factors, including increased chronic inflammation, immune activation [7], microbial translocation [8] and ART [9]. However, to date, the pathogenesis of ASCVD in HIV-treated patients is poorly understood.

Several risk scores [10–12], such as the Framingham Risk Score(FRS), the Data Collection on Adverse Effects of Anti-HIV Drugs (D:A:D) risk equation and the Pooled Cohort Equation (PCEs) have been developed to predict future risk for ASCVD. Compared with established risk prediction tools such as the FRS, the PCEs reported in the 2013 ACC/AHA guideline obtained good discrimination andcalibration with internal validation by 10×10 cross-validation and external validation among Americans [13].

The prevalence of ASCVD in PLHIV differs among geographical regions [14]; this may be related to the distribution of age, living habits, ART regimen, immune function reconstruction and use of different ASCVD risk assessment tools. Limited data on assessment of ASCVD risk factors in PLHIV from low-income countries exist. In Asia, two studies from Thailand found the prevalence of predicted cardiovascular risk in HIV infected Thai patients was relatively low (about 1% by D:A:D scoring systems) [15, 16]. In China, the prevalence of risk factors for ASCVD is high (17% by the 10-year ASCVD risk estimation chart) in the general population [17], however, few study have assessed the underlying prevalence of ASCVD risk factors among PLHIV.

Chongqing is more heavily affected by the HIV epidemic than are other regions in China [18]. The average proportion of PLHIV who were the middle-aged and elderly at HIV diagnosis increased dramatically from 3.6% between 1988 and 2003 to 45.4% between 2013 and 2017 in this region [19], and the main dietary factors were salt, oil and spicy, especially high oil, which may increase the risk of ASCVD; however, data are currently lacking. In this study, the primary objective was to assess the 10-year ASCVD risk by using PCEs and to analyze the influencing factors. The overarching objective was to provide guidance for effective intervention for ASCVD.

Methods

Participants

According to the World Health Organization (WHO) criteria, middle-aged people are defined as those aged 45–59 years, and elderly people are defined as those aged ≥ 60 years [20]. The cross-sectional study was conducted between 1 January and 31 March 2022 at the Chongqing Public Health Medical Center (CPHMC) in China, and the aim was to investigate the risk of ASCVD in middle-aged and older PLHIV. Briefly, referring to previous studies, more than 450 PLHIV on ART were required according to analyses we conducted by Power Analysis and Sample Size (PASS) software, version 11[21].

The inclusion criteria were 1) had a diagnosis of HIV, or infection, HIV infection diagnosed in accordance with the guidelines for HIV/AIDS diagnosis and treatment in China (2021) [22]. 2) were aged ≥ 45 years, 3) had received ART for at least 6 months, and 4) were willing to join the study. The exclusion criteria were: 1)incomplete data, 2) poor adherence to ART (A patient was defined as "poor adherence to ART" when calculated adherence percentage was < 95% of the prescribed doses in the last month)[23]. The CPHMC is a prominent government-funded tertiary referral hospital with Grade A level specializing in the prevention and treatment of infectious diseases. As the designated medical quality control center for HIV, the hospital plays a pivotal role in the diagnosis and treatment of HIV, so survey data of PLHIV in this center are representative.

Questionnaire survey

The survey and interviews were conducted by the same team of trained investigators. A face-to-face questionnaire was used to collect the following information:

Sociodemographic variables (i.e., age, education, occupational status, marital status).
behavioural (i.e., physical exercise, heavy alcohol consumption, smoking, coffee consumption, sleep quality).

Heavy alcohol consumption was defined according to the guidelines for primary care of alcoholic liver disease [24] as long-term alcohol consumption over 5 years, an ethanol content ≥ 40 g/d in men, ≥ 20 g/d for women, or > 80 g/d in 2 weeks.

Smoking and coffee consumption were assessed by several questions: "Have you ever smoked or do you now smoked at least one cigarette per day for more than six months? Have you ever or do you now drink at least one cup of coffee per day for more than one month?" The answers were yes or no.

Low physical activity was defined as less than 150 min of physical activity in a week.

Participants were considered to have "poor sleep quality" if they currently had insomnia, were troubled by poor sleep (i.e., "much" or "very much") or were rating their sleep quality as "fairly bad " or "very bad".

health (i.e., ART regimen, duration of ART, chronic diseases including hypertension, diabetes, fatty liver and so on)
family history of chronic illnesses (hypertension and diabetes)

Anthropometric measurements

Height (m), weight (kg), waist circumference(cm) and blood pressure (mmHg) were measured by trained investigators based on standard methods, and the above indices were all measured twice for five minute intervals and then averaged. Height and weight were measured to calculate body mass index (BMI), i.e., weight divided by the square of the height in meters.

Clinical laboratory tests

All clinical laboratory tests were performed following an 8- to 12-h overnight fast. Total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), triglyceride (TG) and glucose levels were measured. The CD4 + T-cell count and HIV viral load (VL) were the most recent results within six months before the completion of the questionnaire.

ASCVD risk

The American Heart Association (AHA) and the American College of Cardiology (ACC) developed the PCEs. In our study, the 10-year ASCVD risk was calculated by using the PCEs [13]. The ASCVD risk score was defined as a low risk (< 7.5%) or high risk (≥ 7.5%).

Statistical analysis

Continuous data are presented as the means and standard deviations and were compared using Student's t test. Categorical variables are represented by frequencies or percentages and were compared using the chi-square test or Fisher's exact test, where appropriate. Variables with a p value < 0.05 in the univariate analysis were added to the binary logistic regression. A p value of < 0.05 was considered to indicate statistical significance. All the statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) software, version 25.

Results

Descriptive characteristics

We screened a total of 486 PLHIV. Of these, 23 PLHIV were excluded. 18 PLHIV had incomplete data and 5 PLHIV had poor adherence to ART. A total of 463 PLHIV (including 13 PLHIV with a known history of ASCVD at the time of enrollment) were enrolled; 57.0% (306/463) were middle-aged, and 43.0% (157/463) were older. The median age was 55.0 [interquartile range (IQR) (32.0, 55.0)] years, and 68.5% were men; the majority were married, and approximately half lived in urban areas. In addition, 66 PLHIV had previously been diagnosed with hypertension, and 44 had previously been diagnosed with diabetes. There were 79 first-degree relatives with a history of hypertension and 42 first-degree relatives with a history of diabetes. The duration of ART was 38.0 (IQR 15.0, 70.3) months. The median CD4 + T-cell count was 322.0 (IQR 202.0, 472.0) cells/μL, and 402 (86.8%) PLHIV exhibited virological suppression (VS) with a VL ≤ 200 (copies/mL). At the initial initiation of ART, up to 71.5% (331/463) of PLHIV were on non-nucleoside reverse transcriptase inhibitor (NNRTI)-based regimens; of these, 93 PLHIV subsequently converted to integrase strand transfer inhibitor (INSTI)-based regimens for various reasons. Currently, 238 (51.4%) PLHIV have received NNRTI-based regimens, followed by INSTI-based regimens (39.7%) and protease inhibitor (PI)-based regimens (8.9%) (Table 1).

Table 1 Baseline characteristics

Variable	N = 463	low-risk group (310)	high-risk group (153)	P
Gender, n (%)				< 0.001
Male	317 (68.5)	234 (75.5)	83 (54.2)	
Female	146 (31.5)	76 (24.5)	70 (45.8)	
Age, years	55.0 (50.0, 64.0)	52.0 (49.0, 57.0)	66.0 (60.0, 70.0)	< 0.001
BMI, kg/m2	22.9 (21.1, 25.0)	22.9 (21.0, 24.8)	23.0 (21.1, 25.5)	0.633
Residence location, n (%)				0.003
City	215 (46.4)	129 (41.6)	86 (56.2)	
Countryside	248 (53.6)	181 (58.4)	67 (43.8)	
Married status, n (%)				0.174
Married	325 (70.2)	223 (71.9)	102 (66.7)	
Single	138 (29.8)	87 (28.1)	51 (33.3)	
Route of infection, n (%)				0.218
Homosexual	44 (9.5)	34 (11.0)	10 (6.5)	
Heterosexual	318 (68.7)	206 (66.4)	112 (73.2)	
Unknown	101 (21.8)	70 (22.6)	31 (20.3)	
Work status, n (%)				< 0.001
Unemployed	235 (50.8)	131 (42.3)	104 (68.0)	
Employed	228 (49.2)	179 (57.7)	49 (32.0)	
Education level, n (%)				0.053
Elementary school	177 (38.2)	109 (35.2)	68 (44.4)	
Middle school and above	286 (61.8)	201 (64.8)	85 (55.6)	
Smoking, n (%)				0.519
Yes	102 (22.0)	71 (22.9)	31 (20.3)	
No	361 (78.0)	239 (77.1)	122 (79.7)	
Coffee consumption, n (%)				0.007
Yes	42 (9.1)	36 (11.6)	6 (3.9)	
No	421 (90.9)	274 (88.4)	147 (96.1)	
Heavy alcohol consumption, n (%)				0.282
Yes	66 (14.3)	48 (15.5)	18 (11.8)	
No	397 (85.7)	262 (84.5)	135 (88.2)	
Low activity levels, n (%)				0.396
Yes	211 (45.6)	137 (44.2)	74 (48.4)	
No	252 (54.4)	173 (55.8)	79 (51.6)	
Poor sleep quality				0.023
Yes	149 (32.2)	89 (28.7)	60 (39.2)	
No	314 (67.8)	221 (71.3)	93 (60.8)	
Family history of hypertension, n (%)				0.070
Yes	79 (17.1)	46 (14.8)	33 (21.6)	
No	384 (92.9)	264 (85.2)	120 (78.4)	
Family history of diabetes, n (%)				0.156
Yes	42 (9.1)	24 (7.7)	18 (11.8)	
No	421 (90.9)	286 (92.3)	135 (88.2)	
Accompanied hypertension, n (%)				
Yes	79 (17.1%)	20 (6.5)	40 (26.1)	< 0.001
No	384 (82.9)	290 (93.5)	113 (73.9)	
Accompanied diabetes, n (%)				
Yes	42 (9.1%)	11 (3.5)	33 (21.6)	< 0.001
No	421 (90.9)	299 (96.5)	120 (78.4)	
Duration on ART, month	38.0 (15.0, 70.3)	38.0 (15.0, 70.25)	42 (20.0, 60.50)	0.743

Table 1 (continued)

Variable	N = 463	low-risk group (310)	high-risk group (153)	P
ART-based regimen, n (%)				0.163
2NRTI + NNRTIs	238 (51.4)	166(53.5)	72 (47.1)	
2NRTI + PIs	41 (8.9)	30 (9.7)	11 (7.2)	
2NRTI + INSTIs	184 (39.7)	114 (36.8)	70 (45.7)	
CD4 count, (cells/mL)	322.0(202, 472)	331 (200, 481)	308.0 (204, 451)	0.566
Viral load, n (%)				0.368
< 50 (copies/mL)	355 (76.7)	242 (78.1)	113 (73.9)	
50–200 (copies/mL)	47 (10.1)	32(10.3)	15 (9.8)	
> 200 (copies/mL)	61 (13.2)	36 (11.6)	25 (16.3)	
LDL-c (mmol/L)	2.8 (2.4, 3.2)	2.68 (2.3, 3.1)	2.94 (2.6, 3.4)	< 0.001
HDL-c (mmol/L)	1.3 (1.1, 1.5)	1.3 (1.0, 1.5)	1.3 (1.1, 1.6)	0.110
TG (mmol/L)	2.8 (2.4, 3.2)	1.7 (1.1, 2.4)	1.8 (1.2, 2.6)	0.177
TC (mmol/L)	4.9 (4.4, 5.5)	4.85 (4.3, 5.5)	5.13 (4.6, 5.9)	< 0.001

Note: Data are presented as x ± s for normally distributed data or as M (P25, P75) for skewed distributions, or N(%). Abbreviations: BMI, body mass index; ART, antiretroviral therapy; NNRTIs, non-nucleoside reverse transcriptase inhibitors; PIs, protease inhibitors; INSTIs, integrase strand transfer inhibitor; LDL-c, low-density lipoprotein cholesterol; HDL-c, high-density lipoprotein cholesterol; TG, triglyceride; TC, total cholesterol

ASCVD risk score

When evaluating the risk of developing ASCVD events within 10 years according to the PCEs, the median ASCVD risk score was 4.2% [IQR 2.0%, 9.5%]. A total of 153 PLHIV (33.0%) were classified into the high-risk group, and 310 PLHIV (67.0%) were classified into the low-risk group.

Risk factors for ASCVD

Univariate analyses were also conducted to compare the characteristics of PLHIV at high-risk and those at low risk for ASCVD (Table 1). Compared with those in the low-risk group, the participants in the high-risk group were older (median 66.0 vs. 52.0 years, P < 0.001) more likely to be female (45.8% vs. 24.5%, P < 0.001) and more likely to be unemployed (68.0% vs. 42.3%, P < 0.001). PLHIV in the high-risk group had significantly greater LDL-c (P < 0.001) and TC levels (P < 0.001). Coexisting hypertension and diabetes were positively associated with ASCVD ≥ 7.5%(P < 0.001). In addition, coffee consumption was associated with a lower risk of ASCVD. However, there were no differences between the two groups in terms of smoking status, heavy alcohol consumption, physical activity, HIV VL, CD4 + T-cell count, ART duration or ART regimes.

According to the adjusted model, older age [odds ratio (OR) = 62.469, 95% CI = 27.456, 142.134, P < 0.001]; female sex [OR = 9.635, 95% CI = 4.384, 21.179, P < 0.001]; LDL-c levle [OR = 1.018, 95% CI = 1.000, 1.036, P = 0.049]; accompanied hypertension [OR = 8.642, 95% CI = 3.373, 22.143, P < 0.001]; and diabetes status [OR = 10.806, 95% CI = 3.787, 30.834, P < 0.001] were found to be independent risk factors for a 10-year risk of ASCVD (Table 2).

Table 2 Logistic regression analysis of the factors associated with a high risk of 10-year ASCVD

Model	β	SE	t	P	OR (95%CI)
Age	4.135	0.419	97.172	< 0.001	62.469 (27.456–142.134)
Gender	2.265	0.402	31.787	< 0.001	9.635 (4.384–21.179)
residence location	0.615	0.327	3.531	0.060	1.849 (0.974–3.511)
work status	-0.19	0.342	0.307	0.579	0.827 (0.423–1.617)
sleep quality	0.045	0.58	0.006	0.939	1.046 (0.335–3.259)
coffee consumption	-0.498	0.58	0.613	0.434	0.608 (0.175–2.114)
accompanied hypertension	2.157	0.48	20.183	< 0.001	8.642 (3.373–22.143)
accompanied diabetes	2.38	0.535	19.795	< 0.001	10.806 (3.787–30.834)
LDL-c	0.018	0.009	3.861	0.049	1.018 (1.000–1.036)
TC	0.002	0.005	0.106	0.745	1.002 (0.992–1.011)

Discussion

In this study, we we found the occurrence rate of 10-year ASCVD among middle-aged and elderly PLHIV was 33.0% in Chongqing, which was higher than that among HIV-treated patients in Taiwan (22.2%) [25], HIV-naive patients in other 11 provinces of China (10.5%) [6] and HIV-naive patients in Western countries (19.6–21.1%) [14]. These discrepancies might have resulted from the fact that our study population was older, and consisted of HIV-treated patients and from differences in lifestyle and health behavior across regions. Furthermore, The risk factors for the 10-year risk of ASCVD were older age, female sex, elevated LDL-c level, and coexisting hypertension and diabetes.

ASCVD is closely related to abnormal lipid metabolism, and factors significantly associated with ASCVD in our sample population included LDL-c and TC levels according to univariate analyses. Current evidence suggests that abnormalities in the lipid profile may be associated with the HIV-related immune activation and chronic inflammation [26]. After maintaining for possible confounding factors, LDL-c was identified as one of the risk factors independently associated with ASCVD. According to the Chinese Guidelines for Lipid Management, LDL-C is the pathogenic risk factor for ASCVD, and LDL-C is recommended as the primary target for lipid intervention [27]. This finding suggests that we should pay more attention to LDL-c. However, patients have no clinical symptoms when LDL-c abnormalities occur in the early stages, this problem may be ignored by infection doctors. Therefore, it is urgent to improve the ability of specialized infectious department physicians to identify and cure chronic diseases such as hyperlipidemia. If necessary, a multidisciplinary team is also involved to develop better therapeutic strategies to reduce or delay the onset of ASCVD.

Considering the rising age in HIV-infected subjects because of the improved therapeutic options, it is critical to understand what the future might hold for ASCVD in the middle-aged and elderly people. Previous studies have suggested that age is one of the strongest risk factors for ASCVD in PLHIV [25, 27, 28]. Similarly, our study showed that the median age (66.0 years) in the high-risk group was significantly greater than that in the low-risk group (66.0 vs. 52.0)($P=0.000$), indicating that the burden of ASCVD in this group is greater with increasing age. Interestingly, this prevalence is often underestimated owing to a general misperception that females are thought to have fewer risk factors for ASCVD, such as smoking and alcohol abuse. There was also a sex difference in the risk of ASCVD in our study; however, the risk was 9.6 times greater in women than in men, even after adjusting for other factors, which contradicts other findings [29–33]. The possible reasons are as follows: women are significantly more likely to have a raised body mass index and suffer from MetS [34], and in Chongqing, women have hot personalities and are easily impulsive; these are risk factors for ASCVD. In addition, women may be more likely to put their family first than men are, which compromises their own health [34], therefore, it seems that we should pay more attention to females.

Smoking was considered as a traditional risk factor to ASCVD, benefits from smoking cessation to lower ASCVD risk have also been reported [35, 36]. It's reported that smoking is highly prevalent among PLHIV (42% were current smokers and 20% were former smokers in a nationally representative US sample) [37]. Similarly, approximately 50.5% of adult males in China and 2.1% of adult females in smoked cigarettes [37]. Smoking is more prevalent among people with HIV compared with the general population in China. In our study, smoking isn't the risk factor for the 10-year risk of ASCVD, the possible reason is that the proportion of women in the high-risk group is larger ($P<0.001$), while women were less likely to smoke, so that the results of the study was influenced, Further study in a larger population is warranted.

According to our univariate analyses, individuals who were unemployed, living in cities or had poor sleep quality were more prone to developing ASCVD. Unemployment and living in cities are possibly associated with strong stress from social life and unhealthy lifestyles; similarly, poor sleep quality is strongly associated with anxiety and depression [38, 39]. It has been reported that poor sleep quality is linked to greater rates of ASCVD [40]. However, coffee consumption was inversely related to ASCVD. Previous studies have confirmed that coffee may exert a beneficial effect on cardiovascular-related outcomes and cardiovascular protection [41]. However, in the multivariate analysis, there were no significant effects of the above factors on ASCVD incidence after excluding these confounding factors, possibly due to sample size and other complicating factors. In addition, ART regimens, ART duration and CD4 T-cell count were not associated with an increased risk of ASCVD, possibly because many of the participants were receiving NNRTI-based ART before the recent introduction of the INSTI and because of the similar duration of ART.

This study has several limitations. First, this was a single-center, cross-sectional study reporting on associations, which does not imply causality. Second, due to the limitations of the included samples, an in-depth stratified analysis was not performed to determine whether the duration of ART and whether the ART regimen had an impact on the occurrence of ASCVD. Third, the ASCVD risk assessed in this study may not represent actual ASCVD, as clinical events, or surrogate evidence, such as

atherosclerosis and structural changes in the heart, were not determined using computed tomography, carotid artery or cardiac ultrasonography. In addition, Atherogenic index of plasma (AIP) [42], as a robust predictor of cardiovascular risk, should be used in the future study.

Conclusion

In summary, the overall 10-year ASCVD risk is greater for middle-aged and elderly PLHIV in Chongqing, China, particularly for those who are older, female, have elevated LDL-c levels, and have coexisting hypertension and diabetes. Given the significantly high 10-year ASCVD risk among PLHIV, there is a need for an integrative disease management approach for managing both diseases. Comprehensive promotion of multidisciplinary combination diagnosis and treatment modalities is needed to reduce the incidence and case fatality rate of ASCVD.

Abbreviations

ART	Antiretroviral therapy
ASCVD	Atherosclerotic cardiovascular disease
BMI	Body mass index
CPHMC	Chongqing Public Health Medical Center
FRS	Framingham Risk Score
HDL-C	High-density lipoprotein cholesterol
INSTIs	Integrase strand transfer inhibitor;
IQR	Interquartile range
LDL-C	Low-density lipoprotein cholesterol
MetS	Metabolic syndrome
NNRTIs	Non-nucleoside reverse transcriptase inhibitors;
PIs	Protease inhibitors;
PLHIV	People living with HIV
TG	Triglycerides
TG	Triglycerides;
VL	Viral load

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None.

Author contributions

Data collection was carried out by RH and YSW, QL and ML carried out the main analyses.YJF provided critical suggestions for this study, HHY and QC are the co-corresponding authors who contributed to the writing of the paper and performed the analysis. ML is the first author and contributed to the study design, analysis, and writing of the paper. All the authors approved the final version of this manuscript.

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Availability of data and materials

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

The study was approved by the ethics committee of the Chongqing Public Health Medical Center (no. 2021–041-04-KY). Written informed consent for the study was waived by the Ethics Committee of the Chongqing Public Health Medical Center.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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