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Risk Factors Associated with Severe/Critical COVID-19 in People Living with HIV-1

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ABSTRACT

Introduction: Our objective was to determine the risk factors of a "severe/critical" form of COVID-19 in a cohort of people living with HIV-1 (PLWH1) followed in the Bichat University Hospital center in PARIS, FRANCE.

Methods: This study was an observational retrospective monocentric cohort of PLWH1 diagnosed with COVID-19 between February 1 st and November 31 st, 2020. Risk factors associated with "severe/critical" forms were determined using stepwise forward selection.

Results: One-hundred-and-twenty-nine PLWH1 with COVID-19 were included. COVID-19 diagnosis was confirmed in 98 cases (75.9%) and deemed probable according to the association of clinical criteria and contact case in 31 cases (24.1%). Clinical presentation of COVID-19 was "asymptomatic/mild/moderate" in 95 (73.6%), "severe" in 26 (21.7%) and "critical" in eight (6%). Patients with "severe/critical" COVID-19 tended to be older (median 54 year old), have a higher BMI (median 28.8 kg/m²) and were likely to have diabetes (9 versus 5) or chronic kidney disease (5 versus 2). Transgender women had higher risk too (OR: 4.9 (IC95: 1.35-24.0)). No association was observed between severity of COVID-19 and viral suppression or CD4 rates.

Conclusion: Risk factors for severe COVID-19 were similar in PLWH1 than in the general population and PLWH1 transgender women were at higher risk.

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Introduction

Risk factors have been described as associated with severe forms of COVID-19 (Zhang et al., 2020). Persons living with HIV-1 (PLWH1) often carry such comorbidities. As shown by Bhaskaran et al (2021), PLWH1 are at a greater risk of developing a severe form of COVID-19. Our objective was to determine the characteristics associated with the development of a severe or critical form of COVID-19 in a cohort of PLWH1 who were followed up at the Bichat-Claude Bernard University Hospital in Paris, France.

Methods

This study was an observational retrospective monocentric cohort of PLWH1 who were diagnosed with COVID-19 infection between January 2, 2020 and October 31, 2020. Consecutive PLWH1 who were being managed in our department, who developed COVID-19, either confirmed by virological evidence (SARS-CoV-2 serology or SARS-CoV-2 PCR) or deemed probable by the physician, according to the association of clinical criteria and confirmed contact case, were included.

All individuals gave their written informed consent to have their medical chart recorded in the electronic medical record system, Nadis©, from which we extracted anonymized data.

We described the demographic characteristics, comorbidities, clinical variables related with HIV, and the severity form of COVID-19. Given the small number of individuals, we pooled the 'asymptomatic/mild/moderate' patients and 'severe/critical' patients. Data were presented through univariate distributions, Student's *t*-test to compare quantitative, and Fisher exact test to compare qualitative variables between the 'asymptomatic/mild/moderate/' and 'severe/critical' groups, respectively. In the final model, a multivariable logistic regression model (stepwise regression) was performed

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Table 1
Demographic and baseline clinical characteristics

Characteristics	Asymptomatic/ mild/moderate N = 95	Severe/Critical N = 34	Statistical test
Gender			Fisher = 0.213
Women, n	41 (43%)	9 (26%)	
Men, n	45 (47,5%)	21 (61%)	
Transgender women, n	9 (9,5%)	4 (11%)	
BMI			
kg/m², median (IQR)	27 (25.92; 28.07)	28.8 (27.09; 30.66)	t = 0.0379
≥ 30 kg/m², n	23 (24%)	8 (23,5%)	Fisher = 1
Age			
Years, median (IQR)	48 (46;51)	53 (49; 59)	t = 0.0104
≥ 65 years, n	5 (5%)	5 (14%)	Fisher = 0.127
Place of birth			Fisher = 0.206
Sub-Saharian Africa, n	46 (48%)	19 (55%)	
France, Europe, or Central Asia, n	25 (26%)	4 (11%)	
Other, n	24 (25%)	11 (32%)	
Smoking			Fisher = 0.885
Past, n	9 (9,5%)	4 (12%)	
Current, n	13 (13,5%)	4 (12%)	
Never, n	73 (77%)	26 (76%)	
At least one comorbidity			
Diabetes, n	5	9	Fisher = 0.002
Arterial hypertension, n	15	9	Fisher = 0.201
Other cardiac disease, n	4	5	Fisher = 0.054
Chronic kidney disease (creatinine clearance < 60ml/min), n	2	5	Fisher = 0.014
Chronic respiratory disease (asthma, chronic bronchitis), n	2	2	Fisher = 0.283
Active cancer, n	2	1	Fisher = 0.814
≥3 comorbidities	0	5	
Immunovirological status at COVID-19 diagnosis			
CD4			
/mm³, median (IQR)	663 (595;731)	654 (531;777)	t = 0.139
[0, 200], n	10 (10,5%)	3 (9%)	
[≥ 200], n	85 (89,5%)	31 (91%)	
HIV plasma viral load			Fisher = 0.923
During the past 6 months			
2 pVL <50 cp/mL, n	78 (82%)	29 (85%)	
1 pVL <50 cp/mL, n	11 (11, 5%)	3 (9%)	
0 pVL <50 cp/mL, n	6(6, 5%)	2 (6%)	
ARV treatment			Fisher = 0.797
No treatment, n	2 (2%)	0	
2NRTIs + PI, n	11 (11, 5%)	2 (6%)	
2NRTIs + NNRTI, n	26 (27%)	7 (20%)	
2NRTIs + INI, n	46 (48, 5%)	21 (62%)	
NRTI + PI + INI, n	4 (4%)	1 (3%)	
NRTI-sparing regimen, n	6 (6%)	3 (9%)	

to determine odds ratios (ORs) for risk factors associated with 'severe/critical' forms of COVID-19 after adjusting the effects of possible confounding variables. To avoid possible selection bias, the same analysis was repeated, considering the study population with "virological evidence".

Variables in the multivariate analysis were selected on the basis of variables, which were marginally significant with P <0.20 in the univariate analysis. Variables with P <0.05 were retained in the stepwise regression.

Results

A total of 129 PLWH1 with COVID-19 were included between January 2, 2020 and October 31, 2020. Baseline characteristics are shown in Table 1.

Eight individuals had unsuppressed plasma viral load (pVL) before COVID-19 infection. Median pVL among them was 1729 cp/ml and the median CD4+ T cell count was 640/mm^3 (interquartile range [IQR]: 500-795).

COVID-19 diagnosis was confirmed in 98 cases (75.9%) (SARS-CoV-2 antibodies [n = 22], SARS-CoV-2 PCR [n = 76]) and was deemed probable in 31 cases (24.1%).

Clinical presentation of COVID-19 was 'asymptomatic/mild/moderate' in 95 cases (73.6%) 'severe' in 26 cases (21.7%), and 'critical' in 8 cases (6%). Of the 129 individuals with COVID-19, 4 died (of a critical respiratory form of COVID-19).

Patients with "severe/critical" COVID-19 tended to be older (median age 54 years [IQR: 47.6] vs 48 [IQR: 46.5]), have a higher body mass index (BMI) (median BMI 28.8 kg/m² [IQR: 26.7] vs 27 kg/m² [25.9; 28.1]; OR: 4.3 [95% CI: 1.3-13.4]), and were more likely to have diabetes (9 vs 5; OR 4.0 [95% CI: 0.9-17.1]) or chronic kidney disease (5 vs 2; OR: 7.5 [95% CI: 0.9-55.7]). Transgender women had a significantly higher risk of severe COVID-19 (OR: 4.9 [95% CI: 1.3-24.0]).

Neither the CD4 cell count nor HIV-1 pVL at diagnosis of COVID-19 appeared to be associated with the outcome of COVID-19. An analysis restricted to the 98 individuals with virologic evidence of infection yielded the same result.

Discussion

As demonstrated in the general population (Reyes et al., 2022; Zhang et al., 2020), the severity of COVID-19 in the cohort of PLWH1 presented herein was associated with older age, higher BMI, diabetes, and chronical kidney disease. Male gender was also associated with higher risk of severe COVID-19. Although not significant, our results, using stepwise regression, were consistent with the literature (OR: 2.02 [95% CI: 0.68-5.99]).

Transgender women with HIV may engage in behaviors that put them at risk for COVID-19 (Poteat et al., 2020). Our results also suggested they could be at higher risk of severe COVID-19, which leads us to pay particular attention to this population.

Unlike other studies (Nomah et al., 2021; Yang et al., 2021), the number of individuals who were immunocompromised (CD4 $<200/mm^3$) and/or with unsuppressed pVL might be too small in our cohort to allow to show that CD4 rates $<200/mm^3$ might be associated with poor outcomes of COVID-19 infection.

Our study has limitations, including patients with probable COVID-19 as deemed by the physician (i.e., with no virological evidence). To reduce the risk of false-positive diagnosis of "deemed COVID-19", we selected patients who presented with both (i) typical symptoms of COVID-19 and (ii) with a history of recent contact with a patient with COVID-19; and the population described here originates from the pre-Delta variant era/first months of the pandemic and will not be transferable to the present time.

Conclusion

Our study suggests that risk factors for severe COVID-19 were similar in PLWH1 than in the general population (older age, higher BMI, diabetes, chronic kidney disease). We also highlighted, for the first time, that transgender women with HIV-1 were at higher risk for severe COVID-19.

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Ethical approval statement

The participants enrolled in this study gave their written informed consent to have their medical charts recorded in the medical record system, Nadis^{Ò}. The Commission Nationale Informatique & Libertés approved anonymized data extraction from electronic medical records (Commission Nationale Informatique & Libertés number 1171457, May 24, 2006). No further ethical approval is needed for French law on personal data protection.

Declaration of Competing Interest

The authors have no competing interest to declare.

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