

The Case Series of 34 PLWH Diagnosed with COVID-19 from Central and Eastern European Countries – Euroguidelines in Central and Eastern Europe Network Group Data

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HIV; SARS-CoV-2; COVID-19; Central and Eastern Europe; Cases

Abbreviations:

Antiretroviral Therapy – CART; Euroguidelines in Central and Eastern Europe – ECEE; International AIDS Society – IAS; People Living with HIV – PLWH; World Health Organization – WHO; Viral Load – VL

1. Abstract

1.1. Background: A novel coronavirus (SARS-CoV-2) was detected at the end of 2019 in China. The aim of our study was to describe epidemiology and clinical characteristics of PLWH diagnosed with COVID-19 reported from Central and Eastern European Countries.

1.2. Methods: On-line survey was sent to Euroguidelines in Central and Eastern Europe (ECEE) Network Group. Analysis included

all confirmed COVID-19 cases between March 11 and June 26 2020 among PLWH in 12 countries: Albania, Belarus, Bosnia and Herzegovina, Bulgaria, Czech Republic, Estonia, Hungary, Lithuania, Poland, Romania, Russia, and Serbia.

1.3. Results: In total 34 cases were reported. The mean age of those patients was 42.7 years (IQR=35.8-48.5) and most of the patients were male (70.6% vs 29.4%). The mean CD4+ T-cell count prior COVID-19 diagnosis was 558 cells/mm³ (IQR=312-719)

and HIV RNA viral load (VL) was undetectable in 18 of 34 (53%) cases, the data about most recent HIV RNA VL was not available in three cases (8,8%). Comorbidities were observed in 19 (55.9%) patients, mostly cardiovascular disease (27,8%), and in 10 (29.4%) patients had coinfection, mostly chronic hepatitis C (87.5%). The clinical course of COVID-19 was asymptomatic in 4 (12%) cases, mild disease without hospitalization was reported in 11 (32%) cases. Stable patients with respiratory and/or systemic symptoms have been documented in 14 (41%) cases; 5 (15%) patients were clinically unstable with respiratory failure. Full recovery was reported in 31 (91%) cases, two patients died.

1.4. Conclusion: This study indicates no alarming signals of increased morbidity or mortality from COVID-19 among PLWH.

2. Background

The impact of COVID-19 infection on people living with HIV (PLWH) has not yet been fully understood. There is currently no scientific evidence suggesting an increased risk of acquiring the infection and a more severe course of the disease in HIV-infected patients, assuming that these patients have normal CD4 T-cell count and are successfully treated with antiretroviral therapy (cART). Generally, it has been clearly confirmed that older people and people with other comorbidities, including cardiovascular disease, type II diabetes and chronic pulmonary diseases are at higher risk of severe COVID-19 in the general population [1]. HIV-infected individuals might be at higher risk of COVID-19 infection because significant proportion of them are over the age of 50, and the comorbidities such as cardiovascular disease and chronic lung disease are more common than in general population [2-4]. Moreover, little is known about the course of the COVID-19 in PLWH. In addition, we should consider external factors, which could also influence PLWH with COVID-19. A worse access to medical care regarding HIV care in COVID-19 crisis can have a negative impact for future course of COVID-19 [5]. On the other hand, maybe thanks to the COVID-19 pandemic, governments will pay more attention to the importance of public health and greater control of the HIV epidemic will be possible [6]. In our study, we describe epidemiology and clinical characteristics of HIV-positive patients diagnosed with COVID-19 reported from Central and Eastern European Countries.

3. Methods

The Euroguidelines in Central and Eastern Europe Countries (ECEE) Network Group was established in February 2016 to review standard of care for HIV infection and viral hepatitis within the region. The Network includes key experts from the region who are actively involved in HIV care. In March 2020, the group started to collect and analyze all known cases of COVID-19 in PLWH in the CEE. Data were collected through an anonymized on-line questionnaire. This retrospective analysis included all confirmed COVID-19 cases between March 11 and June 26 2020 among

HIV-positive patients in 12 countries (Estonia, Czech Republic, Lithuania, Albania, Belarus, Romania, Serbia, Bosnia and Herzegovina, Poland, Russia, Hungary, Bulgaria). Anonymized data were collected through on-line survey (by the treating physicians). The dataset included age, sex, information about HIV infection (time since HIV diagnosis, baseline HIV RNA viral load (VL), most recent CD 4+ T-cell count prior COVID-19 infection, latest HIV VL prior COVID-19 infection, nadir CD 4+ T-cell count), information about cART regimen at the time of COVID-19 infection, information about comorbidities and coinfections, details about COVID-19 infection (course of the disease: asymptomatic, mild disease, symptomatic patients with respiratory, clinically unstable patients with respiratory failure, patients in critical condition and outcome).

4. Results

In total 34 COVID-19 cases among HIV-positive patients were reported. In 32 (94,1%) cases SARS-CoV-2 infection was confirmed by PCR examination (in 1 case IgG positive, in 1 case clinical course +antibody positivity IgM).

There were 24 (70,6%) male patients recruited to the study, medium age within study cohort was 42.7 (IQR=35.8-48.5). (Table 1).

Two (5,8%) patients were diagnosed with HIV infection because of COVID-19 diagnosis. Among 32 patients with known HIV status before COVID-19 the time since HIV diagnosis ranged between 0.1 to 22 years.

28 patients were on cART regimen at the time of COVID-19 diagnosis. Three (8,8%) patients were on PIs and 12 (35%) patients were on tenofovir (TDF or TAF) containing regimen. Six patients (17,6%) weren't receiving any antiretroviral treatment at the time of SARS-CoV-2 infection Table 2.

The latest median of most recent CD4+ T-cell count prior COVID-19 infection was 558 cells/mm³ (IQR=312-719). The most recent HIV RNA VL (before COVID-19) was <50 copies/ml in 18 cases, the data about latest HIV VL was not available in three cases (8,8%).

In 19 (55,9%) patients there were other than HIV infection comorbidities. The most frequently seen comorbidities were cardiovascular disease in five (27,8%) cases, chronic lung disease or asthma in two (11,1%) cases, diabetes in two (11,1%) cases and obesity in two (11,1%) patients. Coinfection with hepatitis C occurred in 10 cases (29,4%), coinfection with hepatitis B in one case (2,9%) (Table 1).

Respiratory symptoms occurred in 27 (79,4%) cases while 26 (76,5%) patients presented general symptoms like fever, fatigue/malaise, muscle aches; only ten (29,4%) patients had gastrointestinal symptoms (diarrhea, nausea/vomiting, abdominal pain).

The most common symptoms of COVID-19 infection were cough in 24 (70,6%), fatigue/malaise in 24 (70,6%) and fever in 21

(61,8%) cases; muscle aches in 17 (50%) cases, headache in 9 (26,5%) cases, loss of smell in 9 (26,5%) cases and loss of taste in 7 (20,6%) cases Table 2.

Clinically unstable patients with respiratory failure was seen in 5 (15%) cases, stable patients with respiratory and/or systemic symptoms in 14 (41%) cases, mild disease without hospitalization in 11 (32%) cases and asymptomatic course of COVID-19 was only in 4 (12%) cases. Figure 1.

Regarding hospitalization, in one case (2,9%) the data was not available; 22 (64,7%) patients were hospitalized. In three patients hospitalization on intensive unit care was needed, two of them were with detectable HIV RNA needed mechanical ventilation – one of these patients died. Full recovery was reported in 31 (91%) cases, two patients died. (Table 1). Patients were included into analyses according to the STROBE diagram (supplementary file).

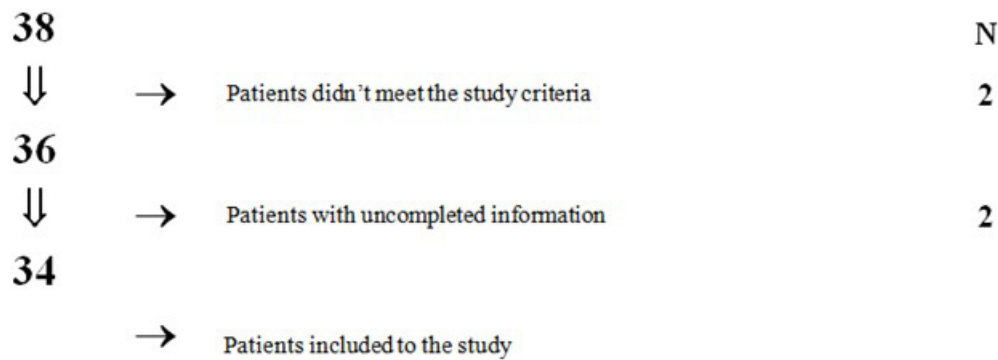
Table 1: Coinfection with hepatitis C occurred in 10 cases (29,4%), coinfection with hepatitis B in one case (2,9%).

Patient	Gender	BMI	Time since HIV diagnosis in years	Nadir CD4 T-cell count (cells/mm ³)	Latest CD4 T-cell count (before COVID-19) (cells/mm ³)	Baseline HIV VL (copies/ml)	Latest HIV VL (before COVID-19) (copies/ml)	cART regimen	Comorbidity	Course of COVID	COVID treatment	COVID outcome
1	Female	Not available	1	381	547	500	<500	TDF+FTC+LPV/r	No	Mild	No	Full recovery
2	Male	21.1	0.1	310	310	Not available	Not available	No cART	Yes	Mild	No	Full recovery
3	Female	26	1	708	708	10 200	<50	ABC/FTC/DLG	No	Stable symptomatic	Yes	Full recovery
4	Male	27	5	219	583	926 000	<50	ABC/3TC+RAL	No	Stable symptomatic	Yes	Full recovery
5	Female	24	13	254	830	118 000	<50	TDF/FTC + DTG	No	Mild	No	Full recovery
6	Female	22	14	28	6	167 000	54 000	No cART	No	Respiratory failure	Yes	Full recovery
7	Male	27	4	1142	880	16 000	Not available	No cART	Yes	Stable symptomatic	Yes	Not available
8	Male	25	13	72	857	22 600	<50	TAF/FTC/EVC/c	Yes	Respiratory failure	No	Full recovery
9	Female	20	1	312	312	17 000	17 000	TDF+FTC+EFV	No	Stable symptomatic	No	Full recovery
10	Male	27	6	318	635	10 000 000	<50	FTC/TDF + DRV/c	Yes	Stable symptomatic	No	Full recovery
11	Female	20	15	200	683	18 000	<50	AZT +Zeffix +NVP	Yes	Stable symptomatic	No	Full recovery
12	Male	29	0	379	630	17 500	66	ABC/3TC/DTG	Yes	Asymptomatic	No	Full recovery
13	Female	Not available	0.1	15	15	Not available	Not available	TDF/FTC/EFV	Yes	Stable symptomatic	Yes	Full recovery
14	Female	26	5	91	204	2 100 000	<500	TDF+FTC+EFV	Yes	Stable symptomatic	No	Full recovery
15	Female	22.5	15	20	20	300 000	300 000	No cART	No	Stable symptomatic	No	Full recovery
16	Male	Not available	1	61	102	4 000 000	7 300	TDF+FTC+EFV	No	Stable symptomatic	Yes	Full recovery
17	Male	24	5	48	362	2 200 000	<500	AZT+3TC+LPV/R	No	Mild	No	Full recovery
18	Female	Not available	22	44	82	110 000	<500	TDF+FTC+LPV/r	Yes	Mild	No	Full recovery
19	Male	Not available	1	520	520	24 000	24 000	No cART	Yes	Respiratory failure	Yes	Death
20	Male	25.8	4	18	491	13 300	<50	ABC/3TC/DTG	No	Stable symptomatic	No	Full recovery
21	Male	23	4	615	1610	0	<50	DTG TAF/FTC	Yes	Stable symptomatic	No	Full recovery
22	Male	27	2	665	1156	84 509	84 509	DTG ABC/3TC	No	Asymptomatic	No	Full recovery
23	Male	27	8	269	423	Not available	<50	FTC/TDF+DTG	Yes	Stable symptomatic	Yes	Full recovery

24	Male	Not available	0	257	257	1 000 000	1 000 000	ABC+3TC+EFV	Yes	Stable symptomatic	Yes	Full recovery
25	Male	29	7	635	936	5 790	<50	TAF/FTC/EVG/c	No	Mild	No	Full recovery
26	Male	25	17	224	493	4 430	<50	TAF/FTC/EVG/c	No	Mild	No	Full recovery
27	Male	26	14	245	547	Not available	<50	FTC/TDF+DTG	Yes	Mild	Yes	Full recovery
28	Male	30.1	5	429	1058	9 257	<50	ABC/3TC+DRV/cobi	Yes	Mild	No	Full recovery
29	Male	28	18	452	673	N/A	<50	FTC/TDF+DTG	Yes	Asymptomatic	No	Full recovery
30	Male	30	21	88	670	80 000	<50	BIC/TAF/FTC	Yes	Respiratory failure	Yes	Full recovery
31	Male	26	22	290	460	226 000	<50	DTG/3TC	Yes	Respiratory failure	No	Death
32	Male	20	4	327	751	78 638	<50	FTC/TDF+DTG	No	Mild	No	Full recovery
33	Male	Not available	7	237	598	132 000	<50	ABC/3TC + DRV/c	Yes	Asymptomatic	No	Full recovery
34	Male	23	7	149	567	1 041 803	289	No cART	No	Mild	No	Full recovery

Table 2. Characteristics of PLWH with COVID-19 diagnosis.

Category	N (%)
Gender	
Male	24 (70,6)
ART regimen	
YES	28 (82)
PIs	3(8,8)
TDF/TAF	12 (35)
Comorbidity	
YES	19 (55,9)
Cardiovascular disease	5 (27,8)
Chronic lung disease/asthma	2 (11,1)
Diabetes	2 (11,1)
Obesity	2 (11,1)
Symptoms	
YES	30 (88,2)
cough	24 (70,6)
fatigue/malaise	24 (70,6)
fever	21 (61,8)
muscle aches	17 (50)
headache	9 (26,5)
loss of smell	9 (26,5)
loss of taste	7 (20,6)
Course of COVID-19	
asymptomatic	4 (12)
mild disease without hospitalization	11 (32)
stable patients with respiratory and/or systemic symptoms	14 (41)
clinically unstable patients with respiratory failure	5 (15)
COVID-19 outcome	
full recovery	32 (88,9)
death	2 (11,1)



Patients' inclusion into analyses according to STROBE diagram

5. Discussion

Our review of 34 cases of patients HIV-positive ensured that COVID-19 presents mostly as mild disease in majority of PLWH having full clinical recovery (91%). In the beginning of SARS-CoV-2 pandemic it could be assumed that in the PLWH group, a significant proportion of this population had an increased risk of developing a more severe form of COVID-19. This hypothesis was based on fact that PLWH population includes patients with a low CD 4 T cell count (<200 cells / μ l) and patients without cART, and therefore in this group are severely immunocompromised patients. In addition, according to the Centers for Disease Control and Prevention (CDC), the risk of immune suppression is unknown, but for other viral respiratory tract infections, in PLWH population the risk of infection is highest with low CD4 T-cell count and without cART [7]. Published data has verified those assumptions. The comparable results to our study were reported by Harter et al. In this case series of 33 PLWH patients with COVID-19 infection it was observed that 91% of the patients recovered and 76% of patients have been classified as mild cases [8]. Another study strongly supports the above data. Study cohort published by Gervasoni et al. consisting of 47 PLWH with COVID-19 infection 96% of patients has fully recovered [9]. In the larger study on 51 group of patients HIV-infected diagnosed with COVID -19 in Madrid Vizcarra et al. found that only six (12 %) of studied patients were critically ill, among which two (4%) patients died [10]. Other recent studies in small cohorts of patients also strongly support the above data [11].

On the other hand, in the study Bhaskaran et al. [12] it was improved that in UK population PLWH were at increased risk of COVID-19 mortality. According to the authors research 25 HIV-positive patients with COVID-19 had higher risk of COVID-19 death than those without HIV after adjusting for age and sex [12]. The preliminary analysis of available evidence shows that PLWH are not protected from COVID-19, they are also not protected from severity of the disease. Authors suggest that HIV-related immunosuppression may increase risk of severity of COVID-19. The study shows that PLWH should be vigilant and adhere strictly to guidelines and recommendations of how to avoid SARS-CoV-2 infection [13].

In our study the most common symptoms of COVID-19 infection

were cough in 24 (70,6%), fatigue/malaise in 24 (70,6%) and fever in 21 (61,8%) cases. In the largest description of COVID-19 in Europe, in prospective observational cohort study of 16 479 patients from 166 UK hospitals Docherty et al. presented cough (70%), fever (69%) and shortness of breath (65%) as the most common symptoms. Only four percent of cases reported no symptoms [14]. In our review four (12%) patients were asymptomatic, which suggest even better clinical outcome of SARS-CoV-2 in PLWH than in general population.

International AIDS Society (IAS) and the World Health Organization (WHO) recommend PLWH to take the same precautions as the general population, as well as follow specific governmental recommendations. PLWH who know their serological status but have not yet received cART should have immediate antiretroviral treatment initiated [15]. Unfortunately, in Central and Eastern European Countries access to cART is insufficient [16]. We observed this fact in our study; only 82.6% of patients were on cART, but despite of that we didn't reported increased morbidity and mortality from COVID-19 among PLWH. Some of the studies suggested, that PLWH receiving TDF/FTC have a lower risk for COVID-19 and related hospitalization than those receiving other therapies [17]. In our study we observed only mild and stable symptomatic COVID-19 disease among HIV-positive patients receiving TDF/FTC regimen. We must admit, that the main limitation of our study is small group of patients. In this study from 12 countries in Central and Eastern Europe region we did not see any clear signals of increased morbidity or mortality caused by COVID-19 among HIV-positive persons. As the studies of SARS-CoV-2 among PLWH are performed in small study groups, there is a need for further research.

6. Conclusions

This study from 12 countries in Central and Eastern Europe region indicates no alarming signals of increased morbidity or mortality from COVID-19 among HIV-positive persons. There is a need for further research in this field.

7. Funding

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