

Consequences of COVID-19 and lockdown measures among People Living with HIV in Italy.

Conseguenze della COVID-19 e delle misure di lockdown tra le persone che vivono con HIV in Italia.

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Abstract

We conducted a survey aimed at estimating the burden of COVID-19 epidemic on HIV-infected patients healthcare during the first pandemic wave. The interview was conducted in a single outpatient clinic for HIV-infected patients at San Gerardo Hospital, Monza from May to Sep 2020. All consecutive patients presenting for scheduled clinical appointment were asked about the impact of COVID-19 on their life, access to health-services and treatment adherence. Possible associations between patients' characteristics and risk of treatment discontinuation or viral rebound were explored using chi-squared test or Fisher's exact test. Two-hundred and forty-three patients were interviewed (76.5% men, 81% Italians, 27.1% MSM, 21.4% >60 years old). Four patients (1.6%) have had COVID-19 diagnosed by a nasopharyngeal swab, 18 (7.4%) had developed symptoms of COVID-19 but were not tested and 31 patients (12.7%) reported a close contact with confirmed/suspected cases of COVID-19. Thirteen had a relative who died of COVID-19. One in 5 patients reported significant economic losses and 1 in 4 reported they had suffered from severe psychological distress. Two thirds of the patients had their HIV-appointments postponed and 21 (8.6%) reported they had unaddressed health problems during the lockdown. Twenty-two patients reported incomplete adherence to ART, 6 had a viral rebound to >50 copies/ml. Migrants had significantly higher rates of treatment interruption (19.6% vs. 2%; $p < 0.001$) and virological failure (8.7% vs. 1%; $p < 0.001$) than Italian-born patients. Containment measures of COVID-19 can have indirect effect on HIV-treatment adherence and patients wellness. However, this may guide future reflexions on new care models.

Riassunto

È stata realizzata un'intervista per indagare le conseguenze della COVID-19 sui pazienti HIV-positivi durante la prima ondata pandemica. L'intervista è stata realizzata presso l'ambulatorio di Malattie Infettive dell'Ospedale San Gerardo di Monza tra maggio e settembre 2020. I pazienti sono stati sottoposti ad un'intervista che includeva domande sull'impatto di COVID-19 dal punto di vista personale, economico e dell'accesso alle cure. Abbiamo inoltre indagato la presenza di fattori di rischio che favorivano l'interruzione della ART e un rebound della carica virale. Sono stati intervistati 243 pazienti (76.5% uomini, 81% Italiani, 27.1% MSM, 21.4% >60 anni). Quattro (1.6%) avevano ricevuto una diagnosi di COVID-19 con conferma microbiologica, 18 (7.4%) avevano manifestato sintomi compatibili ma non avevano effettuato tampone nasofaringeo. Tredici avevano perso un familiare a causa di COVID-19; 1 su 5 riferiva importanti perdite economiche e 1 su 4 stress psicologico. Due terzi dei pazienti avevano dovuto posporre le visite di controllo per l'infezione da HIV e 21 riferivano problematiche di salute che non era stato possibile gestire durante il periodo di lockdown. Ventidue pazienti hanno riferito un'aderenza subottimale alla ART e per 6 è stata documentata una carica virale >50 cp/ml; i pazienti di origine non italiana presentavano un rischio aumentato di interrompere la ART (19.6% vs. 2%; $p < 0.001$) e di fallimento virologico (8.7% vs. 1%; $p < 0.001$). Le misure di contenimento del COVID-19 hanno avuto quindi effetti indiretti sul benessere delle persone HIV-positivo; la stessa epidemia può rappresentare un'occasione per riflettere su possibili nuovi modelli di gestione delle cure.

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Background

During the first wave of the COVID-19 pandemic, Italy implemented the earliest, longest, and most radical lockdown measures outside of China. Between March 9th and May 4th, 2020, non-essential business

activities were closed and restrictions to citizen's free of movement were introduced. Although the access to hospital or other health-care facilities was allowed, "non-essential movements" were discouraged, and a "stay-at-home" order was issued.

Moreover, most services for HIV-positive patients were converted to COVID-units, further reducing access to non-urgent care (1,2). In a context of fear and uncertainty, although we tried to ensure continuity of care, it is foreseeable that the most fragile groups of people living with HIV (PLWH) may have encountered difficulties in accessing care or maintaining their adherence to treatment (3,4).

The present survey was therefore aimed at estimating the burden of COVID-19 epidemic and of the related restrictions on PLWH healthcare. Moreover, we aimed at identifying possible factors associated with treatment discontinuation or reduced adherence.

Methods

Setting

This observational study was conducted in a single outpatient clinic for HIV-infected patients at San Gerardo Hospital, Monza. The clinic takes care of about 1500 patients with HIV infection.

Between March and May 2020, the activity of the HIV clinic was largely reduced. All non-urgent blood tests and in-person visit with the physicians were cancelled and postponed, unless non-deferrable. Successively, the majority of follow up visits were performed using telemedicine. Antiretroviral treatment (ART) distribution at the clinic was never interrupted.

Population

All the first consecutive patients accessing one of the 3 offices at our HIV clinic for a scheduled appointment for the first time after the imposed “lock-down” were enrolled in the study.

Study design

A structured interview involving questions on the impact of COVID-19 on their life (being directly infected by COVID-19 or ill during the previous months, having a relative died by COVID-19, having an increase in psychological stress, having experienced financial loss), on their experience with the accessibility of health-services during the pandemic (access to the HIV clinic and other health-services) and ART adherence was conducted during the visit.

The interview included multiple choice questions and closed-ended question. Adherence to antiretroviral treatment was measured on a Visual Adherence Scale, ranging from 1 (worst adherence) to 10 (best adherence). Adherence was considered incomplete when a score ≤ 9 was marked.

Data on HIV-RNA and CD4+ cells count were retrospectively collected considering the results of the routine blood test regularly performed before the clinical appointment.

Virological rebound and variation of the CD4+ cells count was assessed considering the results of this blood test and the previous blood test available, performed before the onset of COVID-19 pandemic in Monza.

Statistical analysis

Possible associations between patients' characteristics and risk of treatment discontinuation or viral rebound were explored using chi-squared test or Fisher's exact test, where appropriate.

Results

Two-hundred and forty-three patients were interviewed between May 5th and Sep 30th, 2020 (Table 1). Of them, 186 (76.5%) were cis-gender men and 197

Table 1. Characteristics of the study population.

Characteristic (N=243)	N (%) or Mean (SD)
Gender/sex	
Cisgender men	186 (76.5%)
Cisgender women	52 (21.4%)
Transgender women	5 (2.1%)
Age, years	50.7 (11.2)
Risk factors for HIV infection	
Intravenous drug use	29 (11.9%)
Heterosexual intercourses	123 (50.6%)
MSM/TG Female	71 (29.2%)
Other	5 (2%)
Unknown	15 (6.2%)
Country of birth	
Italian born	197 (81.1%)
Foreign born	46 (18.9%)
CD4+ count, cells/mm³	701 (307)
HIV-RNA¹	
<50 copies/ml	226 (93%)
50-200 copies/ml	13 (5.3%)
>200 copies/ml	3 (1.2%)

¹ Latest measurement available before March 2020.

(81.1%) were Italian. Median age was 50.7 years old (SD 11.4); in particular, the 21.4% of patients were older than 60 years. Half of the patients had acquired HIV infection through heterosexual intercourse (123, 50.6%), while 71 (29.2%) were MSM or female transgender and 29 (11.9%) reported a previous intravenous drug use.

Among the study population, 4 participants (1.6%) reported a previous COVID-19 infection which was diagnosed by a nasopharyngeal swab, while 18 participants (7.4%) had developed symptoms of COVID-19 (either fever, respiratory symptoms, or ageusia/anosmia) but were not tested. Moreover, 31 participants (12.7%) reported at least a previous close contact with a confirmed or suspected case of COVID-19. Overall, 19 participants (7.8%) were subject to quarantine during the previous months (**Figure 1**).

In the second part of the interview, we explored indirect consequences of the COVID-19 pandemic on the study population (**Figure 2**). Thirteen participants (7.8%) had relatives or friends who had died of COVID-19. Twelve participants (4.9%) permanently lost their job and one in 5 patients (49/243, 20.2%) reported significant economic losses during the lockdown (**Figure 2**). A quarter of the participants (61/243, 25.1%) reported to have suffered from severe psychological distress. Twenty-one participants (8.6%) reported they had unaddressed health problems during the lockdown and 13 (5.3%) felt abandoned by their treating physicians.

Two thirds (68.3%) of the participants had their HIV-appointments postponed. In the majority of cases, the appointments were postponed for hospital/physician decision, mainly because of work overload (145/166, 87.3%). Only 4 participants (2.4%) had postponed a clinic appointment for personal choice. In addition, half of the patients (121, 49.8%) reported that during the study period one or more other health appointments were canceled or delayed, including radiologic exams or other diagnostics (61/123 answers, 49.6%), specialistic consultations (57/123, 46.3%), periodic screenings (15/123, 12.2%), vaccinations (13/123, 10.6%), elective surgery (5/123, 5.6%), in-vitro fecundation (2/123, 1.6%) and others (7/123, 5.7%).

Incomplete adherence during the lock-down, measured as a score ≤ 9 on a Visual Adherence Scale, was reported by 22 (9%) participant (**Figure 3**).

Thirteen participants reported ART discontinuation for more than 48 hours, while ART interruption lasted

Figure 1. Results of the survey: proportion of COVID-19 infection, close contact with COVID-19 infected people and quarantine among the study population.

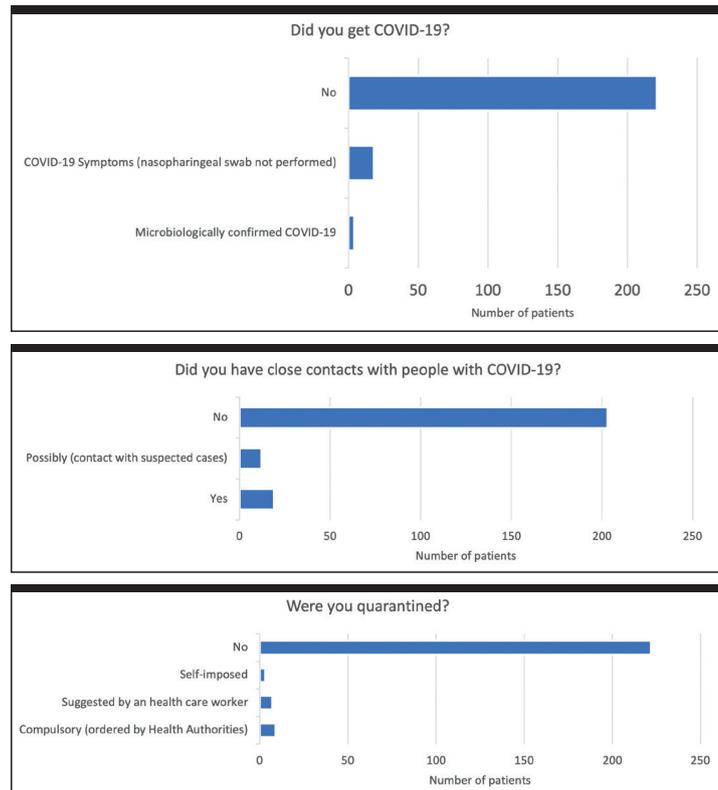
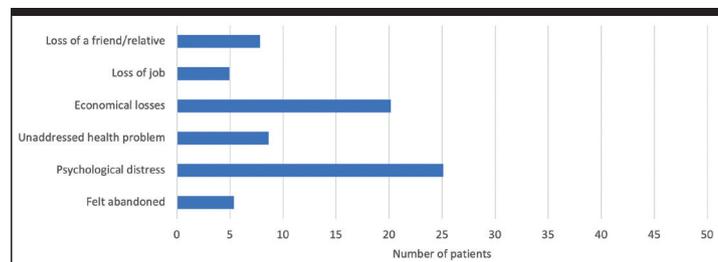
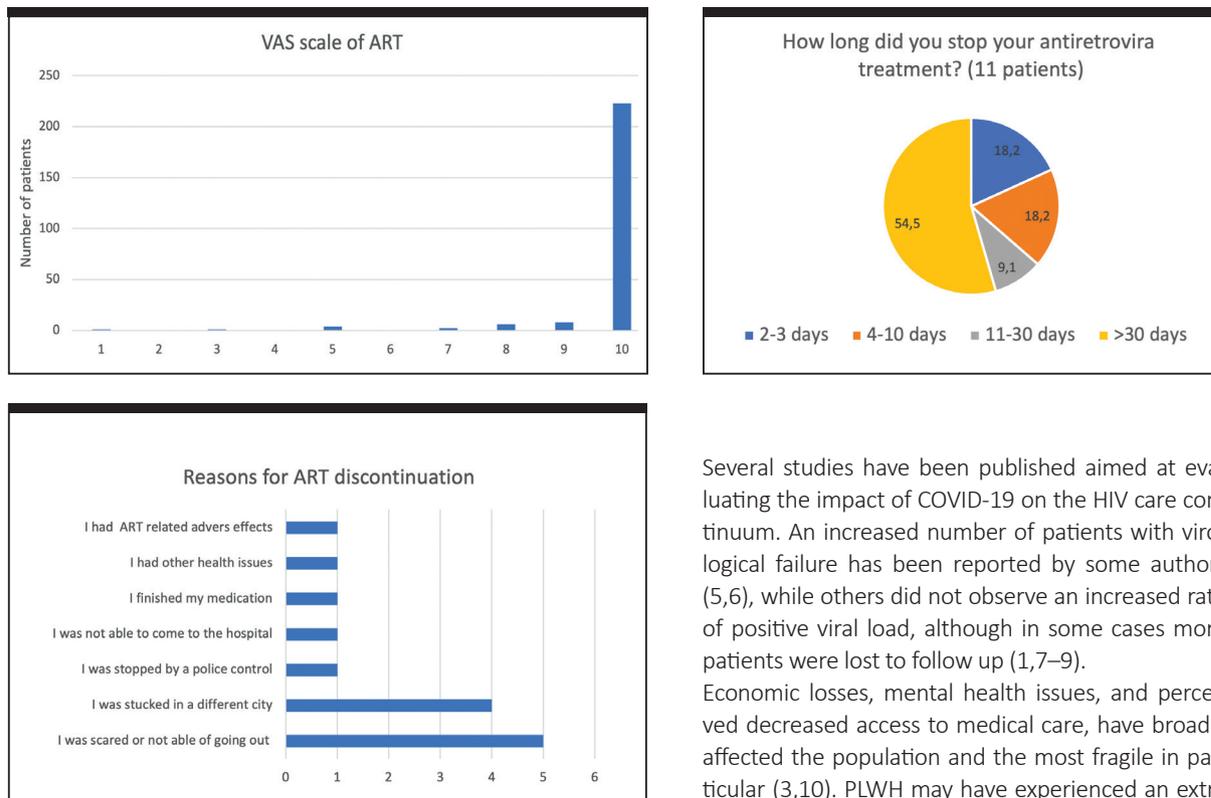


Figure 2. Indirect consequences of COVID-19 pandemic among the study population: economic and psychological issues among the study population.



more than 30 days for 6 of them. The most frequent reason for ART interruption was missed drug refill due to fear of getting infected when leaving home (5 participants) or movement restriction imposed by the government (4 participants).

Six participants who were previously virally suppressed experienced a viral rebound (>50 copies/ml); in four of these, the viral load was >200 copies/ml. Twenty-two patients (9%) experienced a drop in CD4+ cells count of 30% or more, as compared to the levels measured right before the lockdown.

Figure 3. ART adherence: self-reported adherence measured on a Visual Adherence Scale, duration and causes of the ART discontinuation.

Migrants presented both significantly higher rates of treatment interruption (19.6% vs. 2%; $p < 0.001$) and virological failure (8.7% vs. 1%; $p < 0.001$) than Italian-born participants (Figure 4). Although not statistically significant, a trend towards higher rates of treatment discontinuation was observed in women (9.6% vs. 4.2%; $p = 0.126$). No further associations were found considering other patients' characteristics, such as age (<60 or ≥ 60 years old), risk factors for HIV infection acquisition, time since ART initiation and CD4+ cells count.

Discussion

In this observational study, we aimed at exploring the consequences of COVID-19 pandemic on a cohort of HIV-infected patients at a large hospital in northern Italy. We observed a significant impact of the pandemic on the HIV patients of our clinic, ranging from being directly affected by COVID-19 illness, to economic damage or job loss, to the difficult to solve health issues due to inaccessibility of hospitals and finally a reduced adherence to ART and virological rebound.

Several studies have been published aimed at evaluating the impact of COVID-19 on the HIV care continuum. An increased number of patients with virological failure has been reported by some authors (5,6), while others did not observe an increased rate of positive viral load, although in some cases more patients were lost to follow up (1,7–9).

Economic losses, mental health issues, and perceived decreased access to medical care, have broadly affected the population and the most fragile in particular (3,10). PLWH may have experienced an extra psychological distress, fearful of being at higher risk of serious consequences of the infection, or being forced to interrupt ART and therefore to have deterioration of their clinical status, as well as avoidance of HIV appointment in fear of getting exposed to COVID-19 (7,11–13). Moreover, patients may have been modifying their ART regimen in order to “spare tablets”, in fear of running out of the treatment without being able to get supplies (6).

In our study, we observed a correlation between virological rebound and not being Italian born. As previously highlighted, the pandemic increased disparities in the most fragile populations, including migrants. Foreign patients were potentially more affected by all these indirect consequence of COVID-19 pandemic (2,14–16) and this could have negative impact on their retention in care.

Mitigation strategies, could have been less effective for them, as they could be more difficult to reach via phone calls (17).

Moreover, although in Italy patients receive essential health cares (such as ART) irrespectively of their legal status and ART dispensation was granted at the hospital, patients without regular documents may have

avoided more frequently going out from home in fear of police check.

The actual HIV care framework is based on the 90-90-90 targets (90% of PLWH aware of their HIV status, 90% of them on ART, 90% of them with virological suppression, and more recently, 90% of them with a good quality of life)(18). Covid-19 had a variably negative effect on all these targets (7,17,19).

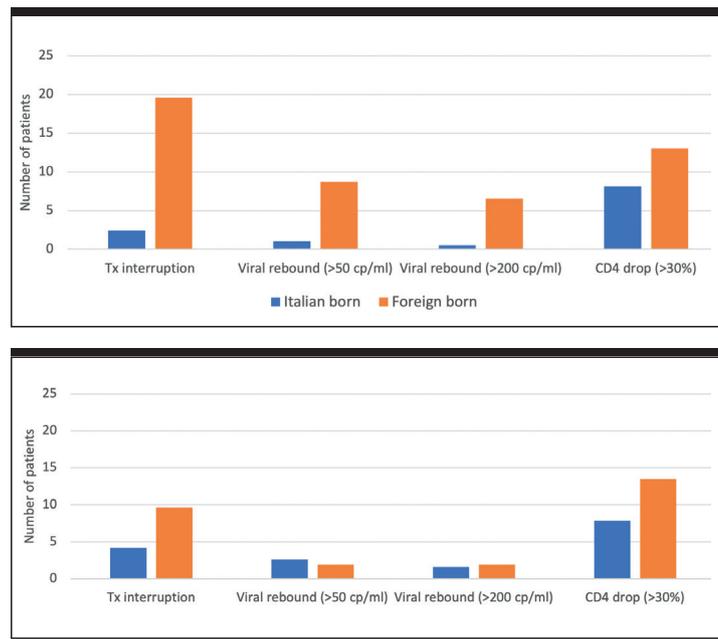
Many strategies measures have been put in place order to guarantee the access to treatment and care for PLWH: transition from clinical visit to phone calls except when in-person evaluation was essential, postponing of all routine blood tests, systematic review of HIV-RNA results, multi month art dispensing, ART home delivery or prescription delivery to local pharmacy (1–3,5,6,11,12).

As HIV care shifts from virological success to patient-centred outcomes, some of the strategies adopted during the covid pandemic may be adapted and integrated into routine care, carefully considering their positive and negative sides (1,12,17).

First of all, although patient-physicians encounter is essential in some situations (e.g. new HIV diagnosis) telemedicine may be integrated in some of the follow up visits allowing to reach a more comprehensive care involving different specialist, as pharmacists or psychologists (12).

Beyond teleconsultations via phone calls, specific apps for different settings, including HIV care, has been developed in the past years and its use has spread since the onset of covid-19 (3,20). Telemedicine could also be useful for PLWH who are still affected by the stigma of being seen in Infectious Diseases clinic, as well as to reduce the illness perception (2). On the other side, reducing in person access can reduce the global support for more fragile patients (5). Home delivery of medications, previously used in settings where distance from the health-care facilities could affect adherence (8), could reinforce ART adherence in some situations, but on the other hand it could not

Figure 4. Virological and immunological outcome according to patient nationality and gender.



be accepted for patients who want to maintain anonymity or privacy at home (11). Finally, the postponing of blood test, may have shifted the attention from lab results to quality of health objectives (17).

Conclusions

In this study, we discuss data collected after the first lock-down in Italy. In the following months, 3 other pandemic waves have hit the country, thus leading to further difficulties in managing healthcare. Care models developed during this difficult time may offer a chance of reflection and a starting point to strengthen the quality of care offered to PLWH.

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