Research Article

SARS-CoV-2 (COVID-19) infection in patients with HTLV-1 infection in Peru - case series

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Abstract

Introduction: Peru has suffered a prolonged sanitary emergency and has the highest COVID – 19 mortalities per capita in the world. Some risk factors (diabetes, HIV, cardiovascular diseases, etc.) are currently considered by the CDC to develop severe COVID-19 infection. CDC considers as possible risk factors (evidence is mixed), other immunodeficiency conditions, one of them would be infection by HTLV-1 (human T-cell lymphotropic virus type 1). It is not known whether subjects with HTLV – 1 infection have a higher risk for severe COVID – 19 disease.

Materials and methods: We identified 51 patients with HTLV-1 and COVID-19. The patients recruited for this article belong to the HTLV-1 cohort of the Institute of Tropical Medicine Alexander von Humboldt - Cayetano Heredia Hospital and to the study cohort: "The effect of Strongyloides Stercoralis on HTLV-1 disease progression". Periodic telemedicine follow-up was carried out on our patients during the lockdown from April 2020 to November 2021, and information related to SARS-CoV-2 infection was recorded.

Results: 51 patients from cohorts were diagnosed with COVID-19 during the pandemic between April 2020 and October 2021. The majority are female (29 patients, 56.85%). 76.47% (39 patients) underwent a molecular/PCR, antigenic or serological test; while 23.53% (12 patients) developed symptoms compatible with COVID-19 in a context of family outbreak and positive direct contact. 74.51% (38 patients) developed a mild form of the disease, 15.69% (8 patients) a moderate form and 9.80% (5 patients) were asymptomatic. The most frequent symptoms were general malaise and/or fever (82.35%), headache (80.39%) and cough (76.47%).

Discussion: the course of SARS-CoV-2 in patients infected with HTLV-1 follows similar patterns in percentage and symptoms compared to the general population. 81% usually develop a mild condition, while for our data 74.51% did. 14% usually develop moderate to severe disease worldwide, in our cohort, 15.69% developed moderate disease. The patients show a clinical picture similar to what is described in the literature as a common presentation of SARS-CoV-2. American studies show that the most frequent symptoms are headache (76%) and sore throat (65%); in our cohort, 80.39% reported headache and 35.29% sore throat.

Conclusion: Patients with HTLV-1 who become infected with SARS-CoV-2 develop mild or moderate disease in similar proportions to the general population. More studies are needed to elucidate the risk of developing severe SARS-CoV-2 disease in patients infected with HTLV-1 and its associated comorbidities.

Keywords: COVID 19, HTLV-1, SARS-Co-V2

Abbreviations: CDC, communicable disease center; HIV, human immunodeficiency virus; ATLL, adult T-cell leukemia/lymphoma; SS, strongyloides stercoralis, TSP, tropical spastic paraparesis

Introduction

The SARS-CoV2 pandemic was declared on March 11, 2020, affecting the entire world, putting all governments in trouble and especially the health systems of underdeveloped countries. In Peru, on March 5, 2020, the first case of SARS-CoV-2 was confirmed and the quarantine began 10 days later.

Since the beginning of the pandemic until the end of mid-April 2022, almost 2 years, there have been 504 919 200 cases and 6 223 910 deaths worldwide.[1,2] In Peru, up to the same date, 3 555 739 cases and 212 630 deaths have been registered, thus suffering a deep health crisis, having one of the highest mortality rates per capita on the planet (629.2 deaths per 100 000 inhabitants).[1-3]

The COVID-19 pandemic has led to accelerating and redirecting research efforts globally to advance knowledge, made possible by partnerships between science, government, and communities.

In the development of SARS-CoV-2 infection, comorbidities are factors that increase mortality from COVID-19. Some risk factors currently considered by the Communicable Disease Center (CDC) are diabetes, serious cardiovascular conditions, smoking, chronic kidney disease, people living with HIV (human immunodeficiency human), etc.[4-6] Additionally, the CDC considers other immunodeficiency conditions as possible risk factors, one of which would be infection by HTLV-1 (type 1 human T-cell lymphotropic virus); however, the evidence is mixed.[7]

Regarding HIV infection, the clinical presentation of COVID-19 seems to be very similar to people who do not carry HIV; however, numerous studies currently describe that HIV infection means a higher risk of developing severe disease from COVID-19 compared to the uninfected population.[8-10] On the other hand, another retrovirus known

as HTLV-1, which is described as generating immunosuppression, apparently does not put the patient at greater risk of developing severe SARS-CoV-2 infection. This information is still scarce and is under study. [11]

This article will explain the experience during these two years of the pandemic with HTLV-1 patients in our cohort and concomitant SARS-CoV-2 infection in this type of patient.

Materials and methods

Study design: descriptive and retrospective observational study, based on the analysis of a database created at the Alexander von Humboldt Institute of Tropical Medicine.

Population: patients in a created (coded) database, who belong to the HTLV-1 cohort of the Alexander von Humboldt Institute of Tropical Medicine, additionally, patients from the study cohort were entered: "The effect of *Strongyloides Stercoralis* on HTLV-1 disease progression". The information was recorded through an interview conducted by an infectious disease doctor and a general practitioner via telephone or video call to the patients mentioned as a virtual follow-up visit, these controls were made temporarily and as part of the interview, the information related to COVID-19 was recorded in a database. The information was collected between the months of April 2020 and November 2021.

Sample: 51 patients duly coded and entered into the database. The information has been recorded by an infectious disease physician and a general practitioner based on a telephone interview.

Operational definition of variables:

HTLV – 1 positive: patient with a confirmed diagnosis of being infected by human T-cell lymphotropic virus type 1 and belonging to one or both of the aforementioned cohorts.

COVID – 19 positives: patient with diagnosis confirmed by diagnostic test (PCR – molecular, antigenic or serological) and/or clinically diagnosed when the diagnostic test could not be performed.

Asymptomatic COVID-19 case: patient diagnosed with COVID-19 and has no symptoms.

Mild COVID-19 case: patient diagnosed with COVID-19 with at least 2 of the following symptoms: cough, malaise, fever, nasal congestion, sore throat, anosmia and dysgeusia. Does not require hospitalization.

Moderate COVID-19 case: patient diagnosed with COVID-19 with any of the following criteria: dyspnea, respiratory rate >22 breaths/minute, oxygen saturation <95%, altered mental status (confusion), low blood pressure, or shock, clinical and/or radiological signs of pneumonia, leukocyte count <1000 cells/μL. May require hospitalization.

Severe COVID-19 case: patient diagnosed with COVID-19 with any of the following criteria: respiratory rate >22 breaths/minute or PaCO2 <32 mmHg, altered mental status, MAP <65 mmHg, PaO2 <60 mmHg or PaFi <300, nasal flaring, use of accessory muscles, serum lactate >2 mosm/L.

Study procedure: as a result of the pandemic, activities in Peru were paralyzed due to quarantine, so the follow-up of the patients of both cohorts proceeded to be carried out virtually by telephone or video call. The virtual interviews were conducted by an infectious disease physician and a general practitioner. The information obtained was recorded in a database created for this purpose in the Microsoft Excel Program. The fidelity and veracity of the data, as well as its homogeneity, are guaranteed. Information was obtained from 51 patients.

Limitations: Small number of patients who could be contacted with the diagnosis of HTLV-1 with concomitant SARS-CoV-2 infection. There is a possibility of under diagnosis of COVID-19 because the vast majorities of patients in the cohorts are poor and could not afford a test in a timely manner despite having positive direct contact.

Ethical aspects of the study: both the HTLV-1 cohort of the Alexander von Humboldt Institute of Tropical Medicine, as well as the study cohort: "The effect of *Strongyloides Stercoralis* on HTLV-1 disease progression", have the permissions by the Ethics Committee to carry out the interviews and the respective follow-ups. The names of the participants are not included in the database and the analyzes were done using coded information.

Analysis plan: the information collected in the interview was entered into the Microsoft Excel Program and the most important variables were chosen. The data was coded in the Microsoft Excel Program, where the results and tables were obtained. The results were analyzed and will be presented below.

Results

From both aforementioned cohorts, 51 patients with HTLV-1 were identified, who in turn were diagnosed with SARS-CoV-2 (COVID-19) infection. All HTLV-1 diagnoses were made by ELISA and/or Western Blot at the time of enrollment in the cohorts. Regarding the demographic data of the patients (Table 1), the majorities are female (29 patients, 56.85%); males are 22 patients (43.14%).

Of those diagnosed with HTLV-1, 78.43% are asymptomatic, 17.65% have a diagnosis of HTLV-1-associated myelopathy/TSP (HAM/TSP), and 1.96% have a diagnosis of ATLL. Regarding ages, 47.06% of patients with HTLV-1 are between 50 and 64 years old, 35.29% between 30 and 49 years old, 9.80% are over 65 years old and only 7.84% are under 30 years old (Table 1).

Table 1 Demographic data of patients diagnosed with HTLV-1

Patients with diagnosis of HTLV-1 (n=51)		
Asymptomatic HTLV-1	40	78,43%
ATLL	1	1,96%
HAM/TSP	9	17,65%
Others (recurrent uveitis, coinfection with SS)	1	1,96%
Sex (n=51)		
Male	22	43,14%
Female	29	56,86%
Age (n=51)		
>65 years old	5	9,80%
50 - 64 years old	24	47,06%
30 - 49 years old	18	35,29%
< 30 years old	4	7,84%

*SS, strongyloides stercoralis; TSP, tropical spastic paraparesis; ATLL, adult t-cell leukemia/lymphoma

51 patients from the HTLV-1 cohorts were diagnosed with COVID-19 during the pandemic between April 2020 and October 2021; 34 (66.67%) were diagnosed in 2020 and 17 (33.33%) during 2021 (Table 2).

To make the diagnosis of SARS-CoV-2 infection, 76.47% (39 patients) underwent a molecular/PCR, antigenic or serological test; while 23.53% (12 patients) developed symptoms compatible with COVID-19 in a context of family outbreak and positive direct contact, through any of the aforementioned tests, during the outbreak (Table 2).

Table 2 Data related to the clinic, diagnosis and severity of COVID-19 in patients with HTLV-1

Diagnosis of COVID-19 (n=51)		
Molecular test - PCR, antigenic or serological	39	76,47%
Symptoms in the context of a family outbreak with direct contact with a positive test	12	23,53%
Year of COVID-19 diagnosis		
2020	34	66,67%
2021	17	33,33%
Clinical presentation of COVID-19 in patients with HTLV-1 (n=51)		
Asymptomatic cases	5	9,80%
Mild cases	38	74,51%
Moderate cases	8	15,69%
Severe cases	0	0,00%
Oxygen requirement (n=51)		
Yes	3	5,88%
No	48	94,12%
Most frequent symptoms		
General malaise and/or fever	42	82,35%
Headache	41	80,39%
Cough	39	76,47%
Sore throat	18	35,29%
Fatigue	12	23,53%
Anosmia and/or dysgeusia	8	15,69%

Of the patients with HTLV-1 and COVID-19, the vast majority of patients (74.51%, 38 patients) develop a mild form of the disease, 15.69% (8 patients) a moderate form and 9.80% (5 patients) were asymptomatic. No patient developed the severe form of the disease in question, no mortality was reported in the cohort product of COVID-19. It should be noted that no patient required admission to the Intensive Care Unit. Only 3 patients (5.88%) required oxygen therapy at some point in the course of their illness (Table 2).

The most frequent symptoms were general malaise and/or fever; it was present in 82.35% of the patients; headache was also widely reported, with 80.39% of the patients; followed by cough (76.47%) (Table 2).

Discussion

Human T-cell lymphotropic virus type 1 or HTLV-1 is an oncogenic virus that can be transmitted through sexual intercourse, blood transfusions or the use of contaminated syringes and the vertical route (breastfeeding).[12] It affects more than 10 million people in the world and is asymptomatic in almost 95% of cases. The prevalence varies according to the region, being more endemic in areas of southern Japan, South America, the Caribbean, Central and West Africa, to name a few examples.[13,14] Very high seroprevalences can be found in the areas mentioned above, reaching 27% in rural areas of southern Japan.[15]

While most infected people remain asymptomatic, a small percentage may develop disabling and fatal clinical illness. The main diseases are HTLV-1-associated myelopathy/ Tropical spastic paraparesis (HAM/TSP) and adult T-cell leukemia/lymphoma (ATLL).[14,16,17] HTLV-1 carriers and especially those with HAM/TSP or ATLL have an impaired immune system caused by HTLV-1 virus itself, this immunosuppression is different from that caused by HIV.[18-20]

HTLV-1 is classified as a retrovirus, like HIV, which primarily infects CD4+ T cells and integrates into their DNA. HTLV-1 favors T cell proliferation and cytokine production, whereas HIV favors T cell depletion.[18,19,21,22]

On SARS-CoV-2 infection in patients with HIV, there is varied literature, where HIV is considered a risk factor for developing severe disease from COVID-19.[9,10]

What is described is that the clinical manifestations in a patient with HIV who becomes infected with SARS-CoV-2 will be similar to the general population. However, various studies show a higher rate of hospitalization and mortality in patients with HIV compared to the population without HIV.[9,10,23] Among the risk factors associated with developing severe COVID-19 in HIV patients we find the presence of multiple comorbidities (cardiovascular disease, diabetes mellitus, obesity, etc.), advanced age and low CD4 count.[23,24]

As mentioned above, information on COVID-19 in patients with HTLV-1 is scarce and not much has been described. The measures taken in this type of patients have been the general prevention measures for COVID-19 for the general population and for the HIV population.[11] Extrapolating knowledge, it could be inferred that patients who develop complications from HTLV-1 such as HAM/TSP and ATLL would be at higher risk of developing severe disease from COVID-19. The latter because patients with ATLL are usually in constant immunosuppression due to their treatment such as chemotherapy or preparing for a bone marrow transplant; in the case of patients with HAM/TSP, some corticosteroids or immunomodulators are usually given for a long time. In both cases (ATLL or HAM/TSP), we could be facing a state of immunosuppression that would put the patient with HTLV-1 at greater risk of complications due to SARS-CoV-2. The information that is handled on what measures to take against COVID-19 when a person is infected with HTLV-1, are the same recommendations that are given for patients with HIV.[11,25,26]

In our experience, we can see that the course of SARS-CoV-2 in patients infected with HTLV-1 follows similar patterns in percentage and symptoms compared to the general population.[27,28] There are several studies that express the percentages on the spectrum of COVID-19 in the general population. For the worldwide population, 81% usually develop a mild condition, while for our data 74.51% did. 14% usually develop moderate to severe disease worldwide; in our cohort, 15.69% developed moderate disease and no mortality was recorded in our cohort. Worldwide, lethality is less than 2% for the general population.[1,2,29,30] It should be noted that these mentioned percentages vary according to the studies, the patient's age, comorbidities and current vaccination status at the time of acquiring the infection. Additionally, from the data shown in the study, only 2 patients with HTLV-1 were vaccinated at the time of developing the clinical picture of COVID-19, the rest (49 patients) were not vaccinated.

Regarding the most frequent symptoms, their proportion is described according to the type of variant (Delta, Omicron, etc), but in general terms, the patients in our cohort show a clinical picture similar to what is described in the literature as a common presentation of SARS-CoV-2. For example, it is described in American studies that

the most frequent symptoms are headache in approximately 76% and sore throat in approximately 65%;[31] in our cohort, 80.39% reported headache and 35.29% sore throat. To cite another example, in other studies it is mentioned that approximately 40% manifest general malaise or fever;[32] for the HTLV-1 cohort in question, these symptoms represented 82.35%, which is the most common symptom manifested by our patients. This information can vary widely between studies because the various variants predominate different types of symptoms. In Peru, during that time, four main variants were registered such as Wuhan, Delta, Gamma and Lambda. More studies are necessary to establish the percentages exactly for each variant because the literature is varied.

It is known that HTLV-1 generates a certain type of immunosuppression, which would expose this population to a risk of developing severe disease from COVID-19. According to our case report, it follows the same trend as the normal population. Studies are needed that can clarify these concepts and ideas in the future. At the moment, being a retrovirus like HIV, the measures and considerations regarding COVID-19 for patients with HTLV-1 are the same as for a patient with HIV.[11,26,33]

Conclusion and recommendations

Human T-cell lymphotropic virus type 1 or HTLV-1 is an oncogenic retrovirus capable of causing immuno suppression, however, it is different from the immunosuppression generated by HIV. In the case of HTLV-1, a lymphoproliferative immunodeficiency pattern is distinguished that will cause adult T-cell leukemia/lymphoma (ATLL) and an inflammatory immuno dysfunctional pattern, which causes HTLV-1-associated myelopathy/ Tropical spastic paraparesis (HAM/TSP).

Patients with HTLV-1 who become infected with SARS-CoV-2 develop mild or moderate disease in similar proportions to the general population. More studies are needed to elucidate the risk of developing severe SARS-CoV-2 disease in patients infected with HTLV-1 and its associated comorbidities.

Currently, HTLV-1 is still a little researched virus and the recommendations given by most experts on the subject are in line with people living with the human immunodeficiency virus (HIV).

For patients with HTLV-1, regarding COVID-19, complete and timely vaccination, social distancing, hand washing/hygiene measures, use of a mask are recommended. Also, continue their follow-ups in their respective cohort.

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Conflicts of interest

The authors declare no conflict of interest.

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