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Clinical Characteristics and Outcome of Patients with HIV and COVID-19 Coinfection in Qatar: A Retrospective Observational Study

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Abstract

Background: People living with HIV might be at an increased risk of SARS-CoV-2 infection or severe COVID-19 disease, especially those with comorbidity, lower CD4+ count, or high HIV RNA load, however, the impact of HIV on COVID-19 course remains a matter for debate. In this report we aim to study patients with HIV/COVID-19 coinfection seen in Qatar and examine the effects of this coinfection on disease course and attempt to identify factors that may be associated with severe disease.

Methods: Review of the medical records of all HIV infected patients who developed COVID-19 infection during the period between 27th February 2020 and 30th June 2021.

Results: Among the 280 HIV infected patients who were living in Qatar during the study period we identified 30 patients with HIV/COVID-19 coinfection. 14 were Qatari and the rest were from other nationalities. 22 patients were males and 8 were females. 23 were known to be HIV infected before COVID-19 diagnosis and 7 were found to have HIV infection at the time of diagnosis or shortly after. 28 patients developed COVID-19 infection either before receiving SARS-CoV-2 vaccine or in less than 14 days after the second vaccine dose. The disease was mild in most patients and only 10 patients needed hospital admission. The clinical and laboratory finding were similar to those reported by others. Virus shedding was prolonged only in the two patients with very low CD4+ cells and high viral load. The outcome was excellent with no significant morbidity and no mortality.

Conclusion: The clinical manifestations of patients with HIV/COVID-19 coinfection seen in Qatar are similar to that reported by others, however, they were younger with male preponderance and is mostly mild to moderate in severity with a favorable outcome and no mortality. In HIV infected patients, COVID-19 vaccine is highly efficacious in preventing severe disease and hospitalization.

Keywords: SARS-CoV-2; HIV; COVID-19; Patients

Introduction

As of June 30, 2021, more than 182,972,000 confirmed cases of COVID-19 have been reported globally with more than 3,963,000 related deaths. Several host susceptibility factors were recognized early in the pandemic and our understanding of risk factors for serious pathology has evolved rapidly over the last year. We now recognize that the disease disproportionally affects older people, those with obesity and those with underlying health conditions such as diabetes, renal and cardiovascular disease [1,2]. This information has allowed the identification of highly susceptible individuals and driven national and regional guidelines for caring of specific groups. The Centers for Disease Control and Prevention (CDC) have cautioned that, compared with the general population, people living with Human Immunodeficiency Virus Syndrome (HIV) may be at a higher risk for complications and death associated with COVID-19 [3,4]. However, whether HIV-infected individuals also fall into this susceptible group remains a matter for debate.

From most of the studies of HIV/COVID-19 co-infection published thus far, there is still no clear understanding of neither whether those SARS-CoV-2 infections aggravate the course of HIV infection in people living with HIV (PLWH) nor if HIV infections worsen the COVID-19 course. People with HIV might be at an increased risk of SARS-CoV-2 infection or severe COVID-19, especially those with comorbidity, lower CD4+ count, or high HIV RNA load. By contrast, the immunosuppression and low CD4+ count might protect HIV-1-infected individuals from developing the cytokine storm observed in patients with COVID-19 [5-7].

As of June 30, 2021, 222,071 cases of COVID-19 have been reported in Qatar with 590 patients dying from their infection giving a mortality rate of 0.27%. Currently there are 280 people living with HIV (PLWH) in Qatar. In this study we aim to describe the SARS-CoV-2 infection rate, the clinical characteristics of COVID-19 and outcome among adults living with HIV in Qatar and to identify factors that may be associated with severe disease.

Materials and Methods

The study was conducted at Hamad Medical Corporation (HMC), which is composed of eight hospitals with over 2300 beds distributed over the country and are the only governmental hospitals. We retrospectively studied all patients diagnosed with HIV infection in the period between 1984 and June 2021 who were co infected with COVID-19. The study period starts from 27th February 2020 to June 30, 2021. HIV infection was diagnosed using ELISA test as screening test followed by Western Blot for confirmation and COVID-19 infection was confirmed by detecting SARS-CoV-2 RNA in nasopharyngeal/throat swab samples using a virus nucleic acid detection kit according to the manufacturer's protocol. Patients were identified using electronic medical records and our registry at the Compromised Host Clinic at the Communicable Diseases Center. Data collected included all the following when available; age, sex, nationality, date of diagnosis of HIV and date of diagnosis of COVID-19 infection. It also included clinical manifestations of COVID-19 infection, comorbid conditions, COVID-19 vaccination history, need for hospital and or ICU admission, viral load and CD4+ cell count at the time or nearest to the time of

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COVID-19 infection diagnosis, complete blood count, renal and liver functions tests, radiologic studies data, treatment given for COVID-19 infections, antiretroviral treatment regimen and outcome. The study was approved by HMC Research Committee.

Results

During the period between February 27, 2020, when the first case of COVID-19 infection reported in Qatar and June 30, 2021, we identified 30 cases of COVID-19 infection among our 280 HIV infected patients who are living in Qatar. 23 patients were known to have HIV infection before the diagnosis of COVID-19 infection and in 7 patients HIV infection was diagnosed at the time or shortly after COVID-19 diagnosis. The date of HIV diagnosis to the time of COVID-19 infection diagnosis in those known to be HIV infected ranged from 1987 to 2020. COVID-19 vaccine was administered to 18 patients and 12 patients never received it before COVID-19 diagnosis. Of the 18 patients who received the vaccine, 10 developed COVID-19 infection prior to receiving the vaccine, 4 after the first dose and before the second dose, 4 after the second dose (4, 12, 40, 100 days). 14 patients were Qatari, and the rest were from other nationalities. 22 patients were males and 8 were females and the median age was 38 years [IQR 29-50]. The most common comorbidities were hypertension, hyperlipidemia and diabetes mellitus (24%, 17% and 14% respectively). 7 of our patients had BMI above 30. The most common presenting symptoms were fever, cough, body pain and loss of smell (55%, 52%, 17% and 17% respectively), however, 13 were asymptomatic. At the time of diagnosis 18 patients had undetectable HIV viral load while the remaining had a median viral load of 22712 copies/mL [IQR 7114-109,425]. The CD4+ cells at COVID-19 diagnosis were above 200 in 23 patients with median CD4+ cells for all patients of 590 cells/mcL [IQR 326-756]. 10 patients needed hospital admission with two requiring ICU care, however none of them needed mechanical ventilation. The median length of hospital stay was 12 days [IQR 3.5-14]. The outcome in our patient was very good with all patients surviving and discharged home with no significant sequalae. Demographic, clinical features, laboratory, and radiologic finding are detailed in Tables 1 and 2.

Characteristic	No (%)
Age (years)	
Median (IQR)	38(21-50)
Sex	
Male	22 (73%)
Female	8 (27%)
Nationality	
Qatari	14 (46%)
Non-Qatari	16 (54%)
Year of HIV diagnosis	
<1990	1(3%)
1991-2000	2(7%)
2001-2010	4(13%)
2011-2020	20(67%)
2021	3(10%)
Year of COVID-19 diagnosis	
2020	16(53%)
2021	14(47%)
HIV diagnosis in relation to COVID-19 diagnosis	
Before COVID-19 diagnosis	23 (77%
Same time or shortly after COVID-19 diagnosis	7 (23%)
Comorbidities	
Hypertension	7 (23%)
Hyperlipidemia	5 (17%)
Diabetes mellitus	4 (13%)
Coronary artery disease	4(13%)
Chronic kidney disease	1 (3%)
Hepatitis C infection	1 (3%)
Bronchial asthma	1(3%)
Malignancy	1 (3%)
Obesity	1 (3%)
Smoking	1 (3%)
Body mass index (29 patients)	
<19	1(3%)
19-24.9	10(34%)
25- 29.9	11(38%)
>30	7(25%)
COVID-19 vaccination	
No vaccination	12 (40%)
Vaccinated	18 (60%)
COVID-19 infection before vaccine	10 (33%)
COVID-19 infection after first vaccine dose and before second dose	4 (13%)
COVID-19 infection after second of vaccine but less than 14 days	2 (7%)
COVID-19 infection after second of vaccine and more than 14 days	2 (7%)
Antiretroviral therapy before COVID diagnosis (23 patients)	
BIC/FTC/TAF	15 (65%)
DAR/COB/FTC/TAF	3 (13%)
RAL/FTC/TDF	1(4.3%)
RAL/FTC/TAF	1(4.3%)
DAR/COB/DTG/3TC/ZDV	1(4.3%)
DTG/ABA/3TC	1(4.3%)
None	1(4.3%)

Note: IQR: Inter Quartile Range; BIC: Bictegravir; FTC: Emtricitabine; TAF: Tenofovir Alafenamide; DAR: Darunavir; COB: Cobicistat; RAL: Raltegravir; DTG: Dolutegravir; 3TC: Lamivudine; ZDV: Zidovudine; TDF: Tenofovir Disoproxil Fumarate; ABA: Abacavir.

Table 1: Baseline characteristics of HIV/COVID-19 co-infected patients.

Characteristic	Number/IQR
Clinical characteristics	
Fever	10
Cough	15
Shortness of breath	2
Runny nose	4
Chest pain	1
Loss of smell	4
Loss of taste	5
Nausea/vomiting	3
Myalgia	5
Heart rate per minute	92(79-101.5)
Respiratory rate per minute	20 (18-20)
Systolic blood pressure	134.5(125.5-140)
Diastolic blood pressure	83.5(74.5-87.75)
Laboratory data (when available)	
HB	14.5 (12.2-15.2)
WBC	5.8(4.4-6.5)
Lymphocytes	1.35(1.2-2)
Platelets	221(206.5-267)
Creatinine	87(80-107)
AST	27(19-40)
ALT	20(15-35)
CRP	7.2(4-86)
D. Dimer	0.57(0.43-0.9)
Ferritin	445(312-1049)
IL6	40(38- 49)
O2 sat	99(94.5-100)
CD4+ 4 cells	590(325-756)
HIV viral load	48,580(8,185-177,770)
Radiologic finding	
Normal	9
Bilateral infiltrate	4

Unilateral	5
Not done	12
Site of care	
Home	14
Quarantine	6
Hospital admission	10
ICU admission	2
Treatment	
Dexamethasone	2
Remdesivir	1
Favipiravir	2
IL6/IL1 inhibitors	0
Duration of Hospital stay (median, IQR)	9 (5-14)
Note: IQR: Inter Quartile Range; WBC: White Blood Cells; HB: Hemoglobin; AST: Aspartate Aminotransferase; ALT: Alanine Transaminase; CRP: C-Reactive Protein; IL6: Interleukin 6; IL1: Interleukin 1.	

Table 2: Clinical, laboratory findings and outcome of HIV/COVID-19 infected patients.

Discussion

Since December 2019, Acute Respiratory Disease (ARD) due to 2019 novel coronavirus (SARS-CoV-2) now named COVID-19 emerged in Wuhan city and rapidly spread throughout China and the rest of the world. As of June 30, 2021, more than 182,972,000 confirmed cases of COVID-19 have been reported globally with more than 3,963,000 related deaths.

Several host susceptibility factors were recognized early in the pandemic and our understanding of risk factors for serious pathology has evolved rapidly over the past year. We now recognize that the disease disproportionally affects older people, those with obesity and those with underlying health conditions such as diabetes, renal and cardiovascular disease [1,2]. Patients living with HIV may be at an increased risk for COVID-19-related complications due to a higher rate of co-existing conditions than the general population, side effects of Antiretroviral Therapy (ART), and traditional cardiovascular risk factors such as obesity, alcohol, and tobacco use disorder, putting many PLWH at increased risk of severe disease or even death [3,4]. However, limited data are available to describe COVID-19 and its outcomes in PLWH [5-7]. Information about the impact of HIV coinfection and anti-HIV drugs on the clinical characteristics and prognosis of COVID-19 patients remains limited.

In this study we describe our experience and report the clinical, laboratory characteristics and outcome of patients living with HIV infection in Qatar who developed COVID-19 coinfection. The first case of COVID-19 infection in Qatar was reported on 27/2/2020. As of June 30, 2021, 222,071 cases of COVID-19 have been reported in Qatar resulting in a rate of approximately 7.9%. Among those infected with COVID 19, and during the same period, 590 patients died due to their infection resulting in a mortality rate of 0.27%. Among the 280 patients with HIV infection who were living in Qatar during the same period, we could identify 30 patients who developed COVID-19 infection. The rate of COVID-19 infection among our HIV infected patients was 10.7% which is higher than that observed among the general population, however we think this is an overestimate because we believe that the number of people living with HIV in Qatar is more than that reported to the ministry of public health. Fortunately, there was no reported death among our COVID-19/HIV co infected patients resulting in zero mortality rates. 14 (47%) of the patients were Qatari. The median age of patients with coinfection was 38 years (IQR: 29-50) and the majority were males (73%). The age of our patients was much younger than that reported by others which was above 50 years [8,9]. This reflects the younger age of our cohort of HIV infected patients in Qatar. The preponderance of males in our HIV/COVID-19 co infected patients is explained by the fact that almost 85% of the population of Qatar is expatriate workers and most of them are young males. In addition, in our community males tend to go out and move around much more than females therefore are more exposed to infection. It is of interest that 7 (23%) of the patients with coinfection were not known to be HIV infected at the time of COVID-19 diagnosis. This finding emphasizes the importance of testing patients presenting with COVID-19 infection for HIV since we think that HIV infection is under diagnosed in our country. Despite of the fact that our cohort is relatively young, however comorbidities were relatively common (63%). The most common comorbidities were hypertension, hyperlipidemia, and diabetes mellitus. Several studies indicated worse outcome in patient with COVID-19 infection who have these comorbidities [1,2], which were present in some of our patients, however we could not demonstrate such effect in our cohort of HIV/COVID-19 coinfected patients. 22 (73%) patients developed COVID-19 infection before receiving vaccination. 6 (20%) patients developed COVID-19 infection after receiving the COVID-19 vaccine but in less than 14 days after the second dose and only two (7%) developed the infection more than 14 days after receiving the second vaccine dose. These findings emphasize the importance of receiving COVID-19 vaccine to HIV infected patients to protect them from getting infected and emphasize the importance of observing precautions to prevent COVID-19 infection even in those who are vaccinated. Unfortunately, we were unable to test antibody levels against the SARS-CoV-2 neutralizing antibodies to identify those with adequate response to the vaccine and to assess the degree of protection by the vaccine among our cohort. 20 patients were either asymptomatic or having mild COVID-19 symptoms and therefore did not require hospital admission. The clinical features, laboratory and radiologic findings in our cohort were similar to those seen in non-HIV infected patients. It is of interest that 13 (43%) were completely asymptomatic. 10 (33%) patients needed hospital admission and two of them were admitted to intensive care. The main indication for hospital admission was pneumonia in 8 patients and probable Pneumocystis jerovicii pneumonia and disseminated tuberculosis in one patient each. 9 of the patients who needed hospital admission developed infection before receiving COVID-19 vaccine and the 10th patient had the infection after receiving the first dose and before the second dose. Both patients who needed intensive care treatment did not receive the vaccine before COVID-19 diagnosis. The median length of hospital stay in those who needed admission was 9 days (IQR 5-14). Two of our patients stayed in the hospital for 68 and 85 days. The first had disseminated tuberculosis and the second had probable Pneumocystis jirovecii pneumonia and acute myocardial infarction. The median time for negative SARS-CoV-2 PCR test was 13 days (IQR: 10-19). Two patients had prolonged positive SARS-CoV PCR test for 103 and 85 days, respectively. Both patients were newly diagnosed HIV infection with very low CD4+ count (9 and 3 cells/mcL respectively. This finding may suggest that patients with very low CD4+ count may continue to shed viruses for a prolonged period and could be a source for spread of the virus to others.

At the time of diagnosis 18 patients had undetectable HIV viral load while the remaining had a median viral load of 22712 copies/mL [IQR 7114-109,425]. Those patients with undetectable HIV viral load were already receiving antiretroviral medication at time of COVID-19 diagnosis. The CD4+ cells at diagnosis were above 200 in 23 patients with median CD4+ cells for all patients of 590 cells/mcL [IQR 326-756]. One patient received remdesivir, two received dexamethasone and two received Favipiravir therapy. We could not comment on the effect of these medications on outcome because of the small number. Two of

our patients required ICU admission however none of them required vasopressor support, interleukin 6 inhibitors or mechanical ventilation. One of these two patients was newly diagnosed HIV infection with CD4+ cells of 3 cells/mL and a viral load of more than 4 million copies/mcl while the other was a previously diagnosed with HIV infection with undetectable viral load and a CD4+ count more than 1200 cells/mcL at the time of COVID-19 infection diagnosis. The outcome in our patients was very favorable with no significant morbidity and no mortality. The zero mortality in our cohort of HIV/COVID-19 coinfected patients is probably related to the younger age of the patients, the fact that the majority had high CD4+ count and undetectable viral load at the time of COVID-19 diagnosis infection and the low mortality of COVID-19 infection in general in Qatar. The effect of HIV infection on the course and outcome of COVID-19 disease has been studied by some investigators with contradictory results. Some research groups, on the basis of investigating sample sets limited in size, concluded that SARS-CoV-2 infection doses do not aggravate the course of HIV infection in people living with HIV (PLWH) nor does HIV infection worsen the COVID-19 course [10,11]. However, there is a contradictory viewpoint. Wanga [12] recently reported a case of one HIV/COVID-19 infected patient with a low CD4+ T cell count who had a longer COVID-19 course and lower antibody level. Furthermore, it has been found that HIV/SARS CoV-2 co-infection may lead to pneumonia complications oftener than COVID-19 itself [13]. The ability of HIV/SARS-CoV-2 co-infection to cause excessive T cell activation has been observed in small sample sets [14,15]. Besides, it has been found that severe symptomatic manifestations of COVID-19 may lead to a more pronounced T cell response than a mild symptomatic clinical course [16]. Furthermore, controversies still exist regarding the role of some antiretroviral in preventing or treating COVID-19. The first randomized clinical trial with ritonavir-boosted lopinavir showed no benefit over standard care in 199 adults admitted to hospital with severe COVID-19 [17]. In another cohort, eight of 947 individuals taking Nucleoside Reverse Transcriptase Inhibitors (NRTIs) plus Non-Nucleoside Reverse Transfer Inhibitors (NNRTIs) were co-infected with SARS-CoV-2, with a similar rate to the general population in Wuhan, indicating that an NRTI plus NNRTI did not prevent COVID-19 [18]. In Vizcarra and colleagues' cohort [8], there was no difference in previous use of anti-retroviral in individuals with and without COVID-19. Neither nadir CD4+ count, nor the use of specific antiretroviral drugs affected the SARS-CoV-2 infection rate. Our study although of small size however suggests that effect of HIV infection on the course of COVID-19 infection especially in those with high CD4+ count and undetectable HIV viral load is not deleterious and is probably related to age and other associated comorbid conditions.

Conclusion

In conclusion, COVID-19 infection among HIV infected patients in Qatar is relatively common. The presentation is similar to that of non-HIV infected patients and to that reported by others. Our study demonstrated that COVID-19 infection in people living with HIV in Qatar is mostly a mild to moderate disease with few patients having severe disease or COVID-19 related complications with most patients not requiring hospital admission. In HIV infected patients, COVID-19 vaccine is highly efficacious in preventing severe disease and hospitalization.

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