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Research Article

HIV and Covid 19 Coinfection, A Local Perspective: A Retrospective Study from Qatar

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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. 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. We also attempt to compare our finding with that of a previous study conducted in Qatar in view of the emergence of new SARS CoV-2 variants and the widespread use of COVID 19 vaccine. **Method**: Review of the medical records of all HIV infected patients who developed COVID 19 infection during the period between 27th February 2020 and 31 December 2022. **Results**: Among the 329 HIV infected patients who were living in Qatar during the study period we identified 136 patients with HIV/COVID 19 coinfection. 90 were Qatari and the rest were from other nationalities. 117 patients were males and 19 were females with a median age of 34 [IQR 28-59] years. 111 were known to be HIV infected before COVID 19 diagnosis and 25 were found to have HIV infection at the time of COVID 19 diagnosis or shortly after. 50 patients developed COVID 19 infection either before receiving SARS CoV-2 vaccine or in less than 14 days after the first vaccine dose and after a median of 246 days from last vaccine dose in the 86 vaccine recipients. Reinfection was relatively common occurring in about 9% of patients, however occurring after a median of 332 and 267 days from previous infection and last vaccine dose respectively. The disease was mild with hospital admission. There was no disease related mortality. **Conclusion**: The clinical manifestations of patients with HIV/COVID 19 coinfection seen in Qatar were similar to that reported by others, however, they were younger with male preponderance and is mostly mild to moderate in severity. Most infections occurred in the third year of the study (57%) when the Omicron variant was the predominant strain circulating in Qatar. Most infections occurred either in unvaccinated patients, within 14 days after the first dose or after a long period form the last vaccine dose. The outcome was excellent with no disease related mortality.

Keywords: SARS CoV 2; HIV; COVID 19; Qatar; Vaccine

Introduction

On Dec 31, 2019, a pneumonia cluster of 44 patients was reported by Chinese authorities. Since then, SARS-CoV-2, the novel coronavirus that causes COVID-19, has caused a devastating pandemic with over 650,000,000 million cases and over 6.66 million deaths reported globally by the end of the year 2022. The reported case counts underestimate the overall burden of COVID-19, as only a fraction of acute infections is diagnosed and reported. Seroprevalence surveys in the United States and Europe have suggested that after accounting for potential false positives or negatives, the rate of prior exposure to SARS-CoV-2, as reflected by seropositivity, exceeds the incidence of reported cases by approximately 10-fold or more [1]. One study that used multiple data sources, including databases on case counts, COVID-19-related deaths, and seroprevalence, estimated that by November 2021, over 3 billion individuals, or 44 percent of the world's population, had been infected with SARS-CoV-2 at least once [2].

The epidemiology of COVID 19 infection has evolved over time with new virus variants with differing clinical presentation and severity and outcome. The latest of these variants, the Omicron sublineage (BA.1, then BA.2, then BA.4 and BA.5) has been associated with local increases in SARS-CoV-2 infections, suggesting a replication advantage over the prior prevailing variant or sublineage. Omicron (specifically the BA.1 sublineage) has also been associated with a higher secondary attack rate compared with Delta [3].

The introduction of vaccination had also affected the epidemiology of disease protecting many and ameliorating the clinical presentation.

At present, more than 38 million people worldwide are living with HIV, approximately 25 million of those in sub-Saharan Africa. Although 26 million people living with HIV are estimated to be receiving antiretroviral therapy (ART), most of those not receiving ART, and those who are immunosuppressed, live in sub-Saharan Africa [4].

Current evidence indicates that people living with HIV represent around 1·0% (95% CI 0·0–3·0) of total hospitalised COVID-19 cases [5,6], whereas SARS-CoV-2 infection prevalence in people living with HIV is between 0·68–1·8%, similar to the SARS-CoV-2 prevalence (0·6–0·8%) reported in the general population [7,8].

In people living with HIV and with symptoms following SARS-CoV-2, 66·5% had mild symptoms, 21·7% reported severe symptoms, and 11·8% needed critical care [9,10], However, asymptomatic infection rates in people living with HIV are most likely underestimated [7]. The epidemiology of COVID-19 in people living with HIV and the overlap between the two pandemics might be affected in the future by SARS-CoV-2 vaccination, depending on the vaccine coverage, vaccination priorities for people living with HIV, and the responses of this population to immunisation by the range of available vaccines. Despite an increasingly consolidated body of evidence on COVID-19 in the general population, the interaction between SARS-CoV-2 and HIV infection is still unclear and data are, at times, conflicting [7].

Material and Method

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 December 2022 who were coinfected with COVID 19. Since the first case of COVID 19 was diagnosed in Qatar was on 27/02/2020, so the study period was from 27th February 2020 till December 31, 2022. HIV infection was diagnosed using ELISA test as screening test followed by Western Blot and HIV PCR for confirmation while COVID 19 infection was confirmed by positive SARS COV-2 PCR and or a positive FDA approved SARS-CoV rapid antigen test obtained from Nasopharyngeal/Oropharyngeal specimens. 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 HIV diagnosis and date of diagnosis of COVID 19 infection. It also included clinical manifestations of COVID 19 infection, comorbid conditions, COVID 19 vaccination history and the type of COVID 19 vaccine administered, need for hospital and or ICU admission, viral load and CD4+ cell count at the time or nearest to the time of 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 December 31, 2022, we identified 136 cases of COVID 19 infection among our 329 HIV infected patients who were living in Qatar. 90 patients were Qatari, and the rest were from other nationalities. 117 patients were males and 19 were females and the median age was 34 years [IQR 28-59]. The most common comorbidities were obesity (defined as BMI $\geq$ 30 kg/m^2), hyperlipidemia, hypertension, and diabetes mellitus (30%,15.5%,15%,12% respectively). 111(82%) patients were known to have HIV infection before the diagnosis of COVID 19 infection and in the remaining 25(18%) 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 2022. 27 patients were diagnosed to have COVID 19 infection in 2020, 31 in 2021 and 78 in 2022. COVID 19 vaccine was administered to 123 patients and 13 patients never received it. The number of COVID 19 vaccine doses ranged from 1-4 doses, however only 2 patients received 4 doses. Pfizer BioNTech vaccine was the main vaccine used in 108 patients (88%). Of the 123 patients who received the vaccine, 37 patients developed COVID 19 infection prior to receiving the vaccine or in less than 14 days after the first dose, with a median of 246 (IQR 103-299) days from the previous vaccine dose among all vaccine recipients. Only 73(54%) of patients were symptomatic at presentation and the rest 64(46%) were asymptomatic. The most commonly presenting symptoms were fever, cough, runny nose, body pain and sore throat (53%,53%,30%,24.5%,18% respectively). At the time of diagnosis 87 patients had undetectable HIV viral load (defined as HIV RNA $\leq$ 200 copies/mL) while the remaining 49 had a median viral load of 35700 copies/ mL [IQR 647-338,000].

The CD4+ cells at COVID 19 diagnosis were above 200 in 116 patients with median CD4+ cells for all patients of 644 cells/ mcL [IQR 338-907]. 24 patients needed hospital admission with two requiring ICU care, however none of them needed mechanical ventilation. The median length of hospital stay was 9 days [IQR 4-14]. 12 patients had re-infection which occurred at a median of 332 (IQR 281-497) days after the first infection. The outcome in our patient was very good with all patients except one surviving and discharged home with no significant sequalae. The patient who died was an elderly woman with advanced HIV with multiple comorbidities including hypertension, Diabetes mellitus, cerebral toxoplasmosis, CMV viremia, and dementia. She died 5 months after COVID 19 diagnosis due to her other medical problems. Demographic, clinical features, laboratory, and radiologic finding are detailed in table 1 & 2.

Table 1: Baseline characteristics of HIV/COVID 19 coinfected patients.

Characteristic	No (%)
Age (years) Mean (IQR)	 34(28-59)
Sex Male Female	 117 (86%) 19 (14%)
Nationality Qatari Non-Qatari	 90 (66%) 46 (34%)
Year of HIV diagnosis < 1990 1990-1999 2000-2009 2010-2019 2020-2022	 2(2%) 10(7%) 8(6%) 44(32%) 72(53%)
Year of COVID 19 diagnosis 2020 2021 2022	 27(20%) 31(23%) 78(57%)
Vaccine administration Yes No	 123 13
Type of vaccine received Pfizer-BioNTech Moderna	 108 15
Number of Vaccine doses Received. No vaccine ≥ 1 dose ≥ 2 doses ≥ 3 doses ≥ 4 doses	 13 123 120 48 2
HIV diagnosis in relation to COVID 19 diagnosis Before COVID 19 diagnosis Same time or shortly after COVID 19 diagnosis	 111 (82% 25 (18%)

COVID 19 diagnosis in relation to COVID 19 vaccination	
COVID 19 infection before vaccine	13 (9.5%)
COVID 19 infection after vaccine	123 (90.5%)
COVID 19 infection in less than 14 days from first dose	37
COVID 19 infection more 14 days from first dose of vaccine	86
Time to COVID 19 infection after COVID 19 vaccine among all vaccine recipients (median, IQR) days	246(103-299)
Comorbidities	
Hypertension	20 (15%)
Hyperlipidaemia	21(15.5%)
Diabetes mellitus	16 (12%)
Coronary artery disease	9(6.5%)
Chronic kidney disease	9 (6.5%)
Hepatitis C infection	1 (0.5%)
Bronchial asthma	2(1.5%)
Malignancy	7 (5%)
Obesity	40 (30%)
Smoking	6 (4.5%)
Body mass index (136 patients)	
19-24.9	46(34%)
25- 29.9	48(35%)
>30	42(31%)
IQR: inter quartile range.	

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

Characteristic	Number/IQR
Clinical characteristics	
Symptomatic	63 (46%)
Asymptomatic	73 (54%)
Fever	39
Cough	39
Shortness of breath	5
Runny nose	22
Chest pain	4
Loss of smell	6
Loss of taste	5
Nausea/vomiting	7
Myalgia/arthralgia	18
Sore throat	13
Heart rate per minute	90(78-99)
Respiratory rate per minute	19 (18-20)
Systolic blood pressure	124(112.5-140)
Diastolic blood pressure	78(68-87)

Laboratory data (when available)	
HB	14.25 (11.7-15.27)
WBC	5.7(3.8-7.1)
Lymphocytes	1.6(1.1-2.07)
Platelets	211(175-276)
Creatinine	92(70-110)
AST	23(18-40.5)
ALT	22(16-37)
CRP	6.8(3.8-45.9)
D. Dimer	0.61(0.43-0.87)
Ferritin	555(286-945)
IL6	38(1805-44.9)
O2 sat	99(97 -99)
CD4+ 4 cells	644(338-907)
HIV viral load	
Undetectable	87
Detectable	49
Median (IQR)	33500(399-38000)
Radiologic finding	
Not done	100
Done	36
Bilateral infiltrate	8
Unilateral	10
Normal	18
Site of care	
Home/quarantine	112
Hospital admission	24
ICU admission	2
Treatment	
Dexamethasone	3
Remdesivir	4
Favipiravir	3
IL6/IL1 inhibitors	0
Hydroxychloroquine	2
Duration of Hospital stay (median, IQR)	9 (4-14)
Duration of ICU stay (median, IQR)	7.5(5.25-9.75)
Reinfection	11(8%)
Time of reinfection after first infection	332(280-497)
Time of reinfection after last vaccine dose	267(156-458)
Outcome	
Survival	135(99.3%)
Death	1(0.7%)

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.

Discussion

On Dec 31, 2019, a pneumonia cluster of 44 patients was reported by Chinese authorities. Since then, SARS-CoV-2, the novel coronavirus that causes COVID-19, has caused a devastating pandemic with over 650,000,000 million cases and over 6.66 million deaths reported globally by the end of the year 2022. The number of people living with HIV infection approaches more than 38 million with the majority of them in sub-Saharan Africa [4].

Current evidence indicates that people living with HIV represent around 1·0% of total hospitalised COVID-19 cases [5,6], whereas SARS-CoV-2 infection prevalence in people living with HIV is between 0·68–1·8%, similar to the SARS-CoV-2 prevalence (0·6–0·8%) reported in the general population [7,8]. 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 [11,12].

Reporting on the clinical manifestation of COVID 19 infection in people living with HIV, initial series showed no clear evidence for higher COVID-19 infection rates or different disease course. However, these series were limited by small sample sizes. Most studies reported a younger age with good overall immunological status with a high proportion of these patients receiving ART [19,20]. However, larger cohort studies which were published later suggested poorer outcomes for individuals with HIV compared with the smaller series, while other studies did not report these outcomes [21].

Comparing people living with HIV with individuals that are HIV-negative, clinical COVID-19 presentation was no different to typical reports in the general population. In people living with HIV and with symptoms following SARS-CoV-2, 66·5% had mild symptoms, 21·7% reported severe symptoms, and 11·8% needed critical care [9,10], Fever, cough, fatigue, and dyspnoea were consistently the most frequently reported signs and symptoms in most of these series [22].

As of December 31, 2022, 489,428 cases of COVID 19 have been reported in Qatar with 685 patients dying from their infection with a mortality rate of 0.14%. 329 HIV infected patients were living in Qatar during the study period. In a previous similar study from Qatar, although the number of patients was small, it was concluded that the disease was mild in most patients and with only 10 patients needed hospital admission and there was no mortality [23]. In the current study with a much larger cohort of HIV/SARS CoV-2 coinfected patients, we examined the impact of HIV coinfection on the clinical manifestation and outcome of COVID 19 infection in Qatar and the possible risk factors that may be associated with worse outcome. We also examined the effect of the more widespread use of SARS CoV-2 vaccination and the effect of the emerging new virus variants on the clinical course and outcome of the disease. We identified 136 cases of COVID-19 infection among the 329 patients with HIV infection who were living in Qatar during the study period suggesting that 40% of our HIV infected patients were infected with COVID 19 during the study period. This is much higher than the rate observed among the general population in Qatar which was about 17%. This high rate could not be explained totally by increased susceptibility secondary to reduced immunity in our cohort since the CD4+ cells at COVID 19 diagnosis were above 200 cells/mcL in 116(85%) patients with median CD4+ cells for all patients of 644 cells/mcL [IQR 338-907]. A possible contributing factor for this high rate is failure to observe infection prevention precautions among our cohort of patients who were relatively young and socially active. Another probable cause is the lower vaccine uptake in our cohort. Although the vaccine was administered to 123 patients, however of the 123 patients who received the vaccine, 37 patients developed COVID 19 infection prior to receiving the vaccine or within less than 14 days after the first dose, while the other 86 developed the infection after receiving the vaccine with a median of 246 (IQR 103-299) days from the previous vaccine dose, suggesting waning vaccine protection after 3 months of administration. It is of interest that 12 patients developed reinfection with COVID 19, however, these patients had re-infection at a median of 267 (IQR 156-458) days after the last vaccine dose emphasizing the importance of receiving booster vaccine dose within the recommended time according CDC guidance.

Almost 60% of COVID 19 cases occurred during the third year of the study probably reflecting the predominance of the Omicron variant which was the prevalent virus strain in Qatar during this period. This virus strain is known to be highly contagious.

The age of our patients (mean: 34 years, IQR: 28-59) was much younger than that reported by others which was above 50 years [24,25]. The younger age of our cohort of HIV infected patients in Qatar reflects the fact that most of our HIV infected patients were young males who acquired infection through unprotected sex, and this emphasize the importance of education and public awareness of safer sex practices and promotion of condom use. The preponderance of males in our HIV/COVID 19 coinfected patients is explained by the fact that almost 85% of the population of Qatar are males. Despite of the fact that our cohort was relatively young, however comorbidities were relatively common (43%). The most common comorbidities were obesity, hypertension, hyperlipidaemia, and diabetes mellitus. Several studies indicated worse outcome in patient with COVID 19 infection who have

these comorbidities [4,5], which were common in our patients, however we could not demonstrate such an effect in our cohort of HIV/COVID 19 coinfected patients. The disease was mild in the majority of patients. 46% of patients were asymptomatic and the most common symptoms among those who were symptomatic were fever, cough, runny nose and body pains (53%, 53%, 30%, 24.5%) respectively. The majority of patients were managed at home with only 24 (18%) needed hospital admission and only 2 required care in intensive care unit. Even those who needed hospital care did not stay for a long time with a median of 9 [IQR4-14] days. There was no COVID 19 related mortality in our cohort. 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 main indication for hospital admission was pneumonia in 18 patients and probable Pneumocystis jirovecii pneumonia and disseminated tuberculosis in one patient each. Antiviral use to treat COVID 19 infection was uncommon with only 9 patients receiving such treatment, Remdesivir and Favipiravir were the most used agents (4 and 3 respectively). Steroids were used in only three patients. Both of these findings reflect the fact that disease was mild in our cohort and most patients were managed at home. 100 patients were receiving antiretroviral treatment at the time of COVID 19 infection. The other 36 patients were not on treatment either because they were diagnosed to have HIV at the time of COVID 19 diagnosis or were known to be HIV infected however they declined HIV treatment. The most commonly used antiretroviral was Bictegravir/Emtricitabine/Tenofovir alafenamide. At the time of diagnosis, 87 patients had undetectable HIV viral load while the remaining had a median viral load of 33500 copies/mL [IQR 399-338000]. Those patients with undetectable HIV viral load were already receiving antiretroviral medication at the time of COVID 19 diagnosis. When compared with our previous study, there was no significant difference in regard to clinical features, however the percentage of patients requiring inhospital care is less, likely related to the finding that most cases in the current study occurred in the third year of the study when the omicron variant was the predominant strain which is known to cause mild disease compared to the delta strain which was the predominant stain in the previous year.

In conclusion, COVID 19 infection among HIV infected patients in Qatar is common and is more than that seen in the general population. The presentation is similar to that of non-HIV infected patients and to that reported by others. The disease is usually mild with a significant proportion of patients being asymptomatic. Infections were mostly seen either in those who did not receive the vaccine, within 14 days after receiving the first vaccine dose or very late after the last vaccine dose. Re-infection was relatively common and mostly occurring after a long period from the last vaccine dose. Administering SARS CoV-2 vaccine in due time and according to guidelines is essential in combating COVID 19 infection. The outcome is excellent with no disease related mortality.

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