



CASE SERIES

Management Outcome of Coronavirus Disease 2019 and Human Immunodeficiency Virus Co-Infection in Nigeria: A Case Series

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Abstract

Introduction: Studies indicate that people with underlying comorbidities and the elderly are susceptible to increased risk of developing severe disease when infected with SARS-CoV-2. This study aims to describe the clinical presentation and treatment outcome of People Living With Human Immunodeficiency Virus (PLWHIV) who had Coronavirus disease 2019 (COVID-19).

Methodology: We conducted a retrospective study of COVID-19 patients with Human Immunodeficiency Virus (HIV) co-infection admitted at the University of Abuja Teaching Hospital (UATH) isolation and treatment centre from March 2020 to September 2020. Data on age, gender, antiretroviral (ART) regimen, CD4 count, symptoms, underlying comorbidity, temperature, blood pressure, pulse rate, oxygen saturation in room air, chest X-ray, urea, creatinine, white cell count, severity of disease, length of hospital stay and outcome were extracted. We categorized patients based on severity of symptoms as mild, moderate and severe.

Results: A total of 280 patients were admitted with a diagnosis of COVID-19 during the study period, 7 (2.5%) of whom were co-infected with HIV and were on Antiretroviral Therapy (ART). The common symptoms at presentation were fever, cough, difficulty in breathing, loss of smell, poor appetite and rhinorrhea. Four cases (57.1%) had mild disease while 3 (42.9%) had severe disease. The 3 cases that had severe disease also had underlying comorbidities

aside HIV infection. The average length of hospital stay among the 7 cases was 12 days (\pm 8.5 days). All seven patients recovered from COVID-19 infection.

Conclusion: COVID-19 in HIV infected persons has a similar clinical presentation and outcome as in HIV uninfected persons. PLWHIV who are on ART do not seem to have any protection from COVID-19; ART may however prevent severe COVID-19 infection. We recommend ART, COVID-19 vaccination and adherence to public health advisories on physical distancing, use of face masks and hand hygiene for all PLWHIV.

Keywords

COVID-19, Human Immunodeficiency Virus (HIV), Comorbidities, Co-infection, Case series, Nigeria

Abbreviations

ART: Antiretroviral Therapy; BSL3: Biosafety Level 3; FCT: Federal Capital Territory; COVID-19: Coronavirus Disease 2019; HIV: Human Immunodeficiency Virus; PLWHIV: People Living with Human Immunodeficiency Virus; RT-PCR: Real-Time Polymerase Chain Reaction; SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus 2; UATH: University of Abuja Teaching Hospital

Introduction

The novel coronavirus disease 2019 (COVID-19) is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The virus is spread from Person-to-person through close-range contact, mainly via respiratory droplets. Infection might also occur if a person's hands are contaminated by droplets or by touching contaminated surfaces and then they touch their eyes, nose, or mouth. Airborne transmission can also occur; however, the extent to which this occurs under natural conditions and how much this mode of transmission has contributed to the pandemic are controversial [1].

Studies have shown that people with underlying comorbidities such as hypertension, diabetes, obesity, chronic kidney disease, Human Immunodeficiency Virus (HIV), malignancies and the elderly are susceptible to increased risk of developing severe disease when infected with SARS-CoV-2 [2]. HIV infection is associated with abnormal humoral and T-cell-mediated immune responses, resulting in increased susceptibility to infections. This complex disorder of the immune system leads to increased susceptibility of HIV patients to opportunistic and conventional pathogens. With 38 million people living with HIV (PLWHIV) worldwide, there have been concerns for increased risk of severe COVID-19 among PLWHIV. It has been postulated that PLWHIV if infected with COVID-19 would have a severe disease with an increased risk of death [3].

Nigeria is the 2nd largest HIV epidemic country in the world [4]. Currently, 1.9 million people are living with HIV in Nigeria, with a national prevalence of 1.4% among adults aged 15-49 years; hence the need to study COVID-19 and HIV coinfection in the country. This study aims to describe the clinical presentation and treatment outcome of PLWHIV who had COVID-19.

Methodology

Study site

The University of Abuja Teaching Hospital (UATH) is located in Gwagwalada, one of the six local area councils managed by the Federal Capital Territory (FCT) Authority, Abuja, Nigeria. It is a tertiary hospital equipped with 520 beds and a biosafety level 3 (BSL3) laboratory and serves as a referral hospital to the FCT and neighboring states of Kogi, Nassarawa, Niger and Kaduna. Patients were admitted into the isolation and treatment centre after they tested positive to COVID-19. UATH was assigned the responsibility for the treatment of moderate to severe cases of COVID-19 patients in the FCT. The majority of cases with severe disease and other co-morbidities were referred from other isolation and treatment centres in the FCT for specialist care.

Study design and population

We conducted a retrospective study (case series) of COVID-19 patients with HIV co-infection that were ad-

mitted at the UATH isolation and treatment centre from March 2020 to September 2020. Data retrieved from the medical record of patients include age, gender, ART regimen, CD4 count, symptoms, underlying comorbidity, temperature, blood pressure, pulse rate, oxygen saturation in room air, chest X-ray, urea, creatinine, white cell count, severity of disease, length of hospital stay and outcome. The diagnosis of COVID-19 was made by real-time polymerase chain reaction (RT-PCR) using nasopharyngeal and oropharyngeal swabs. We categorized patients based on severity of symptoms; mild, moderate and severe. Patients who had no shortness of breath and had oxygen saturation greater than 90% were considered to have mild disease. Those with mild shortness of breath and oxygen saturation greater than 90% were categorized as having moderate disease while those with severe shortness of breath with oxygen saturation less than 90% or who had any organ failure were considered to have severe disease.

Ethical clearance

Secondary data was used to conduct this study and does not require ethical clearance. Permission for obtaining data and the use of data was given by the hospital management (UATH). The data was however de-identified to provide anonymity.

Results

A total of 280 patients were admitted with a diagnosis of COVID-19 during the study period, 7 (2.5%) of whom were co-infected with HIV. A total of 4 cases (57.1%) presented with mild disease while 3 (42.9%) had severe disease. The average length of hospital stay among the 7 cases was 12 days (\pm 8.5 days).

Case 1

S.U was a 34 year male HIV positive patient who had been on antiretroviral medications for 5 years. At the time of admission, he was on Tenofovir, Lamivudine and Dolutegravir. He tested positive to COVID-19 two weeks after returning from a business trip from London and was admitted at the COVID-19 isolation and treatment ward. The only symptom at presentation was a mild fever; he had no other underlying comorbidity. On examination his temperature was 36.5 °C, pulse rate 82 beats/min, blood pressure was 128/83 mmHg, oxygen saturation on room air was 99%. His baseline Full blood count and Electrolytes, Urea and Creatinine, as well as chest X-Ray were essentially normal; CD4 count was 580 cells/ml. He was treated according to the treatment protocol of the facility at that time with Chloroquine 500 mg 12 hourly on the first day, then 250 mg daily for 5 days; Lopinavir/ritonavir 400 mg 12 hourly for 2 weeks; Azithromycin 500 mg daily for 5 days and Vitamin C 600 mg daily for 2 weeks. He also continued with his ARV's. He tested negative to COVID-19 after 15 days and was discharged in a stable condition.

Case 2

M.B was a 38 year male HIV positive patient who was admitted into the COVID-19 isolation and treatment ward after testing positive to COVID-19. He was on Tenofovir, Lamivudine and Dolutegravir at the time he was infected with COVID-19. He presented with a 5 days history of loss of smell and poor appetite. At presentation, his oxygen saturation was 99% on room air, temperature was 36.6 °C, pulse rate was 76 b/min with a blood pressure of 114/77 mmHg. The baseline laboratory and radiological parameters were essentially normal with CD4 count of 450 cells/ml. He was commenced on Chloroquine 500 mg 12 hourly on the first day, then 250 mg daily for 5 days; Lopinavir/ritonavir 400 mg 12 hourly for 2 weeks; Azithromycin 500 mg daily for 5 days and Vitamin C 600 mg daily for 2 weeks, as well as his routine ARV'S. He tested negative to COVID-19 after 10 days of hospital admission and was discharged home in a stable condition.

Case 3

J.T. was a 46 year female HIV positive patient on HAART (Tenofovir, Lamivudine, Dolutegravir) for 6 years and a known hypertensive. She was brought into the COVID-19 isolation and treatment ward after she tested positive to COVID-19. She had mild fever and headache at presentation. On physical examination, her oxygen saturation was 99% on room air, temperature was 36.8 °C, pulse rate 123 b/min, and blood pressure on admission was 163/103 mmHg. Baseline renal function test, liver function test, complete blood count and chest X-ray were all normal; CD4 count was 600 cells/ml. She was commenced on Chloroquine 500 mg 12 hourly on the first day, then 250 mg daily for 5 days; Lopinavir/ritonavir 400 mg 12 hourly for 2 weeks; Azithromycin 500 mg daily for 5 days and Vitamin C 600 mg daily for 2 weeks. The routine HIV and antihypertensive medications were also continued. She tested negative to COVID-19 on the 8th day and was discharged home in a stable condition.

Case 4

O.G was a 53-year male HIV positive patient with background hypertension who was admitted into the COVID-19 isolation and treatment ward after he tested positive for COVID-19. He presented with a history of fever and cough of one week duration and breathlessness of a day's duration. His ART regimen was Tenofovir, Lamivudine and Dolutegravir. At presentation, the temperature was 36.5 °C, blood pressure was 153/68 mmHg, pulse rate was 112 b/m, and oxygen saturation was 58% on room air. Baseline renal function test, liver function test and complete blood count were essentially normal; chest X-Ray showed ground glass opacities involving the lateral aspect of the left middle and lower lung fields. His CD4 cell count was 320 cells/ml. He was immediately given supplemental oxygen via nasal catheter and the saturation improved to 97%. He was

managed as a case of severe COVID-19 with intravenous dexamethasone 6 mg daily, intravenous ceftriaxone 1 g 12 hourly, Hydroxychloroquine 400 mg 12 hourly on the first day, then subsequently 200 mg 12 hourly for the next 5 days; zinc sulphate 220 mg daily for 5 days; Lopinavir/ritonavir 400 mg 12 hourly for 2 weeks and Vitamin C 600 mg daily for 2 weeks. He also continued his routine HIV medications. His oxygen saturation improved to 98% on room air and he was weaned off oxygen on the 6th day of admission. Repeat COVID-19 test done on the 8th day was negative and patient was discharged home in a stable condition.

Case 5

A.P was a 56 year male HIV patient with background type II diabetes mellitus and chronic kidney disease. Patient was on Abacavir, Lamivudine and Lopinavir/ritonavir for his HIV care. He was admitted into the COVID-19 isolation and treatment ward after he tested positive to COVID-19 and presented with a 3 days history of fever, vomiting, irrational behavior and involuntary movements of the hands and legs. On physical examination, pulse rate was 102 b/min, blood pressure was 152/100 mmHg, temperature was 38.2 °C; oxygen saturation was 97% on room air. The random blood sugar was 2.2 mmol/L (normal range is 3.6-7.1) which was immediately corrected with 20 mls of 50% dextrose in double dilution given intravenously. Urgent renal function test showed a markedly elevated serum creatinine of 1392 µmol/L (normal range is 64-104) and a serum urea of 49.4 mmol/L (normal range is 2.1-7.1). His liver function test was normal and chest X-ray showed cardiomegaly, CD4 count was 330 cells/ml. He was commenced on alternate day hemodialysis in view of the deranged renal function; zinc sulphate 220 mg daily for 5 days; Azithromycin 500 mg daily for 3 days. On the second day of admission he developed hyperglycemia with a random blood glucose of 20 mmol/L and was commenced on soluble insulin 10 international units every 8 hours. The blood sugar subsequently normalized; the renal function improved after five sessions of hemodialysis; serum creatinine dropped from 1392 µmol/L to 592 µmol/L. He tested negative to COVID-19 after 17 days in the isolation center and was discharged home to continue care with the nephrologist and his HIV care physician.

Case 6

W.G was a 50 year male HIV positive for 20 years. He was on Atazanavir/ritonavir, Tenofovir and Lamivudine with HIV viral suppression and a CD4 count of 650 cells/ml. He was admitted to the COVID-19 isolation and treatment ward after he tested positive to COVID-19. The only symptom on admission was rhinorrhea. He had no other underlying comorbidity. On admission the temperature was 36.6 °C, oxygen saturation was 99%, pulse rate was 76 b/min with a blood pressure of 150/100 mmHg. All baseline investigations including chest X-ray were essentially normal. He was commenced on Chlo-

roquine 500 mg 12 hourly on the first day, then 250 mg daily for 5 days; Azithromycin 500 mg daily for 3 days; Zinc sulphate 220 mg daily for 5 days; and Vitamin C 600 mg daily for 2 weeks. In addition, he was given Amlodipine 5 mg for control of the blood pressure. A repeat COVID-19 test on the 13th day of admission was negative and patient was discharged home in a stable condition.

Case 7

G.S was a 60 year male HIV positive patient who had been on ARV's for 8 years. He was on Tenofovir, lamivudine, Dolutegravir and was admitted into the COVID-19 isolation and treatment ward after testing positive to COVID-19. He presented with history of cough with difficulty in breathing. Other comorbidities present were diabetes and hypertension. At presentation, oxygen saturation was 88% on room air, temperature was 36.7 °C. He had a pulse rate of 84 beats/min with a blood

pressure of 147/87 mmHg. The random blood sugar was 18.3 mmol/L. Chest X-ray showed ground glass opacities in both lung fields. Baseline liver function test and electrolytes, urea and creatinine and complete blood count were normal, CD4 count was 420 cells/ml. He was commenced on intravenous Remdesivir (now available at the facility at the time of his admission) 200 mg start dose on the first day, then subsequently 100 mg daily for four days; intravenous insulin 16 IU 8 hourly; intravenous ceftriaxone 1 g 12 hourly; Dexamethasone 6 mg daily for 10 days; Zinc sulphate 220 mg daily for 5 days; subcutaneous Enoxaparin 40 mg daily for 10 days. Supplemental oxygen was commenced at 5 liters/min. He made remarkable improvement and was weaned off oxygen on the 5th day of admission. Serum blood sugar levels normalized after 6 days on soluble insulin. The patient was discharged after 13 days of hospitalization in a stable condition (Table 1).

Table 1: Cases and parameters of COVID-19 and HIV co-infection, March 2020 to September 2020, UATH isolation centre Gwagwalada, Abuja, Nigeria, (n = 7).

Parameters	Cases						
	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7
Age (years)	34	38	46	53	56	50	60
Gender	M	M	F	M	M	M	M
ART Regimen	Tenofovir Lamivudine Dolutegravir	Tenofovir Lamivudine Dolutegravir	Tenofovir Lamivudine Dolutegravir	Tenofovir Lamivudine Dolutegravir	Abacavir Lamivudine Lopinavir/ ritonavir	Tenofovir Lamivudine Atazanavir/ ritonavir	Tenofovir Lamivudine Dolutegravir
CD4 count(cells/ml)	580	450	600	320	330	650	420
Symptoms	fever	Loss of smell, poor appetite	Fever, headache	Fever, cough, breathlessness	Fever, vomiting, irrational behavior	Rhinorrhoea	Fever, cough, breathlessness
Underlying comorbidity	None	None	Hypertension	Hypertension	Diabetes Chronic Kidney disease	None	Diabetes Hypertension
Temperature (°C)	35.5	36.6	36.8	36.5	38.2	36.6	36.7
Blood pressure (mmHg)	128/83	114/77	163/103	153/68	152/100	150/100	147/87
Pulse rate (beats/min)	82	76	123	112	102	76	84
Oxygen saturation in room air (%)	99	99	99	58	97	99	88
Chest X-ray	Normal	Normal	Normal	Ground-glass opacities	Cardiomegaly	Normal	Ground-glass opacities
Urea (Mmol/L)	3.3	2.9	4.6	5.1	49.4	3.0	4.0
Creatinine (Pmol/L)	72	80	62	90	1,391	76	65

White cell count ((cells per 10 ⁶ /L)	5.0	4.2	6.7	8.9	5.3	6.6	9.4
Severity of disease	Mild	Mild	Mild	Severe	Severe	Mild	Severe
Length of hospital stay	15	10	8	8	17	13	13
Outcome	Cured	Cured	Cured	Cured	Cured	Cured	Cured

Discussion

Our study revealed that 2.5% of patients admitted during the study period were co-infected with HIV which is higher than what was obtained in a report from Barcelona where 1% of patients with COVID-19 who required admission in a hospital had HIV [5]. This may be related to the high burden of HIV infection in Nigeria. All the HIV co-infected cases were on antiretroviral medications. The majority of the patients (85.7%) were males. The HIV pandemic has disproportionately affected females more than males particularly in sub-Saharan Africa. In Nigeria, women aged 15-49 years are more than twice as likely to be living with HIV than men (1.9% versus 0.9%) [4]. Since the beginning of the COVID-19 pandemic, reports around the globe have shown that males are more susceptible to COVID-19 than females [6]. This report shows that even though more females are living with HIV in Nigeria, the males living with HIV are more likely to get infected with SARS-CoV-2 than females.

The common symptoms at presentation were fever, cough, difficulty in breathing, loss of smell, poor appetite and rhinorrhea. Reports from Nigeria and indeed other parts of the World have shown that these symptoms also occur commonly in HIV uninfected patients with COVID-19 [7,8]. Mirzaei, et al. showed that the main clinical symptoms of COVID-19 in PLWHIV were cough and fever, and comparable to HIV-negative people [9]. Blanco, et al. reporting from Barcelona also showed that HIV patients have a COVID-19 clinical picture resembling the general population [5].

All the 7 cases were on antiretroviral (ART) medications at the time of admission into the isolation and treatment center and had CD4 cells counts ranging from 320-650 cells/ml. The use of ART has resulted in substantial reductions in morbidity and mortality and increased life expectancy in PLWHIV. According to 2019 UNAIDS report, 65% of PLWHIV in Nigeria are on ART. Earlier studies hypothesized that ART could confer protection against COVID-19 in PLWHIV [10,11]. This hypothesis was based on the fact that agents such as Lopinavir showed antiviral activity against SARS-CoV-2 *in vitro* studies. However, the first randomized clinical trial with Lopinavir boosted with Ritonavir showed no benefit over standard of care in 199 adults admitted to hospital with severe COVID-19 [12]. All 7 cases were on ART

at the time they were infected with COVID-19, showing that the hypothesis that ART confer protection against SARS-CoV-2 may be false. In another cohort of HIV patients in Wuhan, it was shown that ART did not prevent COVID-19 [13]. These studies show that standard ART does not seem to shield PLWHIV from COVID-19.

A total of 4 cases (57.1%) presented with mild disease while 3 (42.9%) had severe disease. The activation of the immune system by SARS-CoV-2, leading to the cytokine storm is responsible for disease severity and worse outcome seen in patients with COVID-19. Mascolo, et al. have noted that HIV related lymphopenia can be a protective feature in preventing severe clinical manifestations of COVID-19 infection [14]. This may explain the mild disease seen in 4 out of the 7 cases. Even though all 7 cases had CD4 counts above 200 cells/ml, the relative lymphopenia seen in HIV infection compared to HIV uninfected persons may explain the mild COVID-19 disease seen. Also the fact that all 7 patients were on ART may explain why most of them had mild disease. All 3 cases that had severe COVID-19 disease also had other comorbidities (hypertension, diabetes, chronic kidney disease) in addition to HIV. HIV patients on ART are now living long and are therefore prone to develop cardiovascular diseases just like the general population. It has previously been shown that people with underlying comorbidities are more likely to have severe disease when infected with COVID-19; particularly those with hypertension and diabetes [2]. One could therefore infer that the 3 cases had severe COVID-19 as a result of the other underlying comorbidities that they had.

Unlike the report of Wang, et al. that showed that co-infection of SARS-CoV-2 and HIV may result in a longer hospital stay [15], the average length of hospital stay among the 7 cases was 12 days; which was comparable to the 11.4 days observed among HIV uninfected COVID-19 patients in our facility. Karmen-Tuohy, et al. reporting from New York City also showed that the average length of hospital stay was similar in both HIV and non-HIV patients hospitalized with COVID-19 [16]. No mortality was recorded among the 7 cases; even the 3 cases with severe disease were eventually discharged home with no complications.

Conclusion

COVID-19 in HIV infected persons who are on ART

has a similar clinical presentation and outcome as in HIV uninfected persons. PLWHIV on ART do not seem to have any protection from having COVID-19; however ART may prevent the development of severe COVID-19 infection. We recommend that all PLWHIV should be on ART, get COVID-19 vaccine and adhere to all the non-pharmacological measures that have been put in place to prevent the spread of COVID-19; such as the use of face masks, regular hand washing and social distancing.

Competing Interests

The authors declare no competing interest.

Authors' Contributions

Vivian Gga Kwaghe: Research idea and plan, data collection, data analysis, manuscript draft; Ayi Vandi Kwaghe: Manuscript editing and production of final draft; Vivian Gga Kwaghe, Zaiyad Garba Habib, Bissallah Ahmed Ekele: Read through the final manuscript and approved it.

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Conflict of Interest

The authors declare that there is no conflict of interest.

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