

HIV and SARS COV-2 Co-infection: A systematic review

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ABSTRACT

Introduction: COVID-19 consequences are more likely to affect patients with co-morbidities. According to the recent research, HIV positive individuals are not at a higher risk for COVID-19 than the general population. This systematic study was done to find out how COVID-19 affected individuals who were HIV-positive.

Aim: The aim of the study was to systemic review the recent research studies reported on the impact of HIV and SARS-COV 2 co-infection.

Materials and Methods: A systematic review was conducted according to PRISMA guidelines. A thorough literature search was done in Web of Science, Medline, Google Scholar, Pubmed, Pubmed Central using key words and headings related to HIV and Covid-19 co-infection.

Results: Hundred articles were identified and after duplicates had been removed. Following screening, fourteen studies with a total of 148 HIV-infected patients were evaluated. It was identified that further information is required to establish the outcome of Covid-19 patients and co-infected patients should be screened for opportunistic infections as they are immuno-compromised.

Conclusion: According to the recent studies and current review it was found that patients with less severe Covid-19 symptoms had normal cd4 count. As of now, well controlled HIV infection is not considered as a risk for Covid-19 co-infection. So, more studies are required in this field to identify why patients with low Cd4 count experiences more severe infections.

Key Words: HIV, SARS COV 2

I. INTRODUCTION:

In the Wuhan city, China, the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS COV-2) was first surfaced and the city experienced Corona Virus Disease (COVID) in December, 2019, which is the most calamitous pandemic in the modern era.^[1] Its considered as an global emergency because of its high rate of mortality and rapid expansion.^[2] The World Health Organization (WHO) designated the novel Corona Virus as COVID 19 (Corona Virus Disease 19).^[3] On March 2020, the World Health Organisation (WHO) declared Covid-19 a pandemic due to the widespread distribution and deaths of thousands people through out the world caused by Covid 19, corona virus disease.^[4] The SARS COV-2, beta coronavirus which belongs to the Coronaviridae family, has genomic size of roughly 29 kb. ^[5] Clinical symptoms can be symptomatic or asymptomatic which is subdivided into presymptomatic or asymptomatic infection, mild illness, moderate illness, severe illness and critical illness. Dry cough and fever considered as the first appeared symptoms in persons infected with SARS COV-2. Individuals with asymptomatic infection can be positive by Antigen test or NAAT (Nucleic Acid Based Amplification Test) with no signs and symptoms. Fever, dry cough, headache, muscle pain, sore throat considered as the mild illness. SpO₂>94% along with LRTI considered as the moderate illness, SpO₂<94 and respiratory breath 30 breaths/min considered as the severe illness, respiratory failure, septic shock and multiple organ failure considered as the critical illness ^[6,7]. In addition to respiratory syndrome, COVID-19 may result in cardiac complications, neurological manifestations such as headache, dizziness, intracranial haemorrhage and stroke ^[8,9,10]. However, there is a growing evidence which demonstrate that diabetes, age and hypertension considered as risk factors which are associated with less favourable

outcomes. ^[11,12] As of now, it remains unclear why HIV reactive patients are at a higher risk than healthy individual. ^[13,14] HIV infection results in a CD4 T cell death, impaired mucosal barrier function and chronic immunosuppression. ^[15] Several inflammatory factors, including gut microbial translocation, cause impaired CD4 T cell regeneration and persistently elevated CD8 T cell counts. ^[16,17] In HIV infected patients, there is a decline in CD4 T cell count, which if left untreated turns to AIDS. ^[18,19] According to WHO, “Acquired Immunodeficiency Syndrome is the most advanced stage of the disease” ^[20]. According to Centers for Disease Control and Prevention (CDC), AIDS defines “when the CD4 cell count falls below 200 cells/mm³ or the presence of AIDS defining illness” ^[21]. There is no information on how HIV affects SARS-CoV-2 infection and whether it has any impact on COVID-19 results. The purpose of this systematic review is to locate the studies which addressed HIV patients who had contracted SARS-COV-2 and reported if co-infection increases the probability of negative outcomes.

II. MATERIALS AND METHODS

Search Strategy: A thorough literature review has been executed in PubMed, PubMed Central, Science direct, web of science, Elsevier, Google Scholar to identify why individuals with HIV have a higher risk of contracting SARS-COV 2 infection and what happens to patients who have both infections since they have impaired immune systems in accordance with PRISMA guidelines.

Eligibility criteria: Studies discussed both HIV and SARS COV-2 infection were included in the study. Studies which discussed other co-infections rather than SARS-COV 2 were excluded from the study.

Data extraction: Two authors independently reviewed each paper and the extracted data. Data was validated by the second author.

Statistical analysis: Due to lack of research data in this topic, a suitable meta analysis could not be carried out.

III. RESULTS

First author and Publication year	Article Title	Location	Study design	Population	Outcome
Sun LJ <i>et al</i> , 2020 ^[22]	A case of HIV and SARS-CoV-2 co-infection in Singapore	Singapore	Case study	SARS COV-2 and HIV co-infected patient. 37 years/Male	Patient came with the complaints of having sore throat, fever (38°C) and headache from last 6 days. He had a travel history (returned from Paris and London 1 day before the onset of symptoms). Background medical history: Chronic HIV and the patient was on ART treatment. CBC count, LFT, RFT was normal. RT-PCR was positive for SARS COV-2. After 14 days of isolation and treatment patient recovered and RTPCR came negative.
Feng Zhu <i>et al</i> , 2020 ^[23]	Co-infection of SARS-CoV-2 and HIV in a patient in Wuhan city, China	Wuhan, China	Case study	SARS COV-2 and HIV co-infected patient. 63 years/Male	Patient represented with fever and dry cough from 2 days. SARS COV-2 pneumonia was confirmed from Chest CT report with multiple ground glass opacities in bilateral lungs. Background

					<p>history: Type 2 Diabetes mellitus. RTPCR was positive for SARS COV 2. Lymphopenia with low lymphocyte count and CD4+ T lymphocyte was 4.75%. Antigen/antibody combination test was positive for HIV and ART treatment started(Lopinavir, Ritonavir) along with Moxifloxacin 400 mg. After 18 days of symptoms RTPCR was done and came negative and the very next day patient discharged.</p>
<p>Kulachan ya <i>et al</i> ,2020 ^[24]</p>	<p>Clinical features and outcome of HIV/SARS-CoV-2 co-infected patients in The Bronx, New York city</p>	<p>New York</p>	<p>Case Series</p>	<p>9 HIV patients co-infected with SARS COV-2.</p>	<p>The median age range of the patients was 31-76. Out of which 7 were males and two were females. A positive RT PCR test confirmed the infection of SARS COV-2. CD4+ T cell count in the most recent patients ranges from 179-1827 mm³. In all patients, HIV viral load was very low to undetectable. Six of the eight patients who were on highly active antiretroviral therapy (HAART) reported drug adherence. In four patients, HAART was discontinued. All patients represented with fever, cough, dyspnea. GIT symptoms were present on one patient. Eight patients (89%) had abnormal chest X-rays (CXR) that were consistent with COVID-19 pneumonia, and the severity of the disease corresponded with these abnormalities. Seven patients died (78%), seven of them from multi organ failures and septic shock, with four patients dying from hypoxemic respiratory failure and three from septic shock.</p>

<p>Yifei Hu <i>et al</i>, 2020 ^[25]</p>	<p>Coinfection With HIV and SARS-CoV-2 in Wuhan, China: A 12-Person Case Series</p>	<p>Wuhan, China</p>	<p>Case series</p>	<p>12 HIV infected patients co-infected with SARS-COV 2</p>	<p>12 HIV infected patients(10 men and 2 women) , age range of 25-66 years represented with the mild COVID-19 symptoms. Out of 12 patients, one patient died at home early when healthcare systems was overburdened. two patients, aged 25 years and 37 years, was admitted in ICU with acute COVID-19, both the patients were on ART treatment. With the exception of deceased person, 6 out of 11 co-infected patients reported experiencing depression despite clinical improvements.</p>
<p>Benkovic <i>S et al</i> , 2020 ^[26]</p>	<p>Four cases: Human immunodeficiency virus and novel coronavirus 2019 Co-infection in patients from Long Island, New York</p>	<p>Long Island, New York</p>	<p>Case series</p>	<p>4 HIV infected patients co-infected with SARS-COV 2</p>	<p>4 HIV infected patients diagnosed with SARS COV-2. All 4 patients were on ART regimen. Presented with the symptoms of fever, fatigue, anosmia, ageusia, cough and diarrhea. Out of 4 patients 3 patients were on home isolation and 1 patient was hospitalized for 2 weeks.</p>

Ridgway JP <i>et al</i> , 2020 [27]	A Case Series of Five People Living with HIV Hospitalized with COVID-19 in Chicago, Illinois.	USA	Case series	5 HIV infected patients co-infected with SARS-COV-2.	5 HIV diagnosed patients came positive for SARS COV-2. The patients were between the age range of 38-53. The patients represented with shortness of breath, fever and cough. Three patients experienced diarrhea. All patients were on ART treatment with a reduced HIV viral load and CD4 cells >200 cells/mm ³ . All five patients were admitted to the hospital, supplemental oxygen was required for two patients and all patients were recovered after a median stay of 3 days.
G Härter <i>et al</i> , 2020 [28]	COVID-19 in people living with human immunodeficiency virus: a case series of 33 patients.	Germany	Case series	33 HIV infected patients co-infected with SARS COV-2.	33 HIV infected patients came positive for SARS COV-2. 48 years was the mean age of the patients. All patients were on ART treatment. Prior to SARS-CoV-2 infection, the median CD4+ T-cell count was 670/mm ³ . In 30 patients, HIV viral load was below 50 copies/mL. Coughing was the predominant symptom, followed by fever, arthralgia/myalgia, headache and sore throat. Out of 33, 14 patients were admitted in hospitalized, out of which 6 patients were on ICU.
Patel RH <i>et al</i> , 2020 [29]	COVID-19 in a patient with HIV infection	Florida	Case study	HIV patient co-infected with SARS COV-2. 58 year/Male	Patient represented with the complaints of having weakness, diarrhea, anorexia for 2 weeks. Patient had a history of chronic bronchitis and hypertension and HIV. Patient was on ART regimen. The CD4 cell count was 497 cells/mm ³ . The patient was hospitalized and RT PCR came positive for SARS COV-2. Fever was lasted for 94 hours with a temperature of 37°C. After 5 days patient was discharged and advised home isolation for 14 days.
SR Nagarakanti <i>et al</i> , 2020 [30]	Clinical outcomes of patients with COVID-19 and HIV coinfection	USA	Case series	23 HIV infected patients co-infected with SARS COV-2.	23 patients diagnosed with HIV admitted to hospital. Those patients also came positive for SARS COV-2. The median age of the patients was 59 years. Out of 23, 3 patients presented with AIDS.

KCS Suryana <i>et al</i> , 2021 ^[31]	Coinfection between SARS-CoV-2 and HIV with a low CD4+ T-cells count	Indonesia	Case report	HIV patient co-infected with SARS COV-2. 32 year/Male	The patient was hospitalized with the symptoms of having dry cough, shortness of breath and fever from 3 days. Bilateral infiltration in the lungs was observed in the Chest X-ray. The patient had a weight loss and fever and based on this counselling done and HIV infection was confirmed. SARS-COV 2 infection was confirmed by the RT PCR assay. ART treatment, antibiotics and vitamins was given to the patient. After more than 14 days of hospitalization the patient was discharged.
Yang <i>et al</i> , 2020 ^[32]	The reflection on an AIDS patient with asymptomatic COVID 19	Wuhan, China	Case report	HIV patient co-infected with SARS COV-2. 29 year/Male	Patient was HIV reactive and on ART treatment. Hospitalized for chemotherapy for kaposi's sarcoma. Both nasopharyngeal swab and throat swab came positive for SARS COV-2 by RT PCR assay. The patient had no symptoms of COVID-19 but quarantined in the hospital and recovered without treatment.
Vizcarra P <i>et al</i> , 2020 ^[33]	Description of COVID-19 in HIV-infected individuals: a single-centre, prospective cohort.	Madrid, Spain	Case series	51 HIV infected individuals co-infected with SARS-COV 2	51 HIV infected individuals co-infected with SARS-COV 2. 6 patients were admitted in ICU. All patients patients were on ART treatment and had mild COVID-19 symptoms.
Zhao <i>et al</i> , 2020 ^[34]	Early virus clearance and delayed antibody response in a case of COVID-19 with a history of co-infection with HIV-1 and HCV.	Shenzhen, China	Case report	HIV and SARS COV-2 co-infected patient. 38 years/male.	Patient hospitalized with the symptoms of fever (37.2 °C). Right lower pneumonia was detected in chest CT. RT PCR came negative 3 consecutive times for SARS COV-2. Later, the patient tested positive for IgM IgG antibodies for SARS COV-2. Patient recovered fully without the need for ventilator or ICU

					hospitalisation. The patient also had a history of HIV-1 and HCV co-infection.
Blanco <i>et al</i> , 2020 [35]	COVID-19 in patients with HIV: clinical case series	Barcelona, Spain	Case series	5 HIV infected patients co-infected with SARS COV-2. Median age < 50.	All the patients had fever, cough, dyspnea and malaise. All were on ART treatment. Out of 5, 2 patients were admitted in ICU. All the 4 patients recovered and one patient was in ICU. One patient had <i>pneumocystis jiroveci</i> infection which was treated by antibiotics.

IV. DISCUSSION

In late 2019's SARS COV-2, belongs to the genus Sarbecovirus the causative agent of COVID-19 first detected in a bunch of pneumonia patients in Wuhan, China [36]. Local hospitals in Wuhan discovered the novel coronavirus, SARS-COV 2. WHO declared Covid-19 as a "Public Health emergency of international concern"[37,38]. **Wang *et al*** included 138 patients in his one month of case series where the mean incubation period ranges from 5 days to 8 days [39]. One of the most important things to consider is how COVID-19 is relate to other infectious disease, most importantly HIV. As of now, there are very minimal proof on the affect of HIV on COVID-19 [40]. **KM Byrd *et al*** included 27 HIV diagnosed patients co-infected with SARS-COV 2 in his study. All patients were on ART treatment and had a HIV viral load of <200 copies/ml. CD4 count of the patients ranges from 87-1441 cells/ μ l. Out of 27, 26 patients had mild common symptoms. 9 patients were admitted to hospital, out of those 3 patients were on nursing home and though clinical trial remdesivir was given to 6 patients. However, 8 patients fully recovered and discharged and 1 patient died [41]. **A Parker *et al*** studied a case report of 41 year old patient who was HIV infected and was on ART from 2016 and low, undetectable HIV viral load from last 6 months. Clinical symptoms includes fever, myalgia, diarrhea. Chest radiograph shows diffuse bilateral ground glass infiltrates with patchy areas. The patient was admitted in ICU as differential diagnosis confirmed COVID-19 pneumonia and presence of SARS-COV 2 was confirmed by PCR from endotracheal aspirate [42]. **S Karmen *et al***, included 21 HIV infected patients co-infected with SARS COV-2 in their over one month of study. All the patients were hospitalized with high CRP values. Despite the fact, along with the clinical course, peak levels in HIV reactive patients are frequently high. Three patients died due to concurrent bacteria pneumonia during hospitalisation [43]. **Vizcarra P *et al***, conducted a prospective cohort study. 51 HIV infected patients (mean age of 53.3 years) co-infected with SARS COV-2 were included in the study. Out of 51, 8 were female and 43 were male. 28 patients were admitted to hospital, out of which 22 non-critical and 6 critical. All patients were on ART and had fever, non productive cough, fatigue and dsypnoea. 23 patients (45%) were managed ambulatorily. 6 patients were admitted in ICU. 44 patients were recovered and 5 were in hospital [33].

V. CONCLUSION

Although the evidence is limited, the present review demonstrates that patients with low or undetectable HIV viral loads have a normal/high CD4 count. Most of the patients who have been on ART for a long time experienced mild to moderate symptoms. In some patients, co-morbidities like Type 2 diabetes mellitus, chronic bronchitis, hypertension causes alteration of the symptoms. The death of some patients is due to multiple organ failure or septic shock. Therefore, the analysis concludes that effectively managed HIV infection does not increase the chance of developing COVID-19 of a more severe nature. However, it is unclear if inadequately managed HIV and AIDS increase the risk of developing COVID-19 of a severe nature. Our findings thus emphasise the need for additional and further research to clarify the effect of HIV infection on COVID-19.

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