

# COVID 19 in PLHIV - An Experience Form Tertiary Care Centre

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## ABSTRACT

**Introduction:** Concerns emerged early in the COVID-19 pandemic that immunosuppressed patients (HIV patients) were at a greater threat of a far more serious SARS-CoV-2 illness due to immunosuppression. However, the decreased probability of cytokine storm development and use of antiretroviral drugs (ART) might decrease the probability of HIV patients acquiring COVID 19 infection. Hence, the purpose of this research was to investigate the prevalence and outcomes of COVID 19 in HIV patients in Haryana, India. **Material and Methods:** This was a descriptive retrospective cross-sectional questionnaire-based, single-centre study, carried out at ART centre of Pt. B. D. Sharma Post Graduate Institute of Medical Sciences (PGIMS), Rohtak, Haryana. Every 4th HIV positive patients registered at ART were contacted for conducting the study. All the hospital records available with the patients were analysed. Patients were asked questions regarding COVID 19 illness and its outcomes. If a patient's history for COVID 19 infection was positive, he/she was contacted physically and the hospital records/ discharge card was analysed. In case of death during COVID 19 infection time, detailed history was collected from the relatives and detailed hospital records regarding cause of death, hospital stay, oxygen therapy, medical and interventional treatment, ICU/dialysis requirement were analysed. **Result and Observation:** Out of 10,007 patients attending the ART clinic, 2228 HIV positive patients were interviewed telephonically out of which only 31 patients (1.39 %) had coronavirus infection out of which only 1 expired (3.22 % %) and 30 (96.77 %) got cured of infection. 213 (9.69 %) of COVID 19 negative HIV positive patients died owing to factors other than COVID 19. **Conclusion:** There was no statistically significant difference in COVID 19 prevalence between HIV patients and the general population of Haryana (p value >0.05). Further studies are required to be carried out in order to establish a definitive opinion towards COVID 19 infection in the HIV population.

**Key Words:** COVID-19, HIV, antiretroviral drugs

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## Introduction

Coronavirus, a highly contagious virus, was first discovered in China's Wuhan province on December 31, 2019. Although SARS-CoV-2 infection usually causes asymptomatic or mild respiratory complaints with self-limiting illness, around fifteen percent of patients suffer serious clinical signs such as acute respiratory syndrome and multisystem failure, necessitating oxygen assistance and ICU hospitalisation [1-3]. COVID 19 was designated a global pandemic by the World Health Organisation on March 11, 2020. As of January 2022, more than 336 million confirmed COVID 19 cases have been documented worldwide, with more than 5.5 million fatalities reported, according to the WHO. More than 38 million confirmed cases with more than 487 thousand fatalities have been recorded in India as of January 2022, with more than 873 thousand total cases reported in Haryana, India's northern state, with more than 10,000 deaths [4-6]. The presence of pre-existing comorbidities such as hypertension, diabetes, chronic renal disease and cardiovascular disease, have been linked to severe disease presentation [7-9]. Sex, age and BMI are all linked to COVID-19 illness progression and intensity, according to clinical findings and

COVID-19 cohort investigations [7-10].

AIDS (Acquired Immunodeficiency Virus) is a spectrum of conditions caused by the Human immunodeficiency virus (HIV) characterised by destruction of the immune system. It is a major health problem worldwide and has always been quite a hardship especially for developing and underdeveloped countries, which accounts for more than 80 % of global HIV infection. According to the WHO, 37.7 million people were living with HIV at the end of 2020, with 680,000 HIV-related fatalities documented in 2020 [11]. In India, NACO (National AIDS Control Organisation) reported 2.3 million persons living with HIV (PLHIV) in 2019, with 69 thousand fatalities recorded in the same year [12].

The current COVID-19 epidemic has worsened the plight of HIV-positive patients throughout the globe. HIV individuals were not able to get refills of prescribed antiretroviral treatment (ART) because of a lack of medical services, quarantine procedures, and worries of exposure to COVID 19 [13-16]. Many nations have recently reported difficulties in HIV treatment and care as a result of the COVID-19 epidemic [9]. Beyond individuals infected with COVID-19, this disturbance may enhance morbidity and death

among PLHIV (People Living with HIV) [17,18].

Concerns emerged early in the COVID-19 pandemic that immunosuppressed patients (HIV patients) were at a greater threat of a far more serious SARS-CoV-2 illness, based on facts of other respiratory viral infections suggesting a link between immunosuppression and increased rates of pneumonia, superinfection, and death [17,18]. Moreover, the use of Antiretroviral drugs (ART) and decreased immunity which can decrease the probability of cytokine storm development might decrease the probability of HIV patients acquiring COVID 19 infection. Nevertheless, it's unclear whether weakened immune defences enhance the probability of COVID 19 infection or worsen illness development. Unfortunately, there is little information on the management and prognosis of SARS-CoV-2 infection in PLHIV. As a result, the purpose of this research was to investigate the prevalence and outcomes of COVID 19 in HIV patients in Haryana, India.

## Material and Methods

This was a descriptive retrospective cross-sectional questionnaire-based, single-centre study, carried out at ART centre of Pt. B. D.Sharma Post Graduate Institute of Medical Sciences (PGIMS), Rohtak, Haryana. All these patients were contacted telephonically and physically keeping COVID protocol. The patients were picked up by systematic sampling i.e. every 4th HIV positive patient registered at the centre was included in the study. Patients with psychiatric issues and patients who refused to provide medical records were excluded from the study. Detailed clinical history including viral load and CD4 count was obtained from the patient's records. All the hospital records available with the patients were analysed. Patients were asked questions regarding COVID 19 illness and its outcomes. If a patient's history for COVID 19 infection was positive, he/she was contacted physically and the hospital records/ discharge card was analysed. In case of death during COVID 19 infection time, detailed history was collected from the relatives and detailed hospital records regarding cause of death, hospital stay, oxygen therapy, medical and interventional treatment, ICU/dialysis requirement were analysed.

## Study Tool

A semi structured, pre-tested and pre-validated interview schedule was used to obtain information from the patients for the study. The interview schedule included demographic profile of the patient which included their name, sex, age and address. Information regarding their CD4 count, comorbidities and current medication was also included in the questionnaire. Later part of the questionnaire included the patient's COVID 19 infection status, during the last one and half years, which included questions regarding hospitalisation, oxygen requirement, home isolation, dialysis and steroid requirement. COVID 19 infection was categorised as mild, moderate and severe. As per COVID 19 treatment guidelines, individuals with signs and symptoms (cough, fever, sore throat, malaise, headache, nausea, vomiting, diarrhoea, loss of smell and taste) but no dyspnoea, shortness of breath, or abnormal chest abnormalities were considered mild infections [19]. Moderate infection was considered of individuals with clinical or radiological evidence suggesting lower respiratory disease with oxygen saturation (SpO<sub>2</sub>) > 94% on room air at sea level. Severe infection was considered in individuals having SpO<sub>2</sub> < 94% on room air at sea level, respiratory frequency > 30 breaths/min, or lung infiltrates > 50%.

## Ethical Consideration

As it was a retrospective study no consent or intervention was required. However, consent was taken from the patient's relatives in case of death of the patient. Data collected for the study was kept confidential and only the principal investigator and project supervisor were having access to data. Ethical clearance was obtained before the start of the study from the institutional Biomedical Research Ethics Committee (BREC), Pt. B. D. Sharma PGIMS, UHS, Rohtak and Haryana state AIDS control society.

## Sample population and size

Assuming a prevalence rate of 50% of COVID 19 in aids patients and absolute error of 5%

Sample size thus calculated using formula: -

$$N = (1.96)^2 \frac{pq}{L^2}$$

P= prevalence of COVID 19

Q= 100-p

L= Absolute error (taken 5%)

The minimum sample size from the above calculation came out to be 384

## Result

Out of 10,007 patients attending the ART clinic, every 4th patient was included in the study. 279 out of 2,500 patients did not answer the phones or were excluded from the study as per exclusion criterion. A total of 2228 patients of HIV were interviewed telephonically out of which only 31 patients (1.39 %) had serologically positive coronavirus infection. On pursuing the records and detailed interview, out of the 31 patients who suffered from COVID 19; only 1 expired (3.22 % of COVID positive patients) owing to the symptoms while 30 (96.77 % of COVID positive patients) got cured of infection. Out of the remaining HIV patients who did not suffer from COVID 19, 213 (9.69 % of non-infected individuals) died owing to factors not related to COVID 19 as shown in figure 1.

From all 2500 patients 5 CD4 categories were formed according to which 82 patients had CD4 count less than 50 cells/mm<sup>3</sup>, 351 had CD4 between 50 and 200 cells/mm<sup>3</sup>, 489 had CD4 count between 200 and 350 cells/mm<sup>3</sup>, 530 had CD4 count between 350 and 500 cells/mm<sup>3</sup> while 776 had CD4 count of more than 500 cells/mm<sup>3</sup>.

As depicted in figure 2, among 31 corona positive patients 19(61.29%) patients had CD4 count of more than 500 cells/mm<sup>3</sup>, 4(12.90%) patients had CD4 count between 350 and 500 cells/mm<sup>3</sup>, 4(12.90%) patients had CD4 count between 200 and 350 cells/mm<sup>3</sup>, 3(9.67%) patients had CD4 count between 50 and 200 cells/mm<sup>3</sup> while only 1(3.22%) patient had CD4 count of less than 50 cells/mm<sup>3</sup>. Among 31 COVID positive patients, 23(74.19%) were classed with mild form, 3(9.67%) as intermediate while 5 (16.12%) individuals experienced a severe type of COVID 19 infection.

Age and sex were equally distributed and no significant correlation was found for COVID 19 infection in HIV patients. No patient who experienced mild COVID was hospitalised while individuals suffering from moderate and severe COVID 19 infection were hospitalised as listed in table 2. Hospitalisation ranged from 9-25 days with the average hospital stay of 16.33 days of patients suffering from moderate category COVID 19 while the hospitalisation ranged from 3-14 days with average hospitalisation being 7.8 days of patients suffering from severe form of COVID 19

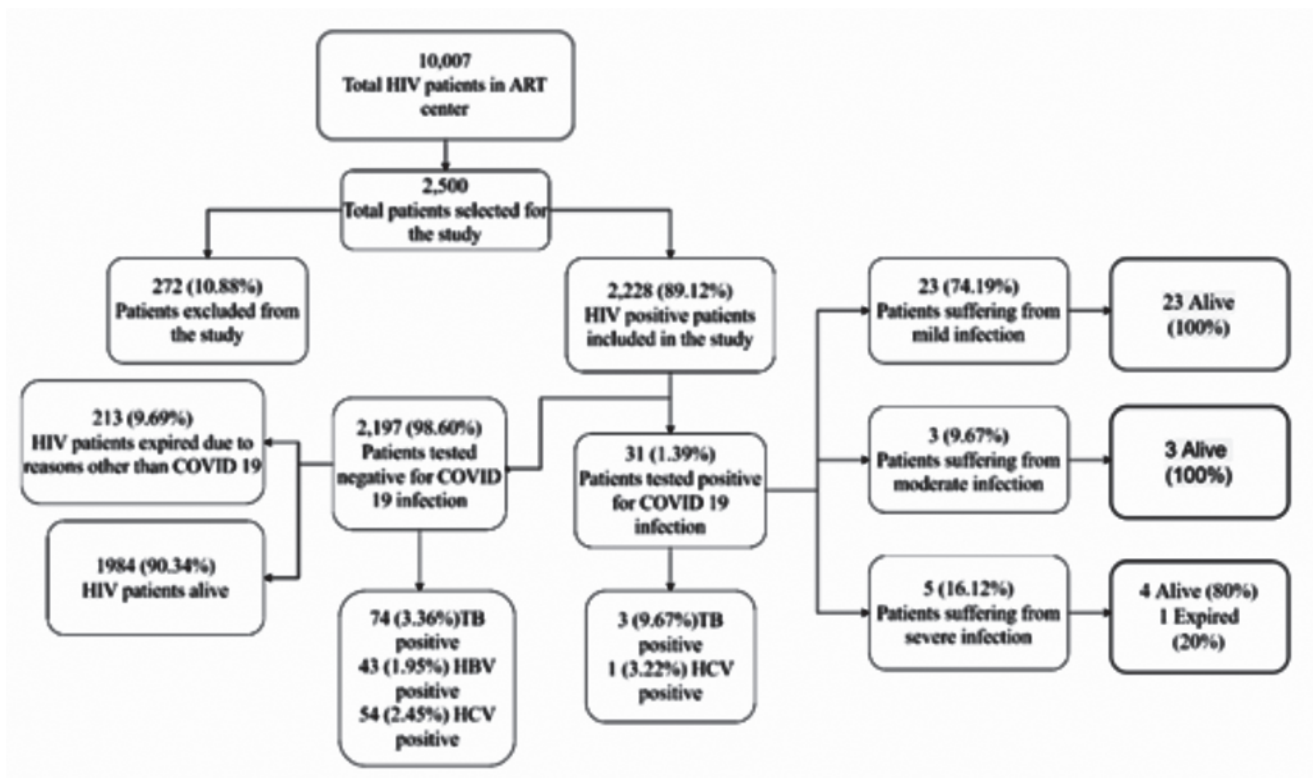


Fig. 1: Flowchart representing the results of the study

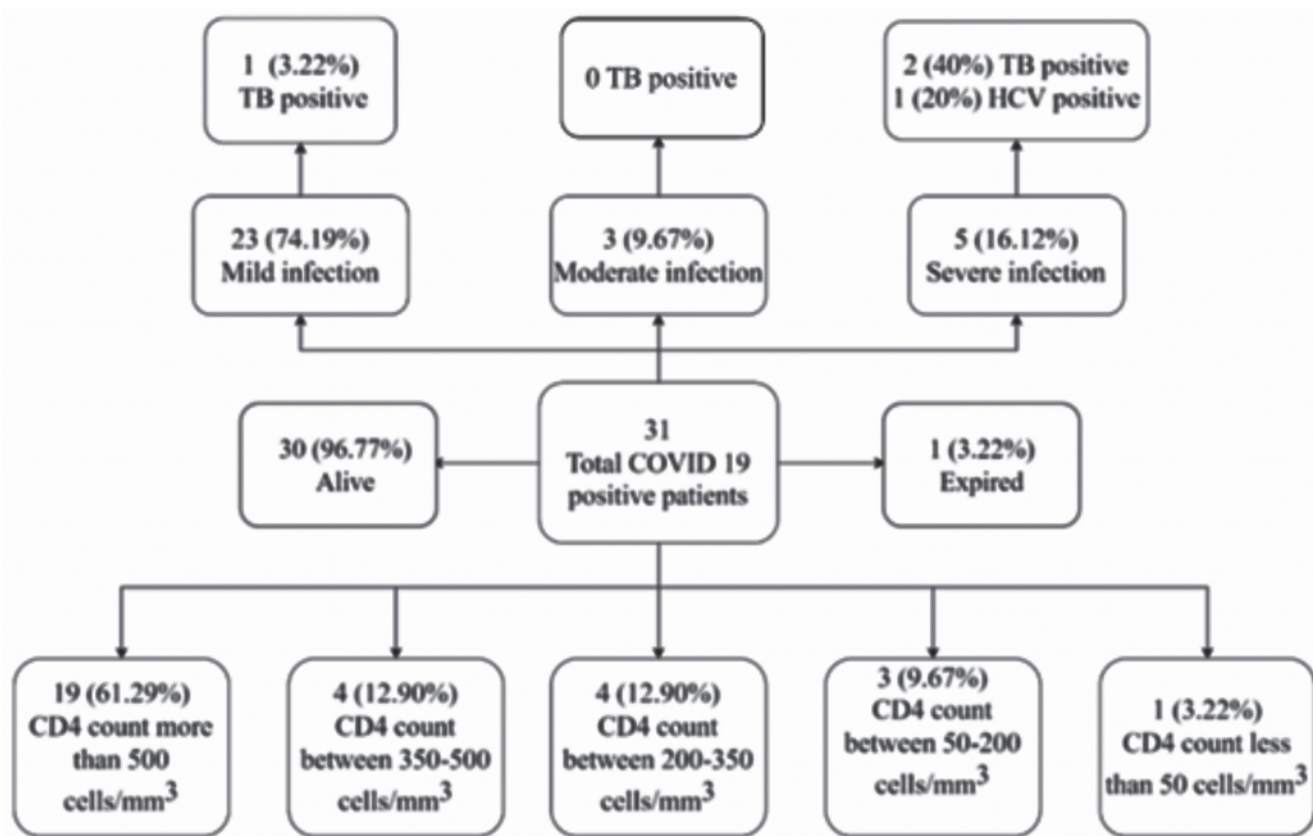


Figure 2: Flowchart representing characteristics of patients suffering from COVID 19 and HIV coinfection

**Table 1: Difference between characteristics of COVID 19 positive patients and COVID 19 negative patients**

	Covid 19 +ve patients	Covid 19 -ve patients
Total Number	31 (1.39%)	2197 (98.60%)
Mean Age (in years)	49.44	42.42
Total Males	18 (58.06%)	1326 (60.35%)
Total Females	13 (41.93%)	859 (39.09%)
Total Transgenders	0	12 (0.54%)
Total Expired	1 (3.22%)	213 (9.695%)
TB Positive	3 (9.67%)	74 (3.36%)
HBV Positive	0	43 (1.95%)
HCV Positive	1 (3.22%)	54 (2.45%)
Mean CD4 count ( in cells/mm <sup>3</sup> )	465	526

**Table 2: Features of mild, moderate, severe infection patients suffering from COVID 19 and HIV coinfection**

	Mild Infection	Moderate Infection	Severe Infection
Total Number	23 (74.19%)	3 (9.67%)	5 (16.12%)
Total Males	14 (60.86%)	1 (33.33%)	3 (60%)
Total Females	9 (39.13%)	2 (66.66%)	2 (40%)
Average Age (in years)	41.56	52.14	54.63
Average CD4 count (in cells/mm <sup>3</sup> )	495.34	437.16	340.16
Total Expired	0	0	1 (20%)
TB Positive	1 (3.22%)	0	2 (40%)
HBV Positive	0	0	0
HCV Positive	0	0	1 (20%)
Diabetes	7 (30.43%)	1 (33.33%)	1 (20%)
Hospitalization Required	0	3 (100%)	5 (100%)
Steroid Administered	0	3 (100%)	5 (100%)
Required Dialysis Therapy	0	0	5 (100%)
Required Invasive Ventilation	0	0	5 (100%)

**Table 3: Prevalence and Mortality of COVID 19 patients. [4,5,51]**

	India	Haryana	HIV COVID 19 study group	p value
Cases of COVID 19	37.8 million	864 thousand	31	>0.05
Prevalence rate of COVID 19	2.73%	3.40%	1.39%	>0.05
Mortality among COVID 19 patients	1.28%	1.15%	3.22%	>0.05

infection. Patients suffering from mild form of COVID 19 infection were kept under home isolation which ranged from 4-15 days with average being 9.61 days. Of the total COVID positive individuals, 14(45.16%) patients additionally suffered from other comorbidities which included 3(9.67%) having TB, 1(3.22%) having HCV infection and 9(29.03%) having diabetes. 20 % patients suffering from severe infection died owing to the infection while no deaths were recorded in patients suffering from moderate and mild infections. All patients suffering from moderate and severe infections received steroids for treatment. All patients suffering from severe infection underwent dialysis therapy and invasive ventilation because of multiorgan failure including acute kidney injury.

In the patient who died owing to COVID 19 infection, the CD4 count was severely low of 43 cells/mm<sup>3</sup> but did not suffer from any other comorbidities. The patient was diagnosed with COVID 19

and reported shortness of breath which later amplified to an extent to place the patient on invasive ventilation who later had renal failure which led to dialysis therapy and expired shortly following hospitalisation.

By the starting of January 2022, COVID 19 cases totalled 8.64 lakhs (864 thousand patients) in Haryana, with more than 10 thousand deaths reported, resulting in a prevalence rate of 3.40%. According to our research, there were 31 cases of COVID 19 in HIV patients, one of which expired, resulting in a prevalence rate of 1.39% as shown in table 3. In the study conducted there was no statistical significance (p value >0.05) found in prevalence of COVID 19 between patients suffering from HIV and the general population of Haryana [4,5]. No statistical significance was observed in deaths of PLHIV patients suffering from COVID 19 and death among the general population of Haryana suffering from

COVID 19 infection.

## Discussion

This study was carried out to explore the influence of a new coronavirus epidemic on PLHIV, to better comprehend their requirements for novel coronavirus prevention and HIV protection services, to offer a foundation for the government's and society's quick reply, and to support enhance healthcare service capabilities and support techniques in urgent circumstances, as well as to offer long-term recommendations for operating processes.

SARS-CoV-2 targets upper respiratory epithelium, and virus generated by affected cells goes down the lower airway, where it affects alveolar and bronchial epithelium, as well as macrophages in alveoli [20]. The epithelial cells infected by the virus suffer cell death and antigen presentation cells (APC) such as macrophages and dendritic cells (DCs) phagocytize these cells as a result of innate immunity. T lymphocytes are presented with viral antigens by the APCs migrating to regional lymph nodes [21]. CD4+ T lymphocytes stimulate B lymphocytes to produce virus-specific antibodies, while CD8+ T - lymphocytes destroy virally contaminated cells directly [21]. HIV can infect macrophages, astrocytes, CD4 positive cells (such as T helper cells) and dendritic cells [22]. HIV pathogenesis is characterised by direct viral cytopathic consequences along with indirect impacts such as host innate immune reaction to viral genome generated throughout abortive infection as well as microbial/endotoxin migration from leaky intestines, prolonged immune stimulation, immune dysfunction, and CD4 T lymphocytes homeostasis malfunction [23-25].

HIV is an immunological dysfunction as well as chronic inflammatory illness which transcends past immunosuppression [26-28]. Hyperinflammation and hypercoagulability have both been linked to COVID 19 [29]. It's possible that the immunological dysfunction caused by HIV might reduce the hyperinflammatory sequence that leads to COVID 19 infection consequences [30]. In addition, the reduction in CD4+ T lymphocytes was prevalent in SARS-CoV-2 patients, according to lymphocyte research studies, and was particularly visible in severe patients [31,32]. When combined with poor CD4 levels in individuals with late HIV illness, SARS-CoV-2's lymphopenia might postpone COVID 19 elimination and hasten progression of the disease.

Antiretroviral therapy (ART) has been found to influence the pathogenesis of HIV COVID coinfection. Tenofovir disoproxil fumarate (TDF) was lately successfully found to interact with COVID 19 RNA polymerase with high binding affinities, equivalent to remdesivir. As a result, TDF has indeed been proposed as prospective COVID-19 therapies [33]. In a recent investigation conducted by Amo et al., the prevalence of identified COVID-19 infections in HIV-infected people receiving a TDF/emtricitabine based combination was decreased than in those receiving alternative strategies [34]. Inflammatory cytokines like IL-8 and IL-10 were shown to be suppressed by tenofovir disoproxil fumarate.

A second perspective concerning the inadequate representation of significant COVID-19 in PLWH comes through a distinct demographic population, people with cancer, who are similarly anticipated to be susceptible. Most of such people are given immunosuppressive drugs on a long-term basis. Provided that numerous innate immunologic factors and proinflammatory cytokines appear to perform a prevailing function in boosting drastic COVID-19 infection, immune suppression associated with cancer chemotherapy, as well as the prolonged immune dysfunction

that accompanies HIV infestation even after efficacious ART, could repress CoV-2 pathological changes as well [35-37].

Low CD4+ levels in HIV positive patients might potentially lead to improved prognosis when coinfecting with COVID 19 because cytokine storm development is less likely [38, 39, 40]. Furthermore, research of the 2015 Middle East respiratory syndrome (MERS-CoV) and 2003 SARS-CoV outbreaks revealed that HIV positive individuals exhibited a decreased likelihood of infection or aggressive disease development. This could perhaps be due to ART suppressed coronavirus proliferation, however patients' immunosuppressive states necessitated a prolonged recuperation period over HIV negative people [38].

Our research results were similar to the study conducted by Guo et al. in China, which shows COVID19 infection being found in 8 of 1178 HIV positive individuals (6 by nasopharyngeal swab and 2 by chest ct). This accounted for 0.68 % of the HIV - infected patients polled, a tiny but not statistically significant increase above the proportion of those tested with COVID19 in Wuhan (0.5 %). 6 patients healed completely following a short sickness, 1 had a serious infection but recovered, and 1 patient died. ART was used to keep all of the patient's HIV under control. Although neither trial was managed or matched for HIV negative individuals, the death rates in Wuhan seem to be comparable to the general population [41].

Up till April 30th, 2020, Vizcarra et al. in Madrid saw fifty one out of 2,873 HIV positive patients who were either laboratory or clinically verified having COVID-19 infection. 35 of the 51 HIV-positive individuals tested positive for COVID-19 in the lab. In the HIV positive group, this culminated in a 1.8 % incidence rate as well as 1.2 % laboratory test validated incidence rate. At the corresponding time period, the general population of Madrid recorded 269,417 instances for COVID-19, with 61,577 occurrences being verified by lab tests. This was responsible for 4.02 % of total incidence and 0.92 % of laboratory-confirmed infections in the overall population. In comparison to HIV positive people coinfecting with COVID-19, the general population (4.02 %) seemed to have a greater total COVID-19 incidence (1.8 %). Perhaps if lab testing confirmed infections are examined, the infection rate is nearly the same, with 0.92 % of the general population affected relative to 1.2 % of HIV-positive people [42].

There was no significant difference in COVID19 results between the general population and PLHIV, according to KarmenTuohy et al. [43]. There were no differences in comorbidities or demographics between twenty-one individuals with COVID 19 and HIV coinfection and forty-two HIV negative patients with COVID 19. 20 of the 21 HIV patients had normal CD4 counts and were suppressed from the virus. These patients do not represent AIDS sufferers in any way. There was a discrepancy between the indications of COVID19 in people with HIV and the indications of COVID19 as specified by the WHO in one case report [44].

On day eight of their complaints with COVID19, Haddad et al. observed seizure and encephalopathy in a patient with managed HIV. This was not seen in other investigations, and the patient recovered completely [45]. No patient in our study suffered from encephalopathy during the infection.

Blanco et al. investigated 5 individuals in Barcelona; they found 4 patients with controlled HIV, out of which 3 were healed from COVID19, one did not require therapy and recovered effectively, and 1 experienced severe COVID19 infection and needed assisted breathing in intensive care. This patient had hypothyroidism and was forty-nine years old. Until they were hospitalised, all of the

patients were on HIV medication. Similarly, in our study no therapy was required for mild COVID 19 cases while patients suffering from severe infection required invasive ventilation and dialysis therapy[46].

In a retrospective case study in Germany, Härter et al. looked at the results of thirty-three individuals who were coinfecting with COVID 19 and HIV. 90 % of the group recovered completely, with seventy-six % reporting just minor symptoms, and a recorded death rate of nine % [47]. The death, hospitalisation, and critical case rate were all greater than in the control group. Because the research primarily focused at symptomatic individuals, this is almost certainly an exaggeration. 1 of the 3 patients who died was eighty years old, had a CD4 count of 69/mm<sup>3</sup>, and had various comorbidities such as type 2 diabetes, hypertension, and the participants in the research were on average forty-eight years old, and ninety % (thirty) of the patients were men, hence this study does not reflect females or senior population with HIV. The technique did not compensate for confounding variables. In our study 4 out of 31 patients (12.90 %) died due to COVID 19 infection.

COVID-19 and SARS have shown no major symptoms in AIDS patients in a couple of case studies [48,49]. Due to the lack of controls and perhaps no big data, the European AIDS Clinical Society issued a preliminary statement stating that “there is insufficient indication for a greater COVID-19 infection incidence or a distinct illness course in persons with HIV than in those without HIV” [50].

According to our study, there was no statistical significance between COVID 19 prevalence in the general population and COVID 19 prevalence in PLHIV. Further research is needed to discover why decreased immunity attributed to AIDS infection does not result in an increase in COVID 19 prevalence. We believe that the use of antiretrovirals in HIV treatment, decreased likelihood of cytokine storm development along with immunosuppression which might decrease the infectivity of COVID 19 are linked to a reduction in the occurrence of COVID 19 in HIV patients receiving ART. The fear of acquiring opportunistic infections in such a population might have led to a decreased exposure to COVID 19 infection.

## Limitations

There are few limitations in our study which includes there being a few patients who did not test for COVID 19 infection but did exhibit some of the symptoms linked to the virus. Such cases are included as negative outcomes. Few patients with severely low CD4 count might have an underlying COVID 19 infection which might be superimposed by other opportunistic infections. Some patients might not have mentioned their past infection history due to societal conventions which might result in bias.

## Conclusion

There was no statistically significant difference in COVID 19 prevalence between HIV patients and the general population of Haryana (p value >0.05). There have not been many studies regarding prevalence of COVID 19 in PLHIV which makes this study essential for prevention as well as treatment purpose to decrease their suffering and increase their prognosis during COVID 19. Further studies are required to be carried out in order to establish a definitive opinion towards COVID 19 infection in the HIV population.

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<b>Conflict of Interest:</b>	All authors declare no COI
<b>Ethics:</b>	There is no ethical violation as it is based on voluntary anonymous interviews
<b>Funding:</b>	No external funding
<b>Guarantor:</b>	Dr. Deepak Jain will act as guarantor of this article on behalf of all co-authors.

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