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Characteristics and outcomes of COVID-19 among people living with HIV at Eka Kotebe General Hospital, Addis Ababa, Ethiopia

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Abstract

Introduction: Evidence on the interplay between HIV and COVID-19 is not entirely consistent.

Methods: A retrospective cohort study was conducted on the medical records of patients who had a positive RT-PCR for COVID-19 and were admitted to Eka Kotebe General Hospital between March 2020 and October 2021.

Results: A total of 427 patients, including 108 people living with HIV/AIDS (PLWH) and 319 people without HIV/AIDS, were included in the study. The median age of PLWH and people without HIV was 49.5 years (interquartile range 40-59 years) and 48 years (interquartile range 32-65 years), respectively. Of these patients, 258 (60.4%) were male and 169 (39.6%) were female. There were significant differences between PLWH and people without HIV in terms of age, tuberculosis, pregnancy, chronic liver disease, complications, shock, white blood cell count, and end outcome (alive or dead). There was no association between HIV status and the need for oxygen, intensive care unit admission, or disease severity. After adjusting for other variables, mortality was significantly higher among PLWH (adjusted odds ratio 2.25, 95% confidence interval 1.11–5.56; P = 0.023).

Conclusions: PLWH with COVID-19 had a higher rate of in-hospital mortality than people without HIV, although no association was found between HIV status and the requirement for intensive care unit admission, mechanical ventilation, oxygen support, or the severity of the disease at the time of admission.

1. Introduction

Worldwide, 537 591 764 COVID-19 cases and 6 319 395 COVID-19-related deaths had been confirmed as of June 21, 2022. At this time, Ethiopia had reported 482 032 COVID-19 cases and 7518 deaths. (WHO Coronavirus (COVID-19), 2020)

Health warnings and preventive measures for people at a higher risk of severe disease and death due to COVID-19 have been issued by the World Health Organization (WHO) and the US Centers for Disease Control and Prevention (CDC). Chronic illness co-morbidities, particularly multimorbidity, appear to be driving COVID-19 mortality. Asthma, chronic lung disease, diabetes, severe cardiovascular problems, chronic renal disease, obesity, chronic liver disease, and immunocompromising conditions, such as HIV, are all reasons that mandate taking extra measures. HIV infection causes aberrant humoral and T-cell-mediated immunological responses, increasing vulnerability to various opportunistic diseases. People living with HIV (PLWH) with a low CD4 cell count, severe illness, a high viral load, or who are not on antiretroviral medication are advised to be cautious. (Ayunbuomwan et al., 2021, Elezkurtaj et al., 2021, Gacche et al., 2021, Kumar et al., 2021, Mylona et al., 2021, Thiabaud et al., 2021)

Do PLWH with COVID-19 have worse outcomes than the general population? There are two opposing possibilities to consider. The first is that immunosuppression may render PLWH more vulnerable to infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the causative agent of COVID-19. However, lymphopenia may guard against the severity of the condition. (Guo et al., 2020) Prior studies have shown that HIV infection is associated with a continuously increased inflammatory state, which will worsen outcomes when paired with the cytokine storm found in severe COVID-19. (Huang et al., 2021, Tesoriero et al., 2020)

However, no large-scale observational studies have been conducted to assess symptoms, disease severity, complications, and the proportion of mortality in patients co-infected with HIV and SARS-CoV-2. The lat-
est evidence consists primarily of case reports and case series, with no reports from Ethiopia thus far. Therefore, the aim of this study was to compare the adverse outcomes of COVID-19 between PLWH and people without HIV/AIDS, and to explore factors that determine the outcomes.

2. Materials and methods

2.1. Study setting and period

The study was conducted in Eka Kotebe General Hospital, Addis Ababa, Ethiopia. This hospital was one of the first COVID-19 treatment centers in the country. It has been designated as a COVID-19 treatment facility since March 2020, when the first case of COVID-19 was discovered in Ethiopia. During the first 6 months of the epidemic, all COVID-19 patients were hospitalized, regardless of disease severity. Later, the practice switched to admitting only individuals with severe illness and major comorbidities.

2.2. Study design

This was a retrospective cohort study that assessed the effect of HIV status on the severity of COVID-19 outcomes.

2.3. Source population

The source population for the study comprised the medical records of all patients with a positive reverse transcriptase polymerase chain reaction (RT-PCR) test result for COVID-19, who were admitted to the COVID-19 treatment facility of Eka Kotebe General Hospital between March 2020 and October 2021.

2.4. Study population

Patients who were RT-PCR-positive for COVID-19, who were admitted to Eka Kotebe General Hospital, were included in the study. SARS-CoV-2 RT-PCR-positive COVID-19 patients with HIV/AIDS were considered exposed, while those without HIV/AIDS were considered non-exposed.

2.5. Sample size determination

The study employed OpenEpi version 2.3 statistical software to determine the sample size for the two patient populations. The assumption was that the proportion of adverse outcomes, i.e. a severe form of COVID-19, among patients without HIV at Eka Kotebe General Hospital would be 3.5%; the severe form is considered a rare disease among non-HIV patients. Regarding PLWH, it was expected that adverse outcomes would increase three-fold. (Rbaskaran et al., 2021) At the 95% confidence level, with 80% power, and a one-to-three ratio of PLWH and people without HIV, it was determined that a minimum of 107 PLWH and 320 people without HIV having COVID-19 were required for the study. The required sample size was increased by 5% to allow for incomplete and missing variable values; as a result, the aim was to include 112 PLWH and 336 HIV-negative people with COVID-19 in the study.

2.6. Sampling procedure

All PLWH admitted to the hospital with COVID-19 between March 2020 and October 2021 were included in the study as the exposed group. For every included PLWH, three patients without HIV admitted subsequently were included as the unexposed group.

2.7. Study variables

The dependent variable was death, while the independent variables included sociodemographic characteristics (age and sex), symptoms (cough, fatigue, dyspnea, fever, arthralgia, headache, anosmia, and sore throat), HIV status, underlying medical conditions (diabetes mellitus, hypertension/cardiovascular disease, chronic pulmonary disease, chronic renal disease, liver disease, tuberculosis (TB), asthma, pregnancy, malignancy, current smoking), patient laboratory tests on admission (white blood cell (WBC) count, absolute lymphocyte count, absolute neutrophil count, neutrophil-to-lymphocyte ratio, platelet count, alanine aminotransferase, urea, and creatinine), and complications (acute respiratory distress syndrome (ARDS), shock, and acute kidney injury) and outcomes (oxygen support, mechanical ventilation, intensive care unit (ICU) admission, severity, and death).

2.8. Operational definitions

COVID-19 cases were patients who had at least one positive RT-PCR test result for SARS-CoV-2. PLWH were all previously and newly diagnosed HIV patients, irrespective of their antiretroviral therapy (ART) status. Severe COVID-19 cases were defined as all patients with SARS-CoV-2 pneumonia and an oxygen saturation level <90%. Critical COVID-19 cases were all of those patients who required critical care level organ support (mechanical ventilation, vasopressors, dialysis). Non-severe COVID-19 cases were all asymptomatic and mild/moderate cases. Severe COVID-19 cases were all severe and critical cases. ARDS was defined using the modified Berlin criteria.

2.9. Data collection procedures and quality assurance

The study collected data on clinical manifestations, demographic characteristics, known co-morbidities, laboratory values, complications, and outcomes of the study patients, using a case reporting format adapted from the WHO case report form. (World Health Organization 2020) Individual patient records were entered into Open Data Kit (ODK). The questionnaire was created using standard questions to address the objectives, based on the literature reviewed, including information on HIV status, ART history, and CD4 count. The questionnaire was pre-tested on 20 patients who were not included in the study. Three physician residents gathered the data after receiving 2 days of training in record abstracting, questionnaire content, and ODK-collect as a data collecting instrument. The primary investigator supervised the data collection. Supervisors also regularly ensured that the data collecting procedure was comprehensive and consistent. The study use of ODK-collect, which is configured to keep questions complete and consistent, and immediately input into a computer server, assured the data quality.

2.10. Analysis plan

The data were exported from ODK, examined for completeness and duplication, and then cleaned before being analyzed. IBM SPSS Statistics version 26 (IBM Corp., Armonk, NY, USA) was used for the statistical analysis. The characteristics of the patients were summarized using percentages for categorical variables and the median and interquartile range (IQR) for continuous variables. In the comparison of groups, continuous variables were compared using the independent t-test, while categorical variables were compared by Chi-square test or Fisher’s exact test. Binary logistic regression was used to identify factors related to inhospital mortality. Variables with a P-value <0.25 in the univariate analysis were included to identify potential significant factors for the final models (Hosmer and Lemeshow test P = 0.6). The odds ratios (OR) with 95% confidence intervals (CI) were calculated, and a P-value <0.05 was considered statistically significant.
Table 1
Comparison of demographic characteristics and symptoms between people with and without HIV/AIDS

| Characteristics | HIV/AIDS status With, n = 108 | Without, n = 319 | Chi square | P-value |
|-----------------|-------------------------------|------------------|------------|---------|
| Age (years), median (IQR) | 49.5 (40–59) | 48 (32–65) | 31.5 | <0.001 |
| 18–39 | 22 (20.4) | 116 (36.4) | 0.0 | 0.865 |
| 40–59 | 62 (57.4) | 88 (27.6) | 0.0 | 0.865 |
| ≥60 | 24 (22.2) | 115 (36.1) | 0.0 | 0.865 |
| Sex, n (%) | | | | |
| Male | 66 (61.1) | 192 (60.2) | 0.0 | 0.865 |
| Female | 42 (38.9) | 127 (39.8) | 0.0 | 0.865 |
| Symptoms, n (%) | | | | |
| Cough | 68 (63.0) | 208 (65.2) | 0.0 | 0.865 |
| Fatigue | 60 (55.6) | 164 (51.4) | 0.0 | 0.865 |
| Dyspnea | 51 (47.2) | 144 (45.1) | 0.0 | 0.865 |
| Fever | 51 (47.2) | 124 (38.9) | 0.0 | 0.865 |
| Arthralgia | 27 (25.0) | 82 (25.7) | 0.0 | 0.865 |
| Headache | 23 (21.3) | 69 (21.6) | 0.0 | 0.865 |
| Anosmia | 15 (13.9) | 33 (10.3) | 0.0 | 0.865 |
| Sore throat | 7 (6.5) | 20 (6.3) | 0.0 | 0.865 |

IQR, interquartile range.
* Significant difference, P < 0.05.

3. Results

Overall, a total of 108 exposed (PLWH) and 319 non-exposed (without HIV/AIDS) COVID-19 patients were included in this unmatched prospective cohort study. Of the PLWH, 87 (80.6%) were on ART; the median duration of illness was 8.5 years and the median CD4 count was 233 cells/μl (IQR 2–14, cells/μl). Among all of the study patients, 258 (60.4%) were male and 169 (39.6%) were female.

A higher proportion of PLWH were in the age group 40–59 years when compared to those without HIV (57.4% vs 27.6%; P < 0.001). However, there was no significant difference in median age between the groups. Cough (n = 276, 64.4%), fatigue (n = 224, 52.5%), and dyspnea (n = 195, 45.7%) were the most common symptoms. There was no difference between the groups with regards to the presenting symptoms (Table 1).

The most common co-morbidities were hypertension/cardiovascular disease (n = 113, 26.5%) and diabetes mellitus (n = 104, 24.4%). TB and chronic liver disease were more prevalent among PLWH than among people without HIV/AIDS (TB: 17.6% vs 1.9%, P = 0.001; chronic liver disease: 4.6% vs 0.3%, P = 0.005). Complications were substantially greater in the PLWH (P = 0.029). In particular, shock was more common in PLWH (21.3% vs 7.8%; P < 0.001). There was no statistically significant difference between the groups for ICU admission, mechanical ventilation, oxygen support, or severity of illness at admission (P > 0.05). PLWH patients had more in-hospital mortality than those without HIV. Thirty PLWH (27.8%) and 47 people without HIV (14.7%) died (P = 0.002) (Table 2).

Laboratory findings showed that a higher percentage of PLWH with COVID-19 presented with a WBC count <4×10⁹/l when compared to people without HIV (24.8% vs 7.7%; P < 0.001) (Table 3).

CD4 count data were available for only a limited number of PLWH (n = 63, 58.3%). In this group, a CD4 count of <200 cells/μl was significantly associated with severe COVID (P = 0.001) and death (P = 0.049) on bivariate analysis (Table 4).

On univariate analysis, HIV/AIDS, age, cough, fatigue, dyspnea, hypertension/cardiovascular disease, diabetes, TB, malignancy, and chronic liver disease were all shown to be significantly associated with in-hospital death (Table 5).

Variables included as possible confounders, including HIV/AIDS, age, dyspnea, diabetes, TB, malignancy, and chronic liver disease, remained significant predictors of death in the multivariable logistic regression (Table 5). The odds of death were 2.2 times higher among PLWH than among people without HIV/AIDS (adjusted OR (AOR) 2.25, 95% CI 1.11–5.56; P = 0.023). Patients aged ≥60 years had a threefold higher risk of death than those under 40 years (AOR 3.03, 95% CI 1.12–8.14; P = 0.028). Patients who reported dyspnea symptoms were approximately four times more likely to die than those who did not (AOR 3.93, 95% CI 1.97–7.83; P < 0.001). Patients with diabetes, TB, malignancy, and chronic liver disease were 3.3, 7.8, 5.4, and 11.7 times more likely to die than those without the condition.

4. Discussion

This study, including data from 108 PLWH and 319 people without HIV, represents the first retrospective cohort study from Ethiopia comparing the adverse outcomes of COVID-19 between people living with and without HIV/AIDS, and exploring the effect of HIV status on COVID-19 outcomes. Age, TB, pregnancy, chronic liver disease, complications, shock, WBC count, and end outcome (alive or dead) differed significantly between the PLWH and those without HIV. There was no significant difference between PLWH and people without HIV in the presenting symptoms. Furthermore, there was no association between HIV status and the requirement for oxygen, ICU admission, or the severity of the condition, but mortality was considerably greater among HIV-positive patients after controlling for other factors.

Co-infection with HIV was found to be associated with a statistically significant increased risk of in-hospital mortality in persons with COVID-19 after adjusting for other possible predicting variables. This finding is consistent with those of previous investigations (Bhoskaran et al., 2021, Danwang et al., 2022, Geretti et al., 2021) and a meta-analysis done by Ssentongo et al. (Ssentongo et al., 2021). The analysis of 22 studies performed in North America, Africa, Asia, and Europe showed an overall pooled relative risk of COVID-19 mortality associated with HIV of 1.78 (95% CI 1.21–2.60). This finding implies a nearly 80% excess risk of death among PLWH when compared to individuals without HIV/AIDS. (Ssentongo et al., 2021) In contrast, a population-level matched retrospective cohort analysis from New York and another retrospective cohort study performed in South Africa, which included 108 PLWH and 276 people without HIV who had COVID-19, found that hospitalized patients with and without HIV died at comparable rates. (Tesoriero et al., 2020, Ventura et al., 2021) Similarly, the present study finding contrasts with those of meta-analyses of different studies, which showed that HIV co-infection was not associated with a statistically significant increase in in-hospital mortality. (Danwang et al., 2022).
In addition, the multivariable regression analysis in the present study showed that age, dyspnea, diabetes mellitus, TB, malignancy, and chronic liver disease were associated with an increased risk of in-hospital mortality, which is similar to the findings of a meta-analysis of other studies. (Sentongo et al., 2021)

The current study also showed significant differences between PLWH and people without HIV in terms of age, TB, pregnancy, chronic liver disease, complications, shock, and WBC count.

A higher proportion of PLWH were in the age group 40–59 years when compared to those without HIV (57% vs 28%). However, there was no significant difference in median age between the groups, which is consistent with other studies from South Africa (Venturas et al., 2021) and the United Kingdom, (Geretti et al., 2021). However, this is in contrast to a New York cohort study that revealed no significant variation in age. (Sigel et al., 2020) The present investigation also showed no significant difference in presenting symptoms between PLWH and those without HIV. This is comparable to the results of another retrospective matched cohort study conducted in Madrid, Spain. (Díez et al., 2021) On the other hand, other large-scale studies discovered a substantial difference in fever, myalgia, headache, runny nose, cough, sore throat, and chest pain presenting symptoms. (Geretti et al., 2021, D’Souza et al., 2020)

This study did not reveal significant differences in underlying medical conditions between PLWH and people without HIV, except for TB, chronic liver disease, and pregnancy. In South Africa, the greater prevalence of TB in PLWH has been documented, (Venturas et al., 2021) consistent with the present study findings. In addition, the results revealed that PLWH had a greater frequency of chronic liver disease than their HIV-uninfected counterparts, which is consistent with research by Sigel et al. (Sigel et al., 2020).
This appears to be the first reported study to assess the outcomes of COVID-19 in HIV patients in Ethiopia. However, there are some limitations to the study. First, due to its retrospective nature and lack of registry, some clinical data such as the HIV viral load and ART regimen type were missing. These factors might have affected the outcomes of the PLWH. Second, this was a single-center study with a convenience sampling method, which may not accurately reflect the situation across the country. Lastly, this study had an unmatched cohort design and confounders were not well accounted for.

In conclusion, HIV patients with COVID-19 were found to have a significantly higher risk of in-hospital mortality when compared to patients without HIV. However, no association was found between HIV status and the need for ICU admission, mechanical ventilation, or oxygen support, or the severity of the disease at the time of admission.

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Ethical approval

The Institutional Review Board of Eka Kotebe General Hospital provided ethical approval (Eka/150/5/88). The study employed an anonymized patient code, and patient anonymity was maintained during the study and subsequently.

Conflict of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Table 4
Comparison of CD4 count according to disease severity and outcome

| Characteristics | End outcome | Chi-square | P-value |
|-----------------|-------------|------------|---------|
| CD4 (cells/μl) (n = 63) | | | |
| <200 | Recovered | 3.84 | 0.049* |
| ≥200 | Died | | |
| Characteristics | Severity at admission | Chi-square | P-value |
| CD4 (cells/μl) (n = 63) | | | |
| <200 | Non-severe | 11.6 | 0.001* |
| ≥200 | Severe | | |

* Significant difference, P < 0.05.

Like previous studies from New York and South Africa, (Tesoriero et al., 2020, Venturas et al., 2021) this study found no significant association between HIV status and ICU admission (P = 0.100) or oxygen needs. While there was no statistically significant difference in ICU admission needs, a greater proportion of PLWH with COVID-19 required ICU admission when compared to those without HIV (24% PLWH and 17% non-HIV patients). This finding is consistent with those of the systematic review and meta-analysis by Ssentongo et al. (Venturas et al., 2021) and a cohort study performed in New York. (Karmen-Tuohy et al., 2020) There was no statistically significant difference between the two groups in terms of ICU admission.

The study findings also showed that PLWH were more likely than those without HIV to experience complications and shock (P = 0.029 and P < 0.001, respectively).

Regarding laboratory findings, it was found that a higher proportion of COVID-19 patients with HIV/AIDS presented with a WBC count <4 × 10^3/L when compared to those without HIV/AIDS (25% vs 8%). This is comparable to the results of a prospective observational study from the UK, (Geretti et al., 2021) which reported that PLWH were more likely to have a decreased WBC count. This might be related to the underlying immunosuppression.

Table 5
Factors affecting in-hospital mortality

| Characteristics | COR (95% CI) | P-value | AOR (95% CI) | P-value |
|-----------------|-------------|---------|-------------|---------|
| HIV | 2.226 (1.320–3.754) | 0.003 | 2.257 (1.117–4.562) | 0.023* |
| Age (years) | | | | |
| 18–39 | 1 | | | |
| 40–59 | 2.684 (1.243–5.796) | 0.012 | 1.420 (0.527–3.829) | 0.488 |
| ≥60 | 5.555 (2.556–11.220) | <0.001 | 3.032 (1.129–8.141) | 0.028* |
| Sex | | | | |
| Male | 1.103 (0.664–1.834) | 0.704 | | |
| Female | 1 | | | |
| Cough | 3.568 (1.859–6.849) | <0.001 | 1.600 (0.690–3.710) | 0.273 |
| Fatigue | 2.312 (1.366–3.911) | 0.002 | 1.169 (0.601–2.275) | 0.645 |
| Dyspnea | 4.764 (2.709–8.315) | <0.001 | 3.931 (1.972–7.837) | <0.001* |
| Fever | 1.333 (0.811–2.189) | 0.256 | | |
| Arthralgia | 0.725 (0.298–1.302) | 0.293 | | |
| Headache | 0.697 (0.365–1.330) | 0.274 | | |
| Anemia | 0.981 (0.133–1.094) | 0.073 | 0.497 (0.153–1.611) | 0.244 |
| Sore throat | 0.966 (0.354–2.636) | 0.946 | | |
| HTN/cardiovascular disease | 2.712 (1.621–4.539) | <0.001 | 1.509 (0.763–2.983) | 0.237 |
| Diabetes mellitus | 3.394 (2.017–5.709) | <0.001 | 3.329 (1.680–6.598) | 0.001* |
| TB | 6.848 (2.974–15.772) | <0.001 | 7.847 (2.682–22.956) | <0.001* |
| Pregnancy | 0.187 (0.025–1.407) | 0.103 | 0.881 (0.995–8.160) | 0.911 |
| Asthma | 0.492 (0.112–2.165) | 0.348 | | |
| Malignancy | 4.097 (1.628–10.221) | 0.003 | 5.411 (1.638–17.877) | 0.006* |
| Chronic kidney disease | 2.631 (0.856–8.083) | 0.091 | 2.236 (5.44–9.191) | 0.264 |
| Chronic lung disease | 0.645 (0.078–5.318) | 0.683 | | |
| Chronic liver disease | 24.236 (2.790–210.269) | 0.004 | 11.747 (1.172–117.775) | 0.036* |
| Current smoking | 1.138 (0.125–10.327) | 0.980 | | |

AOR, adjusted odds ratio; CI, confidence interval; COR, crude odds ratio; HTN, hypertension; TB, tuberculosis.

* Factors associated with a statistically significant increased risk of in-hospital mortality.
