Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
Comparison of outcomes in HIV-positive and HIV-negative patients with COVID-19

Jacqui Ventura, Jarrod Zamparini, Erica Shaddock, Sarah Stacey, Lyle Murray, Guy A Richards, Ismail Kalla, Adam Mahomed, Farzahna Mohamed, Mervyn Mer, Innocent Maposa

A Department of Internal Medicine, Charlotte Maxeke Johannesburg Academic Hospital, and Faculty of Health Sciences, University of the Witwatersrand, 7 York Road, Parktown, Johannesburg 2193, South Africa

B Health Science Research Office and Division of Epidemiology and Biostatistics, School of Public Health, Faculty of Health Sciences, and University of the Witwatersrand, 7 York Road, Parktown, Johannesburg 2193, South Africa

A R T I C L E   I N F O

Article history:
Accepted 20 May 2021
Available online 26 May 2021

Key Words:
HIV
COVID-19
Mortality
South Africa

S U M M A R Y

Background: South Africa has the highest prevalence of HIV in the world and to date has recorded the highest number of cases of COVID-19 in Africa. There is uncertainty as to what the significance of this dual infection is, and whether people living with HIV (PLWH) have worse outcomes compared to HIV-negative patients with COVID-19. This study compared the outcomes of COVID-19 in a group of HIV-positive and HIV-negative patients admitted to a tertiary referral centre in Johannesburg, South Africa.

Methods: Data was collected on all adult patients with known HIV status and COVID-19, confirmed by reverse-transcriptase polymerase chain reaction (RT-PCR), admitted to the medical wards and intensive care unit (ICU) between 6 March and 11 September 2020. The data included demographics, comorbidities, laboratory results, severity of illness scores, complications and mortality, and comparisons were made between the HIV-positive and HIV negative groups.

Results: Three-hundred and eighty-four patients, 108 HIV-positive and 276 HIV-negative, were included in the study. Median 4C score was significantly higher in the HIV-positive patients compared to the HIV-negative patients, but there was no significant difference in mortality between the HIV-positive and HIV-negative groups (15% vs 20%, p = 0.31). In addition, HIV-positive patients who died were younger than their HIV-negative counterparts, but this was not statistically significant (47.5 vs 57 years, p = 0.06).

Conclusion: Our findings suggest that HIV is not a risk factor for moderate or severe COVID-19 disease neither is it a risk factor for mortality. However, HIV-positive patients with COVID-19 requiring admission to hospital are more likely to be younger than their HIV-negative counterparts. These findings need to be confirmed in future, prospective, studies.

© 2021 The British Infection Association. Published by Elsevier Ltd. All rights reserved.

Introduction

SARS-CoV-2 has rapidly spread across the globe with more than 100 million people reported to be infected, as of the 27th of January, and a large number of these manifesting with the associated disease, COVID-19 (coronavirus disease-2019). Overall, 1,423,578 of these cases have occurred in South Africa.1 In the majority of cases, COVID-19 is a mild influenza-like illness; however, severe disease occurs in approximately 14%, and critical illness in 5% of cases.2 Risk factors for progression to severe illness include age, male sex, hypertension, cardiovascular disease, obesity and diabetes, amongst others.3,4

There is still no clarity as to the impact of HIV infection on the risk of contracting SARS-CoV-2, nor on the outcome of COVID-19. This is critically important as South Africa has the highest prevalence of people living with HIV (PLWH) in the world.5 Fourteen percent of the population are HIV-positive and of those only 55% are virally suppressed.5,6 It has been suggested that PLWH are not
at an increased risk of severe disease from COVID-19 infection; especially in those who are using antiretroviral therapy (ART), are virally suppressed, and have a CD4 cell count ≥ 200 cells/mm³.³⁻⁷⁻⁹

A retrospective matched cohort analysis of HIV-positive and HIV-negative patients, amongst several hospitals in the United Kingdom (UK), showed similar outcomes in COVID-19, PCR-positive patients, with respect to the need for ventilation and mortality,⁰ and a matched cohort from New York demonstrated similar findings.¹¹ A study from Spain, demonstrated a lower risk for COVID-19 in the HIV-positive population compared with the general population, especially in those patients taking a combination of tenofovir and emtricitabine.¹² In contrast, population-based data from the Western Cape, South Africa¹³ and from the UK,¹⁴ showed an increased mortality from COVID-19 amongst PLWH. In the former study this association was present irrespective of HIV viral load.¹⁵ Data from the International Severe Acute Respiratory and Emerging Infection Consortium (ISARIC)¹⁵ also showed an increased 28 day mortality amongst PLWH; however, the data were incomplete and did not adjust for confounding factors, such as socioeconomic status, nor the effects of ART, CD4 cell count and HIV viral load.

There is significant heterogeneity in the prevalence of HIV in different regions of the world, and within South Africa. Statistical power may be an issue in areas where prevalence of HIV is lower, such as in Europe, which may lead to conflicting results when compared with a country such as South Africa with a very high burden of HIV infection. In addition, differences seen in the various studies may also represent factors that have not been accounted for, such as frailty and socioeconomic status.

Molecular docking studies have demonstrated binding of the HIV nucleotide reverse transcriptase inhibitor (NRTI), tenofovir, to an RdRp model, suggesting that this agent may also have activity against SARS-CoV-2.¹⁶ Other in vitro data are however conflicting, as one study corroborated the anti-viral effects of tenofovir¹⁷, whereas two others did not.¹⁸,¹⁹ In addition, there is no evidence that pre-exposure prophylaxis (PrEP) with tenofovir, prevents SARS-CoV-2 infection and COVID 19 disease.²⁰ Despite this, a study from the Western Cape province in South Africa showed a reduction in COVID-19 mortality amongst those patients on tenofovir disoproxil fumarate (TDF) therapy, when compared to those on other anti-retroviral therapies, similar to the findings from the Spanish study.¹²,¹³ More data are needed to determine the in vitro and clinical efficacy of tenofovir therapy against SARS-CoV-2. There has also been interest in the potential use of HIV protease inhibitors, as these inhibit the activity of Mpro.²¹ and in vitro studies have shown that the use of nelfinavir significantly blocks SARS-CoV-2 viral replication in cell cultures.²² Despite this, randomised controlled trials have demonstrated no benefit of lopinavir/ritonavir compared to standard care in patients with COVID-19 disease,²³,²⁴ and similarly in a case series, darunavir failed to prevent progression of disease.²⁵

The aim of this study was to determine the impact of HIV infection on the clinical characteristics, disease course and outcome of patients with COVID-19 admitted to a tertiary academic teaching hospital in Johannesburg, Gauteng, South Africa.

Methods

This was a retrospective analysis of prospectively collected data on all adult patients with reverse-transcriptase polymerase chain reaction (RT-PCR)-confirmed COVID-19, admitted to the medical wards and multidisciplinary intensive care unit (ICU) of Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) between 6 March and 11 September 2020. Patients with known HIV status or those with an HIV ELISA performed during the current admission were included in the final analysis.

Patient data was initially captured using dedicated data collection sheets, which were subsequently transferred onto a password-protected database (REDCap version 9.7.8, Vanderbilt University, 2020). The database was supplemented with laboratory information from the National Health Laboratory Service (NHLS) results system (TrakCare, Intersystems, Cambridge, MA, USA). Data was exported into Microsoft Excel 16.4 (Microsoft Corporation, Redmond, USA) and missing data was obtained through review of physical patient files and the NHLS laboratory system and entered directly into Microsoft Excel.

Patient reported comorbidities assessed in our analysis, were the presence of cardiovascular disease (including hypertension, ischaemic heart disease and atrial fibrillation), diabetes mellitus (diagnosed prior to admission), obesity, dyslipidaemia, chronic kidney disease (including prior renal transplant), chronic lung disease (including asthma and chronic obstructive pulmonary disease (COPD)), prior tuberculosis, chronic liver disease, malignancy, neuropsychiatric illness (including dementia, prior stroke, epilepsy and psychiatric disorders), thyroid disease and rheumatological conditions (including systemic lupus erythematosus, rheumatoid arthritis and ankylosing spondylitis).

Clinical severity was analysed by a number of scoring systems, namely the CURB-65 score, the National Early Warning Score 2 (NEWS2) and the 4C mortality score. CURB-65 was chosen as it forms part of the South African community-acquired pneumonia guideline,²⁶ whilst NEWS2 was chosen as it has previously been validated for use in COVID-19.²⁷ The 4C score was used as it was developed for use in predicting mortality in patients with COVID-19.²⁸

Routine admission investigations performed for all patients included: full blood count (FBC), urea, creatinine and electrolytes (U&E), liver function tests, C-reactive protein (CRP), procalcitonin (PCT), lactate dehydrogenase (LDH), D-dimer levels, highly sensitive troponin T (hs-Trop-T), ferritin, beta-d-glucan (BDG), HIV ELISA (with CD4 and viral load if positive) and blood cultures. Presence of SARS-CoV-2 infection was confirmed by RT-PCR on a nasopharyngeal swab and sputum investigations for bacteria were undertaken using microscopy, culture and sensitivity (MC&S). Testing for Mycobacterium tuberculosis and Pneumocystis jirovecii pneumonia (PJP) infection were performed, as appropriate.

Laboratory results used in the current analysis were those taken within 24 hours of hospital admission. The absolute CD4 cell count and HIV viral load, taken at the time of admission diagnosis of HIV were utilised for analysis, whereas in the case of known HIV-positive patients, the most recent viral load and CD4 cell counts, within the six months prior to admission, were used. An HIV viral load of less than 20 copies per millilitre was considered in the current study to represent viral suppression, as this is the detection limit of the assay used at our centre (Roche cobas® 6800/8800 HIV-1 test).

A complication was defined as a new event that occurred during hospital admission. Complications included cardiovascular events (new onset cardiac failure, myocardial infarction, arrhythmias, cardiac arrest), pneumothorax, thromboembolic events, endocrine complications (diabetic ketoacidosis, Addisonian crisis), neuropsychiatric events, nosocomial infections, and gastrointestinal events (GIT bleed and hepatitis).

All patients with moderate/severe COVID-19 disease, as defined by the National Institute of Communicable Diseases (NICD),²⁹ received a standard treatment protocol, which included corticosteroids, anticoagulation, empiric antibiotic therapy (including therapy for opportunistic infections (OI)) and in some cases tocilizumab.
Statistical analysis

Categorical variables were presented as frequencies and percentages. The Chi-square or Fishers’ Exact tests were used to assess the association between categorical variables as appropriate. Continuous variables were described with mean and standard deviations (SD) for normally distributed data while non-normal data were described using the median and interquartile range (IQR). The means for normally distributed continuous variables were compared using the Student’s independent t-test, or analysis of variance (ANOVA) for three or more groups. The Mann-Whitney U test was used for comparing two groups of non-normally distributed data, while the Kruskal-Wallis test was used for analysis of three or more of such groups.

Multivariable logistic regression was used to determine the association between HIV status, and mortality, adjusting for different variables. Variables for the logistic regression model were selected using a stepwise regression, with variables with a p value less than 0.1 being selected for inclusion in the models. These were subsequently analysed together with risk factors that were noted as confounding the association of interest, and so these known confounding risk factors were then included for the various models, regardless of the results of the stepwise regression. The separate multivariable logistic regression models used to assess association of HIV status on in-hospital mortality controlling for different characteristics, included demographics and comorbidities, or demographic and laboratory markers variables, and lastly combining all selected variables.

The data were analysed using Microsoft Excel 16.4 (Microsoft Corporation, Redmond, USA) and Prism 8.4.3 (GraphPad Software Inc, California, USA). The multivariable logistic regression analysis were performed in STATA 16 (StataCorp LLC, Texas, USA) and p values of <0.05 were used to ascertain statistical significance.

Ethics approval

The University of the Witwatersrand Human Research Ethics Committee (Medical) approved both the establishment of the CMJAH COVID–19 Database (Ethics Certificate M200458) and this retrospective review (M2008109).

Results

Demographics

At the time of analysis the CMJAH COVID–19 Database included 676 adult patients with RT-PCR-confirmed COVID-19. Two-hundred and forty two patients had no recorded HIV status and 32 had been admitted to non-medical wards. The remaining 402 patients included one duplicate entry and 15 patients with incomplete data, resulting in a total cohort for analysis of 384 patients (Fig. 1). Overall, 276 patients were confirmed to be HIV-negative with the Roche cobas® HIV-1/HIV-2 Qualitative Test and 108 patients were HIV-positive. Thirteen HIV-positive patients were newly diagnosed, on the current admission, and 95 had been previously diagnosed.

Table 1 shows demographic and comorbidity data for the entire cohort. Patients were predominantly black, largely representing the demographics served by our hospital, and male. The median age of the total cohort was 50 years with the HIV-positive group being significantly younger than the HIV-negative group (45 vs 52 years, respectively p=0.01). Overall, 270 (70%) patients of the total cohort had one or more comorbidities with 72 HIV-positive patients (67%) having at least one comorbidity in addition to HIV infection. There was a significant difference in the number of patients with current or previous tuberculosis (TB) between the two groups. Overall, 79 HIV-positive patients were on ART and 17 were ART-naive at the time of admission. ART data was missing for 12 patients.

Clinical and Laboratory Data

Table 2 depicts clinical and laboratory data for the entire cohort. Interestingly, the median oxygen saturation was higher, and the systolic and diastolic blood pressure lower in the HIV-positive group compared to the -negative group (P<0.05 for all, Table 2), but there was no difference in pulse rate, respiratory rate or temperature between the two groups. Although median neutrophil count, ferritin, LDH, d-dimer level and CRP were elevated in the entire cohort, there was no significant difference in these variables between the two groups. In addition, the median lymphocyte count was reduced in the entire cohort. Interleukin-6 (IL-6) levels were elevated in both the HIV-positive and -negative groups; however, IL-6 levels were only available for 16 and 60 patients in the two groups, respectively, due to limitations in the availability of the assay in this setting. There was a significant difference in haemoglobin, total protein, alkaline phosphatase and gamma-glutamyl transferase levels between the HIV-positive and negative groups, respectively (P<0.05 for all, Table 2). Median CD4 cell counts were 210 cells/mm³ in the HIV-positive group.

Factors associated with mortality in the entire group

Mortality data is shown in Table 3. Overall, patients who died were older than those who survived (54.5 vs 48 years; p=0.01). There was no mortality difference according to gender or race. In terms of comorbidities, diabetes mellitus and obesity were more frequent amongst those who died than those who lived. Respiratory rate, pulse rate and oxygen saturation were all significantly associated with mortality. The patients who died had higher white cell and neutrophil counts, neutrophil/lymphocyte (N/L) ratios, and more severe renal dysfunction (i.e. elevated urea and creatinine). Furthermore, aspartate transaminase (AST), CRP, PCT, d-dimers, ferritin and hs-Trop-T were all higher and the albumin lower in those who died. Patients who developed neuropsychiatric disease and nosocomial infections during their hospital admission had a higher rate of mortality. In addition, the need for respiratory support and ICU care was associated with a higher chance of dying.

Severity of illness and mortality

Severity of illness and mortality data for the entire cohort is shown in Table 4. The median 4C score was significantly higher in the HIV-positive patients compared to the HIV-negative patients. There was no difference in CURB-65 or NEWS2 scores between the groups. The overall mortality in the cohort was 18% with a non-significant difference between the HIV-positive and HIV-negative groups (15% vs 20%, p = 0.31). Furthermore, there was no difference in ICU survival between the two groups.

Subgroup analysis: HIV-positive died vs HIV-negative died

Among the patients that died, the HIV-positive patients were younger than those that were HIV-negative, 47.5 vs 57 years (p = 0.06). There was a significantly higher incidence of neuropsychiatric disease (p = 0.04) and smoking (p = 0.04) in the HIV-positive group, and of obesity (p = 0.05) in the HIV-negative group. The haemoglobin, sodium and albumin levels were all significantly lower in the HIV-positive group, whereas serum urea, ALP and PCT were all significantly higher. There was no significant difference in the CURB-65, NEWS2 or 4C scores between patient groups, and there was no difference in need for respiratory support, admission to ICU, or length of stay. This data is available in Supplementary Table 1.
### Table 1
Demographic and comorbidity data in the entire cohort.

| Age          | Entire cohort (n=384) | HIV-positive (n=108) | HIV-negative (n=276) | p value |
|--------------|----------------------|---------------------|---------------------|---------|
| Median (IQR), (years) | 50 (39–60) | 45 (38–56) | 52.5 (39.8–61) | 0.008 |
| Gender       |                       |                     |                     |         |
| Male         | 204 (53%)            | 94 (50%)            | 150 (54%)           | 0.50    |
| Female       | 180 (47%)            | 54 (50%)            | 126 (46%)           |         |
| Race         |                       |                     |                     |         |
| Black        | 322 (84%)            | 100 (92.6%)         | 222 (80.4%)         |         |
| White        | 27 (7%)              | 6 (5.6%)            | 21 (7.6%)           |         |
| Indian       | 10 (3%)              | 1 (0.9%)            | 24 (8.7%)           |         |
| Mixed race   | 25 (6%)              | 1 (0.9%)            | 9 (3.3%)            |         |
| Comorbidities|                       |                     |                     |         |
| Cardiovascular disease | 148 (39%) | 36 (33.3%) | 112 (40.6%) | 0.20 |
| Chronic kidney disease | 35 (9%) | 10 (9.26%) | 25 (9.06%) | 1.0 |
| Chronic liver disease | 6 (2%) | 2 (1.85%) | 4 (1.45%) | 0.68 |
| Chronic lung disease | 16 (4%) | 6 (5.56%) | 10 (3.62%) | 0.40 |
| Tuberculosis | 14 (4%)              | 8 (7.41%)           | 6 (2.17%)           | 0.03    |
| Diabetes mellitus | 88 (23%) | 18 (16.67%) | 70 (25.46%) | 0.08 |
| Dyslipidaemia | 15 (4%) | 4 (36.76%) | 11 (35.67%) | 0.08 |
| Obesity      | 60 (16%)             | 13 (12.04%)         | 47 (17.03%)         | 0.27    |
| Thyroid      | 16 (5.6%)            | 1 (0.93%)           | 5 (1.81%)           | 1.0     |
| Malignancy   | 20 (5%)              | 5 (4.63%)           | 15 (5.43%)          | 1.0     |
| Neuropsychiatric disease | 30 (8%) | 12 (11.11%) | 18 (6.52%) | 0.14 |
| Rheumatological disease | 6 (2.08%) | 0 (0%) | 8 (2.90%) | 0.11 |
| Smoking      | 23 (6%)              | 6 (5.56%)           | 17 (6.16%)          | 1.0     |

IQR – Interquartile range

### Table 2
Vital and Laboratory Data in the entire cohort, median (IQR).

| Vitals on admission | Entire cohort (n=384) | HIV-positive (n=108) | HIV-negative (n=276) | p value |
|---------------------|----------------------|---------------------|---------------------|---------|
| Haemoglobin (g/dl)  | 13.5 (11.9-14.8)     | 12.9 (12.3-16)      | 13.7 (13.4-14)      | 0.01    |
| Platelets (x10^3)  | 249 (183-325)        | 240 (228-269)       | 256 (242-271)       | 0.73    |
| White cell count (x10^9) | 7.7 (5.6-10.4) | 7.4 (4.8-8.5)      | 8.7 (4.8-8.5)       | 0.17    |
| Neutrophil count (x10^9) | 5.8 (4-8.5)  | 5.0 (4.4-6.2)      | 5.9 (5.4-6.5)       | 0.09    |
| Lymphocyte count (x10^9) | 1.2 (0.8-1.8) | 1.1 (1-1.3)       | 1.15 (1.1-1.3)      | 0.83    |
| N/L Ratio | 2.9-8.6 | 298 | 4.6 (3.9-5.4) | 5.1 (4.6-5.7) |
| Sodium (mmol/l)    | 138 (134-141)        | 137 (135-138)       | 138 (137-139)       | 0.04    |
| Potassium (mmol/l) | 4.6 (4.1-5.2)        | 4.6 (4.3-4.8)       | 4.6 (4.5-4.7)       | 0.45    |
| Urea (mmol/l)      | 5.7 (3.9-8.9)        | 6.5 (5.3-6.7)       | 5.6 (5.2-6)         | 0.43    |
| Creatinine (umol/l) | 93.5 (75-135) | 98 (88-111)       | 95 (88-103)         | 0.79    |
| Total protein (g/l) | 72 (66-78) | 74 (72-76)         | 71 (70-72)          | 0.0007  |
| Albumin (g/l)      | 37 (33-42)           | 37 (35-39)          | 37 (37-38)          | 0.08    |
| Total bilirubin (umol/l) | 8 (5-12) | 7 (6-8)           | 8.5 (8-9)           | 0.004   |
| Conjugated bilirubin (umol/l) | 3 (2-5) | 3 (2-3)           | 3 (3-3)             | 0.29    |
| ALT (UI)           | 27 (18-43)           | 32 (26-33)          | 27 (25-30)          | 0.77    |
| AST (UI)           | 42 (30-63)           | 435 (35-50)         | 42 (40-45)          | 0.41    |
| ALP (UI)           | 84 (64-112)          | 78 (79-83)          | 78 (79-83)          | <0.0001 |
| GGT (UI)           | 63 (35-119)          | 85 (63-108)         | 55 (49-64)          | 0.0007  |
| LDH (UI)           | 478 (338-641)        | 502.5 (396-557)     | 471 (423-527)       | 0.85    |
| C-reactive protein (mg/l) | 92 (36-191) | 107 (70-136)      | 91 (76-101)         | 0.46    |
| Procalcitonin (ng/ml) | 0.22 (0.1-0.8) | 0.265 (0.16-0.53) | 0.21 (0.17-0.27) | 0.31 |
| Interleukin 6 (pg/ml) | 106 (47-466) | 57.8 (17-170)    | 108.9 (87.4-203.1) | 0.12    |
| Beta-D-glucan (pg/ml) | 47 (30-100) | 58.5 (31-99)      | 45 (38-51)          | 0.19    |
| D-dimers (mg/l)    | 0.75 (0.4-2.0)       | 0.79 (0.51-1.5)     | 0.75 (0.66-0.94)    | 0.26    |
| Ferritin (ng/ml)   | 631 (299-1555)       | 635 (488-1045)      | 624 (530-770)       | 0.78    |
| hs Tropomin T (ng/l) | 12 (6-29) | 13 (8-15)         | 11 (9-15)           | 0.58    |
| CD4 (cells/μl^3)   | 210 (144-458.5)      | 210 (180-339)       | 210 (180-339)       | N/A     |

IQR – Interquartile range, ALT- Alanine transaminase, AST- Aspartate transaminase, ALP - Alkaline phosphatase, GGT - Gamma-glutamyl transferase, LDH - lactate dehydrogenase, Nl - neutrophil/lymphocyte, hs - Highly sensitive
Table 3
Mortality data for the entire cohort

| HIV status | Entire cohort n = 384 | Lived n = 314 | Died n = 70 | P value |
|------------|-----------------------|---------------|-------------|---------|
| Positive   | 108 (28%)             | 92 (85%)      | 16 (15%)    | 0.278   |
| Negative   | 276 (72%)             | 222 (80%)     | 54 (20%)    |         |
| Gender     |                       |               |             |         |
| Male, n (%)| 204 (53%)             | 163 (80%)     | 41 (20%)    | 0.31    |
| Female, n (%)| 180 (47%)             | 151 (84%)     | 29 (16%)    |         |
| Race       |                       |               |             |         |
| Black      | 322 (84%)             | 264 (82%)     | 58 (18%)    |         |
| White      | 27 (7%)               | 20 (74%)      | 7 (26%)     |         |
| Indian     | 10 (3%)               | 10 (1000%)    | 0 (0%)      |         |
| Mixed race | 25 (6%)               | 20 (80%)      | 5 (20%)     | 0.34    |
| Age        |                       |               |             |         |
| Median (IQR) (years) | 50 (39–60)    | 48 (38–59)    | 54.5 (44–62) | 0.01    |

Comorbidities n (%)  
Cardiovascular Disease 148 (39%)  
Chronic Kidney Disease 35 (9%)  
Chronic Liver Disease 6 (2%)  
Chronic Lung Disease 16 (4%)  
COPD 3 (1%)  
Diabetes mellitus 88 (23%)  
Dyslipidaemia 15 (4%)  
Malignancy 20 (5%)  
Neuropsychiatric disease 30 (8%)  
Stroke 6 (2%)  
Obesity 60 (16%)  
Tuberculosis 14 (4%)  
Smoking 23 (6%)  

Vitals  
Median (IQR)  
Temperature (°C) 36.7 (36.4–37.2)  
Respiratory rate (rpm) 22 (18–26)  
Pulse rate (bpm) 80 (98–106)  
Oxygen saturation (%) 89 (90–94)  
Systolic BP (mmHg) 125 (115–140)  
Diastolic BP (mmHg) 79 (68–88)  

Laboratory Data  
Median (IQR)  
Haemoglobin g/dl 13.5 (11.9–14.8)  
Platelets (x10^9) 249 (183–325)  
White cell count (x10^3) 7.7 (5.6–10.4)  
Neutrophil count (x10^3) 5.8 (4–8.5)  
Lymphocyte count (x10^3) 1.2 (0.8–1.8)  
NLR 5.2 (2.9–8.6)  
Sodium (mmol/l) 138 (134–141)  
Potassium (mmol/l) 4.6 (4.1–5.2)  
Urea (mmol/l) 5.7 (3.9–8.9)  
Creatinine (umol/l) 93.5 (75–135)  
Total protein (g/l) 72 (66–78)  
Albumin (g/l) 37 (33–42)  
Total Bilirubin (umol/l) 8 (5–12)  
ALT (IU/l) 27 (18–43)  
AST (IU/l) 42 (30–63)  
ALP (IU/l) 84 (64–112)  
GOT (IU/l) 63 (35–119)  
LDH (IU/l) 478 (338–614)  
C-reactive protein (mg/l) 93 (36–191)  
Procalcitonin (ng/l) 0.22 (0.1–0.8)  
Interleukin 6 (pg/ml) 106 (47–466)  
D-Glucan (pg/ml) 47 (30–100)  
Ferritin (ng/ml) 631 (299–1555)  
hs Tropinin T (ng/l) 12 (6–29)  
CD4 count cells/mm^3 243 (145–458)  

Severity of Illness Scores  
Median (IQR)  
CURB 65 score 1 (0–2)  
NEWS 2 score 6 (3–8)  
AC score 22 (22–24)  
Co-existing Pathogens 20 (5.2%)  
Respiratory support 225 (63%)  
ICU required 70 (18%)  

Complications n (%)  
Acute Kidney Injury 76 (20%)  
Cardiovascular 32 (88%)  
Gastrenteritis 4 (1%)  
Infections 10 (3%)  
Metabolic 19 (5%)  
Neuropsychiatric 10 (3%)  
Pneumothorax 1 (0.3%)  

IQR – Interquartile range, ALT- Alanine transaminase, AST- Aspartate transaminase, ALP- Alkaline phosphatase, GGT- Gamma-glutamyl transpeptidase, Hb- Hemoglobin, HCT- Hematocrit, HbA1c- Hemoglobin A1c, LPS- Lipopolysaccharide, CRP- C reactive protein, IL- Interleukin, GDF- Growth Difinition Factor, hs- Highly sensitive, COPD- Chronic obstructive pulmonary disease, BMI- Body Mass Index, Lived- Survived, Died- Died, % - Percentage, n - Number of cases.
Enrolled (n = 384)

Excluded (n = 292)
   - No HIV Result (n = 242)
   - Non-medical complaint (n = 32)
   - Missing vital data (n = 17)
   - Duplicate entry (n = 1)

HIV-negative (n = 276)
   - Known diagnosis (n = 95)
   - Newly diagnosed (n = 13)

HIV-positive (n = 108)
   - Known diagnosis (n = 95)
   - Newly diagnosed (n = 13)

RT-PCR confirmed COVID-19 patients on database at date of analysis (n = 676)

Fig. 1. is a description of the study cohort.

Table 4
Severity of Illness and Mortality according to HIV status.

| Score          | Entire cohort (n = 384) | HIV-positive (n = 108) | HIV-negative (n = 276) | P value |
|----------------|-------------------------|------------------------|------------------------|---------|
| CURB-65        | 22 (20–24) n = 370     | 23 (20–25) n = 105     | 21 (20–23) n = 265     | 0.004   |
| NEWS2          | 6 (3–8)                 | 5 (3–7)                | 6 (3–8)                | 0.28    |
| 4C Score       | 1 (0–1)                 | 0 (0–1)                | 1 (0–1)                | 0.09    |
| Total Complications n (%) | 150                    | 40 (37.04%)            | 106 (39.86%)           | 0.64    |
| Outcomes       |                         |                        |                        |         |
| Died overall - n (%) | 8 (5–12)               | 8.5 (5–12)             | 8 (5–12)               | 0.52    |
| Died in ICU - n (%) | 33 (8.6%)              | 6 (46%)                | 27 (47%)               | 1.0     |

IQR – Interquartile range
Analysis of mortality in HIV-positive patients

Mortality in the HIV-positive patient group is shown in Table 5. There was no significant difference in age between the HIV-positive patients who died and those who survived nor was there a difference in gender. However, smoking and diabetes mellitus were associated with a higher mortality. Amongst the HIV-positive patients who died, there were significant differences in vital signs on admission, with higher respiratory and pulse rates; however there was no difference in oxygen saturation between the two groups. The median haemoglobin and albumin levels were lower in patients who died whereas the white cell and neutrophil counts, N/L ratios, CRP, PCT, urea, creatinine, d-dimers, hs-trop-T, LDH and AST were significantly higher in those that survived. This was similar to the findings in the whole cohort. The median CD4 count was lower in the HIV-positive patients who died than in those who survived and lower in those who required admission to ICU than those who did not; however this was not significantly different in both cases. HIV-positive patients with a suppressed viral load had a lower mortality rate than those with an unsuppressed viral load but again this was not significant. There was, however, a significant difference in the 4C and NEWS-2 scores between HIV-positive patients who lived and those who died.

Multivariate analysis

When adjusting the data only for demographic, clinical features and comorbidities, being HIV-positive was associated with a 14% higher risk of mortality compared to being HIV-negative, although this was not significantly different (aOR=1.14; 95% CI: 0.50–2.60; p = 0.75). Female gender was also non-significantly protective (aOR=0.70; 95%CI: 0.32–1.40; p = 0.319). The requirement for respiratory support and/or ICU admission and having liver cirrhosis were all significantly associated with mortality. However, after adjusting for demographics, clinical and laboratory markers, a non-significant protective effect of HIV-positivity on mortality was noted. These data are available in Supplementary Table 2.

Discussion

Similar to other international studies our findings suggest that HIV is not a risk factor for severe COVID-19 disease, neither is it a predictor of the need for supplementary oxygen, ICU care or mortality. Two studies from New York showed no significant difference in mortality, ICU care and oxygen requirements in PLWH. In addition, although there was a higher proportion of HIV-positive patients who smoked, had COPD, cancer or cirrhosis in one of the studies, this had no impact on outcome. Other studies from China, Italy, France and Germany did not report an excess mortality in patients with HIV infection, and suggest that the risk of severe COVID-19 disease in these patients is the same as that of the rest of the general population. In one observational, prospective study overall mortality in the HIV-positive cohort was 4% compared with 20% in reports from the general population. However higher mortality was noted in 50-59 year olds in the HIV-positive group (8% vs 4%), and an overall higher incidence of severe disease and need for ICU admission was noted in this age group.

Two population based cohorts, one from the Western Cape, South Africa and the other from the UK have documented a higher mortality from COVID-19 in patients with HIV infection. In the Western Cape this was demonstrated across viral loads and CD4 cell counts, and the association with death persisted when hospitalised patients were analysed. In addition, 39% of the HIV-positive patients who died were younger than 50 years old compared to 13% of the HIV-negative patients in this age group.

The median age in our cohort was 50 years; HIV-positive patients were significantly younger than HIV-negative patients (45 vs 52.5, p=0.008), and younger than cohorts from other countries. In addition, the HIV-positive patients who died were younger than their HIV-negative counterparts, but this was not statistically significant. This trend is similar to that seen in the Western Cape, where mortality was higher in HIV-positive patients under 50 years old and is representative of the South African situation where the majority of patients with HIV are in the 25–49 year age group. In the HIV-positive group who died, there was no difference in mortality noted between men and women, nor according to age or in relation to antiretroviral use. The mortality differences in this study should be seen in the light of the fact that studies using epidemiologic models have shown that despite the use of ARV therapy, HIV-positive individuals are chronologically 4.9 years older than HIV-negative controls and have an expected mortality risk of 19%, independent of the duration on antiretroviral therapy.

Similar to other studies, a large proportion of patients in our cohort had comorbid disease, with comorbidities documented in 70% of all cases and 67% of those with HIV co-infection. With the exception of previous TB, there were no differences in type of comorbidity between the HIV-positive and HIV-negative groups. HIV is a risk factor for TB infection, and this may explain the higher percentage of patients with previous TB in the HIV-positive group. Contrary to the Western Cape data, we found that previous tuberculosis infection was not a predictor of mortality. The fact that the incidence of TB in the Western Cape (681/100,000) is far higher than that in Gauteng (330/100,000), may possibly explain these differences.

Other local South African data, drawn from COVID-19 deaths reported to the National Department of Health, determined that 95.8% of patients who died had one comorbidity, and 58.6% had two or more. Hypertension (60.5%) and diabetes mellitus (54.9%) were the most common comorbidities, followed by HIV at 13.9%, which is similar to the overall prevalence of HIV in South Africa. In the entire cohort, diabetes mellitus and obesity were both associated with mortality; however, in the HIV-positive group, although there was a trend to increased mortality with obesity, this was not significant (p=0.05). Finally, despite no differences in overall rates of smoking in the two groups, smoking was significantly more common in the HIV-positive group who died (18.75%) compared to those who lived (3.26%; p=0.04), and was also significantly more common in the HIV-positive group who died (18.75%) compared to the HIV-negative group who died (1.85%; p=0.036). Sigel et al. found a higher proportion of smokers in their HIV-positive cohort, but with no difference in mortality. Our numbers were much smaller and this may account for the difference.

Severity of illness scores

Overall, 4C scores were high with most patients fitting into a “high risk” group (score ≥15), and it performed well as a predictor of mortality. The 4C score was also higher in HIV-positive patients, which is likely accounted for by an extra comorbidity, but this trend did not persist when looking at mortality in this subgroup, and thus 4C may not be a useful tool in HIV-positive patients. We noted no differences in the CURB-65 scores in any group and no differences in CURB-65 scores when compared between patients who lived and died, irrespective of their HIV status. This differs from data from China where a higher CURB-65 score was associated with an increased mortality, again probably because the Chinese cohort was older than our cohort. Using the NEWS2 score, most patients fitted into a “medium clinical risk” category, and a higher NEWS2 score was noted in the patients who died, which was also observed when comparing the HIV-positive subset. This
Table 5
Mortality in the HIV-positive group.

| HIV total Cohort | HIV-positive Died | HIV-positive Lived | P value |
|------------------|-------------------|--------------------|---------|
| n = 108          | n = 16            | n = 92             |         |

**Age**
- Median (IQR, years)
  - Male: 45 (38–56)
  - Female: 45 (38–56)

**Gender**
- Male: 54 (50%)
- Female: 54 (50%)

**Race**
- Black: 100 (93%)
- White: 6 (5%)
- Indian: 1 (1%)
- Mixed race: 1 (1%)

**Comorbidities**
- Cardiovascular disease: 36 (33.3%)
- Chronic kidney disease: 10 (9.26%)
- Chronic liver disease: 2 (1.85%)
- Chronic lung disease: 6 (5.56%)
- Tuberculosis: 8 (7.41%)
- Diabetic mellitus: 18 (16.67%)
- Obesity: 13 (12.04%)
- Dyslipidaemia: 4 (3.70%)
- Thyroid disease: 1 (0.93%)
- Malignancy: 5 (4.63%)
- Neuropsychiatric disease: 12 (11.11%)
- Rheumatological disease: 0
- Smoking: 6 (5.56%)

**Vitals**
- Temperature (°C): 37 (36–37)
- Respiratory rate (rpm): 20 (18–24)
- Pulse rate (bpm): 102 (86–117)
- Oxygen saturation (%): 92 (85–95)
- Systolic BP (mmHg): 120 (108–133)
- Diastolic BP (mmHg): 75 (64–84)

**Laboratory**
- Haemoglobin (g/dl): 12.9 (12–13.6)
- Platelets (x10^9/l): 240 (228–269)
- White Cell Count (x10^9/l): 7 (6.4–8.3)
- Neutrophil count (x10^9/l): 5.08 (4.4–6.2)
- Lymphocyte count (x10^9/l): 112 (1.3–1.3)
- Neutrophil/Lymphocyte ratio (NLR): 4.6 (3.9–5.4)
- Sodium (mmol/l): 137 (135–138)
- Potassium (mmol/l): 4.6 (4.3–4.8)
- Urea (mmol/l): 6 (5.3–6.7)
- Creatinine (umol/l): 93 (88–111)
- Total protein (g/l): 74 (72–76)
- Albumin (g/l): 37 (35–39)
- Total bilirubin (umol/l): 7 (6–8)
- Conjugated bilirubin (umol/l): 3 (2–3)
- ALT (UI): 28 (26–33)
- AST (UI): 43.5 (38–50)
- ALP (UI): 102 (87–112)
- GGT (UI): 85 (63–108)
- LDH (UI): 502.5 (396–557)
- C-reactive protein (mg/l): 107 (70–130)
- Procalcitonin (ng/ml): 0.265 (0.16–0.53)
- Interleukin 6 (pg/ml): 57.8 (17–170)
- Beta-D-glucan (gg/ml): 58.5 (31–99)
- D-dimers (mg/l): 0.79 (0.51–1.5)
- Ferritin (ng/ml): 635 (488–1045)
- hs Tropinin T (ng/l): 3 (2–15)
- CD4 cells/mm3: 210 (180–339)
- CD4 >200, n (%): 48 (54%)
- Suppressed VL, n (%): 39 (90.7%)
- Unsuppressed VL, n (%): 29 (85.3%)

**Severity of Illness**
- CURB-65 Score
  - 0 (0–1): n=108
  - 1 (0–1): n=16
- NEVIS2 Score
  - 0 (0): n=108
  - 1 (0–1): n=16
- 4C Score
  - 0 (0): n=108
  - 1 (0–1): n=16

**Medication**
- Steroids: 72 (66.67%)
- Tocilizumab: 5 (4.63%)
- ART: 79 (82.3%)

**Outcomes**
- Length of stay (days)
  - Total: 8.5 (5 – 12)
  - Length of stay in ICU: 5.5 (4 – 10)

IQR – Interquartile range. ALT– Alanine transaminase, AST– Aspartate transaminase, ALP – Alkaline phosphatase, GCT– Gamma-glutamyl transferase, LDH – lactate dehydrogenase, N/L – neutrophil/lymphocyte, hs – Highly sensitive.
is likely due to the fact that NEWS2 relies on clinical data and not on age and comorbid disease, and therefore NEWS2 could serve as a good predictor of disease severity in HIV-positive patients.

Laboratory results

Haemoglobin and albumin levels were lower in the HIV-positive group who died compared to those who survived, this probably being as a result of chronic illness. PCT was elevated in all patients who died, and was significantly higher in the HIV-positive group who died, compared to the HIV-positive group who lived.

Potential limitations

Firstly, this is a single centre study, and so the data may not be generalizable, either to other parts of South Africa, or to other regions of the world. Secondly, although the study and the database were initially set up to collect data prospectively, some data capturing was retrospective, due to rapidly increasing patient numbers and staff shortages, and as a result some data were missing. Specifically, details regarding occupations were not available for the study and for PLWH we did not have accurate data on the duration of ARV therapy nor time since diagnosis or nadir CD4 cell counts. CMJAH is a tertiary public facility that manages indigent patients from the inner city and throughout Johannesburg. In South Africa, lower socioeconomic, disadvantaged individuals are reliant on state facilities which serve 86% of the total population, compared to the private healthcare system which serves the remaining 16% who can afford health insurance. Levels of poverty in Johannesburg, which has a Gini coefficient of 0.62, are as high as 45.85%. Therefore, although this study lacks a formal index of deprivation score, it is likely that a significant proportion of the patients ranked on a low decile. Thirdly, the cases and the controls were not matched in any way for the comparison. Fourthly, we excluded more than one third of patients on our database as HIV status was not recorded. Informed consent is a requirement for HIV testing in South Africa, and it is likely that a significant proportion of our patients were unable or unwilling to give consent. Lastly, patients with asymptomatic and mild disease not requiring hospitalisation were excluded from the cohort, so the data refers only to hospitalised cases. Possible strengths include the relatively large number of cases from a single centre, where all patients were treated according to a standardised management protocol.

Conclusion

These findings suggest that HIV is not a risk factor for moderate or severe COVID-19 disease neither is it a risk factor for mortality. However, HIV-positive patients with COVID-19 requiring admission to hospital are more likely to be younger than their HIV-negative counterparts. Amongst the HIV positive cohort with COVID19, the NEWS2 score was a useful predictor of mortality. Other laboratory findings which were associated with a poorer outcome are similar to previous studies but also include lower haemoglobin, hypoalbuminemia and elevated PCT. These findings need to be confirmed in future, prospective, studies.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declarations of Competing Interest

None
### Supplementary Table 2

Multivariable logistic regression analyses of the associations between HIV status and mortality in a COVID hospitalized cohort of patients.

| Variables                              | Mortality in hospitalized COVID patient cohort |
|----------------------------------------|-----------------------------------------------|
|                                        | Model 1: Demographics, clinical and complications aOR (95% CI) | P-Value | Model 2: Demographics, clinical and laboratory markers aOR (95% CI) | P-value | Model 3: Demographics, clinical, complications and laboratory markers aOR (95% CI) | P-value |
| HIV status                             |                                              |         |                       |         |                                               |         |
| Negative                               | Ref (0.50–2.60)                              | 0.750   | Ref (0.20–1.40)        | 0.179   | Ref (0.12–1.66)                               | 0.231   |
| Positive                               | 1.14 (1.05–3.5)                              | 0.001   | 1.8 (0.4–7.5)          | 0.019   | 6.0 (0.5–3.2)                                | 0.002   |
| Race                                   |                                              |         |                       |         |                                               |         |
| Black                                  | Ref (0.32–3.60)                              | 0.916   | 1.8 (0.34–1.83)        | 0.576   | 0.6 (0.21–1.72)                              | 0.340   |
| White                                  | 1.10 (0.32–1.40)                             | 0.319   | 0.80 (0.34–1.83)       | 0.576   | 0.6 (0.21–1.72)                              | 0.340   |
| Other*                                 | 0.60 (0.15–2.20)                             | 0.416   | 0.6 (0.2–2.6)          | 0.541   | 0.73 (0.12–4.3)                              | 0.729   |
| Gender                                 |                                              |         |                       |         |                                               |         |
| Male                                   | Ref (0.32–1.40)                              | 0.319   | 0.80 (0.34–1.83)       | 0.576   | 0.6 (0.21–1.72)                              | 0.340   |
| Female                                 | 0.70 (0.32–1.40)                             | 0.319   | 0.80 (0.34–1.83)       | 0.576   | 0.6 (0.21–1.72)                              | 0.340   |
| Age                                    | 1.04 (1.01–1.07)                             | 0.024   | 1.02 (0.99–1.06)       | 0.125   | 1.04 (0.99–1.08)                             | 0.076   |
| Respiratory support                    |                                              |         |                       |         |                                               |         |
| No                                     | Ref                                           | 3.3 (1.2–9.0) | 0.019 | 3.04 (0.88–10.5) | 0.078 | 5.6 (1.0–31.3) | 0.05 |
| Yes                                    | Ref                                           | 3.4 (1.2–9.0) | 0.019 | 3.04 (0.88–10.5) | 0.078 | 5.6 (1.0–31.3) | 0.05 |
| ICU required                           |                                              |         |                       |         |                                               |         |
| No                                     | Ref                                           | 4.1 (2.0–9.4) | 0.001 | 9.4 (3.9–22.9) | <0.001 | 6.0 (2.0–18.8) | 0.002 |
| Yes                                    | Ref                                           | 4.1 (2.0–9.4) | 0.001 | 9.4 (3.9–22.9) | <0.001 | 6.0 (2.0–18.8) | 0.002 |
| Chronic-Liver cirrhosis                |                                              |         |                       |         |                                               |         |
| No                                     | Ref                                           | 13.6 (2–109) | 0.014 | - | - | 2.7 (1.4–5.0) | 0.501 |
| Yes                                    | Ref                                           | 13.6 (2–109) | 0.014 | - | - | 2.7 (1.4–5.0) | 0.501 |
| Complication_neuropsychiatric          |                                              |         |                       |         |                                               |         |
| No                                     | Ref                                           | 7.1 (1.2–42) | 0.031 | - | - | 73 (2.6–1998) | 0.011 |
| Yes                                    | Ref                                           | 7.1 (1.2–42) | 0.031 | - | - | 73 (2.6–1998) | 0.011 |
| Complication_cardiovascular            |                                              |         |                       |         |                                               |         |
| Chronic-Coronary                       |                                              |         |                       |         |                                               |         |
| No                                     | Ref                                           | 3.6 (0.13–0.60) | 0.003 | - | - | 0.4 (0.13–1.3) | 0.124 |
| Yes                                    | Ref                                           | 3.6 (0.13–0.60) | 0.003 | - | - | 0.4 (0.13–1.3) | 0.124 |
| Chronic-Kidney Disease                 |                                              |         |                       |         |                                               |         |
| No                                     | Ref                                           | 6.1 (2.0–21) | 0.004 | - | - | 5.0 (0.8–29.5) | 0.075 |
| Yes                                    | Ref                                           | 6.1 (2.0–21) | 0.004 | - | - | 5.0 (0.8–29.5) | 0.075 |
| Chronic -Cancer                        |                                              |         |                       |         |                                               |         |
| No                                     | Ref                                           | 1.9 (0.5–8.1) | 0.370 | - | - | - | - |
| Yes                                    | Ref                                           | 1.9 (0.5–8.1) | 0.370 | - | - | - | - |
| Complication_infection                 |                                              |         |                       |         |                                               |         |
| No                                     | Ref                                           | 20.3 (3.3–121) | 0.001 | - | - | 37 (4.4–309) | 0.001 |
| Yes                                    | Ref                                           | 20.3 (3.3–121) | 0.001 | - | - | 37 (4.4–309) | 0.001 |
| Complication_AKI                       |                                              |         |                       |         |                                               |         |
| Chronic-Diabetes mellitus              |                                              |         |                       |         |                                               |         |
| No                                     | Ref                                           | 2.3 (1.0–5.4) | 0.05 | - | - | 1.7 (0.5–5.5) | 0.349 |
| Yes                                    | Ref                                           | 2.3 (1.0–5.4) | 0.05 | - | - | 1.7 (0.5–5.5) | 0.349 |
| Chronic-Obesity                        |                                              |         |                       |         |                                               |         |
| No                                     | Ref                                           | 1.4 (0–6.3) | 0.434 | - | - | - | - |
| Yes                                    | Ref                                           | 1.4 (0–6.3) | 0.434 | - | - | - | - |
| Haemoglobin g/dl                       | -                                              | 1.04 (0.89–1.22) | 0.631 | - | - | - | - |
| Platelets x10^9/l                      | -                                              | 0.99 (0.98–0.998) | 0.007 | - | - | - | - |
| Urea mmol/l                            | -                                              | 1.05 (1.01–1.10) | 0.011 | - | - | - | - |
| D-dimers mg/l                          | -                                              | 1.01 (0.97–1.05) | 0.494 | - | - | - | - |
| Total Protein g/l                      | -                                              | 1.08 (1.03–1.14) | 0.004 | - | - | - | - |
| Albumin g/l                            | -                                              | 0.88 (0.80–0.95) | 0.002 | - | - | - | - |
| Total bilirubin umol/l                 | -                                              | 0.89 (0.80–0.98) | 0.001 | - | - | - | - |
| Conjugate bilirubin                    | -                                              | 1.15 (1.01–1.31) | 0.037 | - | - | - | - |
| umol/l                                 | -                                              | 1.15 (1.01–1.31) | 0.037 | - | - | - | - |
| Gamma-glutamyl transferase U/l         | -                                              | 1.0 (0.99–1.003) | 0.767 | - | - | - | - |

Notes: Model 1 adjusts for demographics, clinical and comorbidities/complications, Model 2 adjusts for demographics, clinical and laboratory variables while Model 3 adjusts for demographics, clinical, selected comorbidities/complications and laboratory variables. Gender, age, race; HIV status, respiratory support and whether ICU was required were included in all models.
Acknowledgements

The authors would like to thank the staff of the Departments of Medicine and Critical Care for their ongoing commitment to treating patients with COVID-19 as well as the management of CMJAH for their approval of this study.

Supplementary materials

Supplementary data associated with this article can be found in the online version, at 10.1016/j.jinf.2021.05.020.

References

1. Coronavirus Update (Live): 100,971,153 Cases and 2,169,285 Deaths from COVID-19 Virus Pandemic - Worldometer. Available at https://www.worldometers.info/coronavirus/
2. Guan W, Ni Z, Yu H, Liang W, Wu C, He J, et al. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med 2020;382(18):1708–20. doi: 10.1056/NEJMoa2002032.
3. Zhou F, Yu T, Du R, Fan G, Liu Y, Yu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet 2020;395(10223):1054–62. doi: 10.1016/S0140-6736(20)30566-3.
4. Richter D, Herbst J, Narasiman N, Crawford J, McGinn T, Davidson K, et al. Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York City area. JAMA 2020;323(20):2052–7. doi: 10.1001/jama.2020.6775.
5. AIDSInfo UNAIDS. Available at https://aidsinfo.unaids.org. Accessed 14 August, 2020.
6. Jarrod Z, Venturas J, Diana N. COVID-19 and the uniqueness of South Africa. South Afr J Infect Dis 2020;35(1):1. doi: 10.1016/j.jsaids.2020.01.008.
7. GMH BlueMouse. EACSA, a joint statement 30 April. EACSA. Available at https://www.eacsociety.org/home.html. Accessed 14 August, 2020.
8. Carlucci P, Fervenza F, Zacharioudakis I, Reiberg B, Klein-Kermou 😀礫 Salvanna. Carlucci Philip M, Fervenza Fanarietti N, Zacharioudakis Ioannis M, Reiberg Gabriel, Khoo Fung, et al. Outcomes among HIV-positive patients hospitalized with COVID-19 JAIDS J Acquir Immune Defic Syndr 2020;85(1):3–10. Published Ahead of Print. doi: 10.1097/QAI.0000000000002423. E et al. Outcomes among HIV-positive patients hospitalized with COVID-19 JAIDS J Acquir Immune Defic Syndr 2020;85(1):3–10. Published Ahead of Print. doi: 10.1097/QAI.0000000000002423.
9. Guo W, Ming F, Dong Y, Ziang Q, Zhang X, Mo P, et al. A Survey for COVID-19 Among HIV/AIDS Patients in Two Districts of Wuhan, China Res Q 2020;83(2):53351. Published 2020 Aug 10. Rochester, NY: Social Science Research Network; 2020.
10. M.Lee, C. Smith, S. Douthwaite, S. Figler, N. Fitzgerald, L. Goodwin. 2021. Clinical Outcomes of Patients With and Without HIV Hospitalised with COVID-19 in England Early Stages of the Pandemic: A Matched Retrospective Multicentre Analysis (RECDE-C19 Study) SSRN Electronic Journal. Available at 10.2139/ssrn.3771328. Accessed May 13, 2021.
11. Sigel K, Swartz T, Golden E, Parajpe I, Soman S, Richter F, et al. Coronavirus 2019 and people living with human immunodeficiency virus: outcomes for hos- pitalized patients in New York City. Clin Infect Dis 2020;ciaa880. doi: 10.1093/cid/ciaa880.
12. del Amo J, Rosa P, Moreno S, Diaz Asuncion, Martinez E, Arribas Jose, et al. Incidence and severity of COVID-19 in HIV-positive persons receiving antiretro- viral therapy: a cohort study. Ann Intern Med 2020;M20-3689. doi: 10.7726/AnnIntMed.2020-M20-3689.
13. Boule A, Davies MA, Hussey H, Ishmael M, Morden E, Ziyanda V, et al. Risk factors for COVID-19 death in a population cohort study from the Western Cape Province. South Africa. Clin Infect Dis 2020;ciaa1198. doi: 10.1093/cid/ciaa1198.
14. Bhaskaran K, Rentisch C, Mackenna B, Schultzke A, Mehrkar A, Bates C, et al. HIV infection and COVID-19 death: a population-based cohort analysis of UK primary care data and linked patient death registrations within the OpenSafely platform. Lancet 2020;S2532301820300520. doi: 10.1016/S2532-3018(20)30305-2.
15. Govaert A, Stockdale A, Kelley S, Cevik M, Collins S, Waters L, et al. Outcomes of COVID-19 related hospitalized patients among people with HIV in the ISRCRO WHO Clinical Characterization Protocol (UK): a prospective observational study. Clin Infect Dis 2020 https://academic.oup.com/cid/article-advance-article/doi/10.1093/cid/ciaa1605/5937135. Epub ahead of print. PMID: 32090533; PMID: PMC7665382. doi: 10.1093/cid/ciaa1605.
16. Elfishy A, Ribarvsk, Rennsdorfs, Sofosbuvir, Galidesvir, and Tenofovir against SARS-CoV-2 RNA dependent RNA polymerase (RdRp): A molecular docking study. J Biomol Struct Dyn 2020;117592. doi: 10.1080/07391102.2020.117592.
17. Clososki G, Soldi R, da Silva R, Thais G, Lopes J, Pereira Pamela, et al. Tenofovir disoproxil fumarate: new chemical developments and encouraging in vitro biological results for SARS-CoV-2. J Braz Chem Soc 2020;31(8):1552–6. doi: 10.1590/s0103-5053202030106.
18. Choy KT, Wong Y, Kaewpreechee P, Sia S, Dongdong C, Van HKP, et al. Rennsdor- sivir, lonipravin, emetine, and homoharringtonine inhibit SARS-CoV-2 replication in vitro. Antiviral Res 2020;178:104786. doi: 10.1016/j.antiviral.2020.104786.