

Outcomes of COVID-19 related hospitalisation among people with HIV in the ISARIC WHO Clinical Characterisation Protocol (UK): a prospective observational study

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Objective

To compare the presentation characteristics and outcomes of people with and without HIV hospitalised with COVID-19 at 207 centres across the United Kingdom.

Background

Evidence is conflicting about how the human immunodeficiency virus (HIV) modulates COVID-19.^{1,2} We compared the presentation characteristics and outcomes of adults with and without HIV who were hospitalised with COVID-19 at 207 centers across the United Kingdom and whose data were prospectively captured by the International Severe Acute Respiratory and Emerging Infection Consortium (ISARIC) World Health Organization (WHO) Clinical Characterisation Protocol (CCP) study.³

Methods

We used Kaplan-Meier methods and Cox regression to describe the association between HIV status and day-28 mortality, after separate adjustment for sex, ethnicity, age, probable or indeterminate hospital acquisition of COVID-19 (definite hospital acquisition excluded), presentation date, ten individual comorbidities, and disease severity at presentation (as defined by hypoxia or oxygen therapy).

Results

Among 47,573 patients, 123 (0.26%) had confirmed HIV infection and 111/123 (90.2%) had a record of antiretroviral therapy. At presentation, HIV-positive people were younger (median 56 vs. 74 years; $p < 0.001$) and had fewer comorbidities, more systemic symptoms and higher lymphocyte counts and C-reactive protein levels (Figure 1, Table 1). The cumulative day-28 mortality was similar in the HIV-positive vs. HIV-negative groups (27.3% vs. 32.1%; $p = 0.22$), but in those under 60 years of age HIV-positive status was associated with increased mortality (22.4% vs. 9.6%; $p < 0.001$ [log-rank test]) (Figure 2). Mortality was higher among people with HIV after adjusting for age (adjusted hazard ratio [aHR] 1.52, 95% confidence interval [CI] 1.05–2.20; $p = 0.03$), and the

association persisted after adjusting for the other variables (aHR 1.68; 95% CI 1.14–2.78; $p = 0.009$) and when restricting the analysis to people aged < 70 years (aHR 1.92; 95% CI 1.22–3.00; $p = 0.004$) (Table 2).

- Within the HIV positive group those who died were more likely to have diabetes with complications and obesity compared to those discharged (Table 3). However the effect of HIV status remains significant after adjustment for co-morbidities in the main model.
- After adjustment for sex, ethnicity, age, baseline date, indeterminate/probable hospital acquisition of COVID-19, and ten comorbidities, the odds of admission to critical care were similar regardless of HIV status (odds ratio 1.27; 95% CI 0.85–1.91; $p = 0.24$).

Conclusions

HIV-positive status was associated with an increased risk of day-28 mortality among patients hospitalised with COVID-19.

Figure 1 Kernel density plot of age distribution of study participants stratified by HIV status

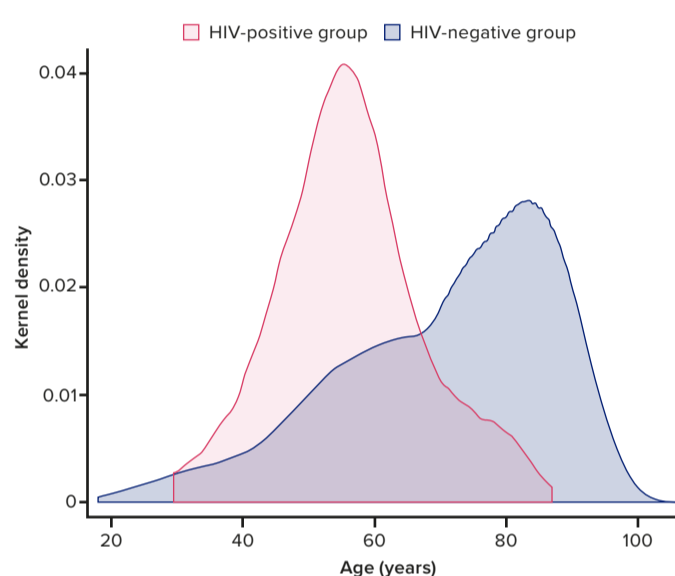


Figure 2 Kaplan-Meier survival graphs, stratified by HIV status, sex, and age group

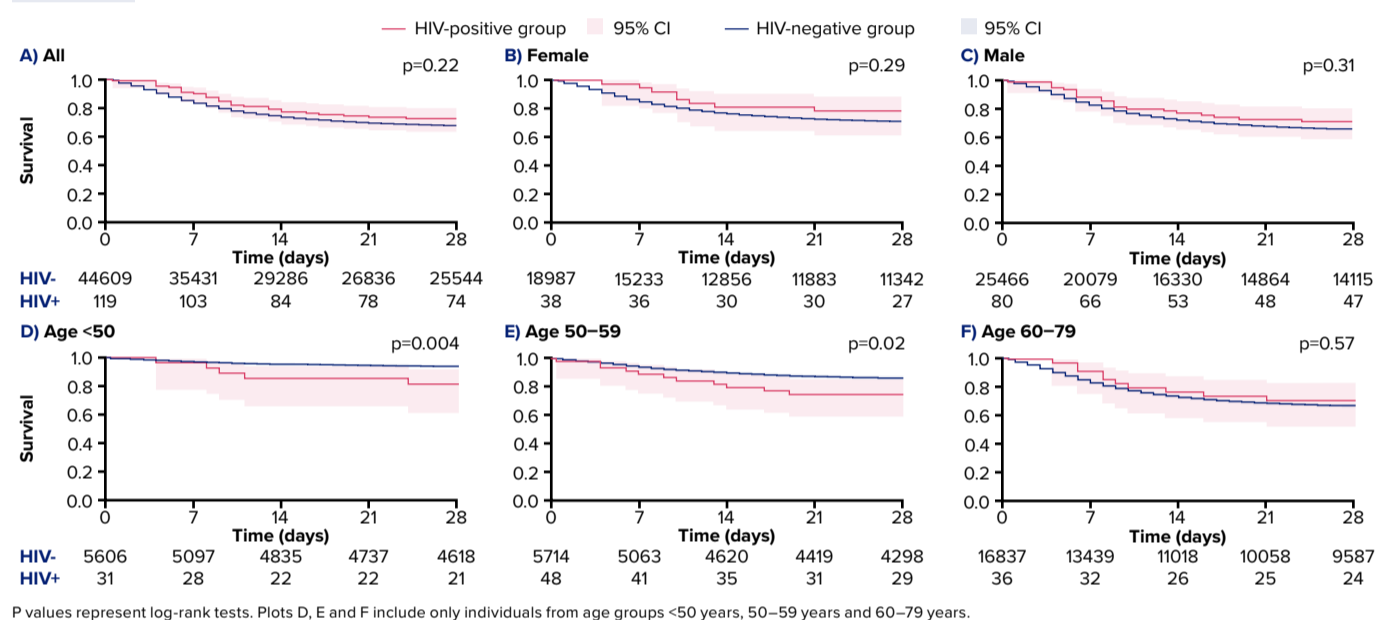


Table 1 Summary of participant characteristics, presenting symptoms, observations and laboratory measurements, stratified by HIV status

Participant characteristics, symptoms, observations, laboratory parameters	HIV-positive (n=123)	HIV-negative (n=47,450)	P value
Age, median years (IQR)	56 (49, 62)	74 (60, 84)	<0.001
Female, n (%)	40/122 (32.8)	20,293/47,283 (42.9)	0.02
Ethnicity, n (%)			<0.001
White	51/114 (44.7)	35,525/42,189 (84.2)	
Black	48/114 (42.1)	1,475/42,189 (3.5)	
Asian	1/114 (0.9)	2,248/42,189 (5.3)	
Other	14/114 (12.3)	2,942/42,189 (7.0)	
Smoking, n (%)			0.01
Never	64/95 (67.4)	17,388/30,364 (57.3)	
Former	20/95 (20.1)	10,637/30,364 (35.0)	
Current	11/95 (11.6)	2,339/30,364 (7.7)	
Comorbidities, median number (IQR)	1 (1, 2)	2 (1, 3)	<0.001
Type of comorbidities, n (%)			
Chronic cardiac disease	22/118 (18.6)	14,611/45,034 (32.4)	0.001
Chronic pulmonary disease ^a	13/121 (10.7)	8,051/44,898 (17.9)	0.04
Asthma	12/117 (10.3)	6,236/44,738 (13.9)	0.25
Chronic renal disease	21/117 (18.0)	7,869/44,708 (17.6)	0.92
Diabetes, no complications	18/118 (15.3)	7,779/43,843 (17.7)	0.48
Diabetes, with complications	9/118 (7.6)	3,304/43,568 (7.6)	0.99
Obesity	19/113 (16.8)	4,592/40,442 (11.4)	0.07
Chronic neurological disorder	8/117 (6.8)	5,585/44,458 (12.6)	0.06
Dementia	3/119 (2.5)	7,462/44,534 (16.8)	<0.001
Mild liver disease	3/119 (2.5)	632/44,208 (1.4)	0.24
Moderate/severe liver disease	6/119 (5.0)	860/44,261 (1.9)	0.02
Malignancy	4/119 (3.4)	4,593/44,339 (10.4)	0.009
Chronic haematological disease	4/119 (3.4)	1,927/44,291 (4.4)	0.82
Rheumatological disease	6/119 (5.0)	4,872/44,163 (11.0)	0.04
Malnutrition	5/113 (4.4)	1,132/41,834 (2.7)	0.24
Presenting symptoms, n (%)			
Fever	99/121 (81.8)	30,637/47,065 (65.1)	<0.001
Myalgia	27/104 (26.0)	6,351/34,825 (18.2)	0.04
Headache	18/96 (18.8)	3,661/34,779 (10.5)	0.009
Cough	96/122 (78.7)	31,017/47,057 (65.9)	0.003
Dyspnoea	88/122 (72.1)	32,124/47,023 (68.3)	0.37
Chest pain	25/109 (22.9)	5,225/38,288 (13.7)	0.005
Sore throat	13/100 (13.0)	2,804/34,283 (8.2)	0.08
Asymptomatic	0/123 (0)	888/47,450 (1.9)	0.18
Symptom group ^b , n (%)			<0.001
Systemic	108/122 (88.5)	32,254/47,099 (68.5)	<0.001
Respiratory	108/122 (88.5)	38,718/47,138 (82.1)	0.07
Gastrointestinal	45/111 (40.5)	13,439/41,296 (32.5)	0.07
Symptom duration, median days (IQR) ^c	5 (1, 9)	3 (0, 7)	0.002
Presenting signs			
Temperature, median °C (IQR)	37.8 (36.9, 38.1)	37 (36.6, 38.1)	0.005
Fever ≥37.8 °C, n (%)	60/118 (50.9)	16,441/45,438 (36.2)	0.001
HR, median beats/min (IQR)	96 (81, 110)	90 (78, 105)	0.004
Tachycardia ^d , n (%)	52/118 (44.1)	15,072/45,412 (33.2)	0.01
RR, median breaths/min (IQR)	20 (18, 27)	21 (18, 26)	0.89
Tachypnoea ^e , n (%)	54/114 (47.4)	23,296/45,190 (51.6)	0.37
Hypoxia ^f /on oxygen, n (%)	55/115 (47.8)	23,960/45,223 (53.0)	0.27
Infiltrates visible on CXR, n (%)	49/75 (65.3)	19,054/30,552 (62.4)	0.60
Systolic BP, median mmHg (IQR)	130 (117, 145)	130 (114, 147)	0.92
Diastolic BP, median mmHg (IQR)	80 (68, 86)	74 (65, 84)	0.009
Haemoglobin, median g/L (IQR)	130 (117, 144)	129 (113, 143)	0.68
Anaemia ^g , n (%)	40/108 (37.0)	15,561/40,072 (38.8)	0.70
WBC, median count x10 ⁹ /L (IQR)	6.6 (4.8, 9.1)	7.4 (5.4, 10.4)	0.01
Lymphocytes, median count x10 ⁹ /L (IQR)	1.0 (0.8, 1.5)	0.9 (0.6, 1.3)	<0.001
Lymphopenia ^h , n (%)	51/109 (46.8)	23,004/39,740 (57.9)	0.02
Platelets, median count x10 ⁹ /L (IQR)	198 (150, 258)	217 (164 to 286)	0.02
Thrombocytopenia ⁱ , n (%)	26/106 (24.5)	7,435/39,719 (18.7)	0.13
Prothrombin time, median sec (IQR)	13.7 (11.2, 15.0)	13.2 (11.8, 15.0)	0.82
Creatinine, median μmol/L (IQR)	89 (72, 134)	86 (67, 121)	0.25
eGFR, median mL/min/1.73m ² (IQR)	75 (52, 101)	73 (48, 97)	0.33
ALT, median U/L (IQR)	27 (19, 46)	26 (17, 43)	0.26
Glucose, median mmol/L (IQR)	6.9 (5.8, 10.3)	6.8 (5.8, 8.9)	0.39
Hyperglycaemia ^j , n (%)	11/54 (20.4)	2,900/19,531 (14.9)	0.26
C-reactive protein, median mg/L (IQR)	107 (51, 200)	83 (36, 157)	0.02

^aExcludes asthma. ^bSystemic symptoms: ≥1 of fever, myalgia or headache; Respiratory symptoms: ≥1 of cough, dyspnoea, chest pain, sore throat, wheeze; Gastrointestinal symptoms: ≥1 of diarrhoea, nausea, vomiting or abdominal pain. ^cBased on the onset of symptoms relative to the date of admission, COVID-19 acquisition was classified as community (<3 days), indeterminate (3–7 days), probable hospital (8–14 days), and definite hospital (>14 days). ^dDefined as HR >100 beats/min. ^eDefined as RR >20 breaths/min. ^fDefined as SpO₂ <94% on air. ^gDefined as haemoglobin <130 g/L in males and <115 g/L in females. ^hDefined as lymphocyte count <1.0 x10⁹/L. ⁱDefined as platelet count <150 x10⁹/L. ^jDefined as glucose >11 mmol/L.

Table 2 Cox proportional hazards model of the association between HIV status and day-28 mortality

HIV-positive vs. HIV-negative	Hazard ratio	95% CI	P value
Unadjusted	0.80	0.56 to 1.14	0.22
Adjusted for sex	0.77	0.53 to 1.10	0.15
Adjusted for ethnicity	0.91	0.62 to 1.32	0.61
Adjusted for age	1.52	1.05 to 2.20	0.03
Adjusted for sex, ethnicity, age, baseline date, indeterminate/probable hospital acquisition of COVID-19, and 10 comorbidities ^a	1.54	1.06 to 2.26	0.03
Adjusted for sex, ethnicity, age, baseline date, indeterminate/probable hospital acquisition of COVID-19, 10 comorbidities ^a and hypoxia/receiving oxygen at presentation ^b	1.68	1.14 to 2.78	0.009
Adjusted for sex, ethnicity, age, baseline date, indeterminate/probable hospital acquisition of COVID-19, 10 comorbidities ^a and hypoxia/receiving oxygen at presentation ^b among individuals aged <70 years	1.92	1.22 to 3.00	0.004

^aThe model adjusted separately for the following comorbidities: chronic cardiac disease, chronic pulmonary disease, chronic renal disease, diabetes, obesity, chronic neurological disorder, dementia, liver disease, malignancy, and chronic haematological disease. ^bHypoxia was defined as SpO₂ <94% on air; a record of hypoxia or receiving oxygen at presentation was used as an indicator of disease severity.

Table 3 Characteristics of patients with HIV, stratified by outcome at day 28, selected variables^a

Characteristic	Died (n=31)	Alive (n=92)	P value
Age, median years (IQR)	58 (55, 69)	55 (49, 61)	0.01
ART recorded, n (%)	25/31 (80.7)	86/92 (93.5)	0.04
Type of comorbidities, n (%)			
Chronic pulmonary disease ^a	1/30 (3.3)	12/91 (13.2)	0.18
Diabetes, with complications	5/31 (16.1)	4/87 (4.6)	0.04
Obesity	8/29 (28.6)	11/84 (13.1)	0.07
Symptom group, n (%)			
Respiratory ^b	29/30 (96.7)	79/92 (85.9)	0.18
Laboratory parameters			
WBC, median count x10 ⁹ /L (IQR)	8.1 (5.5, 11.7)	5.6 (4.6, 8.7)	0.008
Glucose, median mmol/L (IQR)	10.4 (6.4, 13.2)	6.4 (5.8, 8.3)	0.02
Hyperglycaemia ^c , n (%)	6/15 (40.0)	5/39 (12.8)	0.05
C-reactive protein, median mg/L (IQR)	193 (97, 260)	91 (40, 153)	<0.001

^aExcludes asthma. ^bRespiratory symptoms: ≥1 of cough, dyspnoea, chest pain, sore throat, wheeze. ^cDefined as glucose >11 mmol/L.

Abbreviations: aHR: adjusted hazard ratio; ALT: alanine transaminase; ART: antiretroviral therapy; BP: blood pressure; CI: confidence interval; CXR: chest x-ray; eGFR: estimated glomerular filtration rate; HR: heart rate; IQR: interquartile range; RR: respiratory rate; WBC: white blood cells.

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