CLINICALIMAGE

Revised: 21 August 2021

Health Science Reports

WILEY

.....

Predictors of mortality and ITU admission for COVID-19 patients admitted to a London district general hospital: A retrospective cohort study

Michel Alhilani ^{1,2}		Martin Cohn ¹	Ι	Ma	ria Nakhoul ³	Τ	Jonathan Than ⁴
Sing Yue Sim ^{4,5}	Ву	ung Choi ^{1,6}	La	vand	an Jegathees	war	an ^{1,2}
Amal Minocha ^{1,2}	E	rnest Mutenges	a ^{1,2}	<mark>2</mark>	Ashik Zala ^{1,7}	7	Georgios Karagiannis ^{1,8}

¹Department of Medicine, The Hillingdon Hospitals NHS Foundation Trust, London, UK
²Department of Medicine, Imperial College NHS Healthcare Trust, London, UK
³Division of Informatics and Analytics, Dana Farber Cancer Institute, Boston, Massachusetts, USA
⁴Department of Ophthalmology, Moorfields Eye Hospital NHS Foundation Trust, London, UK
⁵Department of Ophthalmology, The Hillingdon Hospitals NHS Foundation Trust, London, UK
⁶Department of Medicine, Chelsea and Westminster Hospital, London, UK
⁷Department of Medicine, London North West University Healthcare NHS Trust, London, UK
⁸Transplant Department, Harefield Hospital, Royal Brompton & Harefield NHS Foundation Trust, London, UK

Correspondence

Michel Alhilani, Department of Medicine, The Hillingdon Hospitals NHS Foundation Trust, London, UK. Email: michel.alhilani@nhs.net

1 | INTRODUCTION

The coronavirus disease 2019 (COVID-19) outbreak that originated in Wuhan, Hubei Province in China, was classified as a global pandemic by the World Health Organisation (WHO) on March 11, 2020.¹ As of April 8, 2021, the causative virus SARS-CoV-2 has spread to 219 countries and territories around the world, with 133 897 605 individuals infected and 2 904 686 deceased as a result.² COVID-19 manifests as a wide spectrum of disease ranging from asymptomatic infection to multiple organ failure requiring ITU admission and potentially leading to death.³⁻⁵

In the United Kingdom (UK), the first confirmed cases were reported on January 27, 2020⁶ and London has comprised the epicenter of its outbreak, bearing the highest rate of admission and mortality from COVID-19 in the country.⁷

A number of cohort studies from Italy, China, the United States (USA), and early UK studies have demonstrated the clinical characteristics and outcomes of patients with COVID-19 within their individual populations.^{5,8-11} Risk factors for ITU admission and mortality identified by these studies vary, with factors such as increasing age and various comorbidities showing consistent association, whereas other factors such as gender, ethnicity, antihypertensive medication use, and hematological laboratory results are inconsistently reported to predict adverse outcomes.

We therefore present the demographic, laboratory, and clinical features of patients with COVID-19 admitted to a district general hospital in London and assess predictors of mortality and ITU admission outcomes, in order to identify parameters aiding risk stratification of such patients in a secondary care setting.

2 | METHODS

2.1 | Study design

We conducted a retrospective cohort study on all patients with COVID-19 admitted to The Hillingdon Hospital (THH), The Hillingdon Hospitals NHS Foundation Trust, between March 16, 2020 and April

Michel Alhilani, Martin Cohn, and Maria Nakhoul contributed equally to this study.

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made. © 2021 The Authors. *Health Science Reports* published by Wiley Periodicals LLC.

14, 2020. We have included all patients aged >18 years with reverse transcription-polymerase chain reaction (RT-PCR) confirmed SARS-CoV-2 infection via nasopharyngeal swab. Age under 18 years was the only exclusion criterion. The primary outcome of the study was all-cause mortality by the end of the study period. The secondary outcome was ITU admission during hospitalization. The data collection period commenced at the time of admission until May 1, 2020, all-owing a minimum of 17 days from the date of admission to achieve a definitive outcome.

This study was approved by the Health Research Authority of England (IRAS project ID 284077, REC reference 20/HRA/2581), which waived the need for written informed consent due to the study's retrospective character.

2.2 | Data collection

The demographics, clinical characteristics, imaging data, and laboratory parameters on presentation, and the study outcomes were extracted retrospectively from electronic medical health records. All data were collected by medical doctors (M.C., M.A., S.Y.S., B.C., L.J., A.M., E.M., and A.Z.) and then reviewed by a senior consultant physician (G.K.).

Demographic characteristics collected included age, sex, and ethnicity. Ethnicity was divided into four main groups: Asian, black, white, and other (comprising mixed/multiple ethnic groups and other ethnic groups).¹²

Clinical characteristics collected included pre-existing medical conditions and presenting symptoms. The following chronic comorbidities were recorded: hypertension (HTN), ischemic heart disease (IHD), diabetes mellitus (DM), chronic kidney disease (CKD), asthma, chronic obstructive pulmonary disease (COPD), active cancer (Ca), cerebrovascular accident (CVA), dementia, and congestive cardiac failure (CCF). Information regarding current smoking status and use of angiotensin-converting enzyme inhibitors (ACEis) or angiotensin II receptor blockers (ARBs) were also collected. All information related to comorbidities was checked against previous hospital admission letters, clinic letters, and GP health records where accessible.

Presenting symptoms collected on admission included shortness of breath (SOB), fever (sublingual temperature of >37.9°C), cough, myalgia, production of sputum, fatigue, diarrhoea, nausea and vomiting, and chest pain.

Blood test results collected included routine hematology and biochemistry panels. Arterial blood gas results were collected where performed. In cases where venous instead of arterial blood gas was performed, only pH, lactate, and bicarbonate measurements were reviewed.¹³

Chest X-rays (CXRs) of our patient cohort were reported by the Hospital Radiology Department according to the British Society of Thoracic Imaging CXR reporting guidelines,¹⁴ which deemed a CXR (a) Normal (CVCX0), (b) Classic/Probable COVID-19 (CVCX1), (c) indeterminate for COVID-19 (CVCX2), and non-COVID-19 (CVCX3). In our study, we categorzsed CXR reports into two groups: (a) patients with CXRs showing classic/probable COVID-19 (CVCX1) and (b) patients with CXRs that were normal, indeterminate, or not showing classic signs of COVID-19 (CVCX0, CVCX2, CVCX3).

2.3 | Statistical analysis

Data collected from our patient cohort were subject to analysis using R version 3.6.1. Characteristics of the cohort were described with categorical variables represented as n (%), and continuous variables were represented as median with interquartile range (IQR). Wilcoxon ranked tests, Student's *t*-tests, chi-squared tests, and fisher-exact tests were used to compare differences between features for surviving and deceased patient groups when appropriate. The normality of variables was assessed using the Shapiro test, and all *P*-values were corrected using Bonferroni correction. Ethnicity was analyzed using two approaches: The first approach was to compare all ethnic groups against each other, whereas the second was to compare white ethnicity vs all other ethnicities.

To assess the association between outcomes and variables, univariate and multivariate logistic regressions were used with results presented as odds ratios with a 95% confidence interval. When choosing our predictors for the multivariate regression, the regsubsets R function was used to obtain the different model subsets—chooses variables based on the branch and bound algorithm.¹⁵ Models having either the highest adjusted R², or lowest Akaike information criterion (AIC), or lowest Bayesian information criterion (BIC) were extracted, and the subset of the variables were chosen based on being selected by at least two of the models. Variables with greater than 20% missing data, or for which an odds ratio for the univariate analysis could not be retrieved, were excluded from the multivariate regression model.¹⁰

Since our primary outcomes were of competing risks, this as well as right-censored data were accounted for. Cumulative incidence plots were used to evaluate the proportion of patients who were either deceased or discharged from the hospital over time.

3 | RESULTS

3.1 | Baseline demographic characteristics

Amongst our cohort of 383 patients were included in the study analysis (Figure 1). The median age was 71 years (54, 82), and 210 (54.8%) were male (Table 1). White ethnicity was the most prevalent in our study cohort. White patients had a higher median age compared to other ethnicities, and the median age amongst the four groups was statistically different (P < .001), with white having the highest median age of 78.5, followed by Asian 63, other 60.5, and black 54.

Of these 383 patients, 311 (81.2%) had definite outcomes at the end of the study period; 72 (18.8%) were considered censored, or with incomplete outcomes, due to being transferred or still hospitalized at the date of the last recorded follow-up on May 12, 2020



*Including those with incomplete ITU admission outcomes

FIGURE 1 Patient cohort pathway

(Figure 1). Of those with definite outcomes, 184 patients (59.2%) were discharged from hospital, and 127 (40.8%) died during their stay.

Furthermore, 295 patients had complete outcomes with regard to ITU admission. The median age, sex, ethnicity along with certain comorbidities, symptoms, and laboratory findings were significantly different between those who were admitted to ITU and those who were not (Table 2).

Median length of stay for all patients was 7 (IQR 3-12) days. Median length of stay for deceased patients was 6 (IQR 2-11) days. White ethnicity was associated with increased length of hospital stay compared to the other ethnicities (P = .0021).

3.2 | Predictors of mortality

In univariate logistic regression, age was the only significant demographic variable that was associated with an increased risk of mortality (Table 3).

Within our cohort, black, Asian, and other minority ethnicity (BAME) groups were overrepresented in terms of both hospital and ITU admission; 51.2% of admitted patients, and 76.4% of ITU patients were from BAME groups despite comprising only 39.9% of the

London Borough of Hillingdon population.¹² Despite this overrepresentation, there was no statistically significant association between ethnicity and odds of mortality in our study, in both univariable and multivariable analysis controlling for potential confounders including sex, age, and comorbidities.

Cough and myalgia were associated with lower odds of mortality, whereas SOB was linked to increased odds (Table 3). Classic finding of COVID-19 on CXR was associated with increased odds of mortality. Comorbidities that had a significant association with outcome were HTN, COPD, cancer, CCF, and dementia (Table 3). Laboratory results that had a significant association on outcome were WCC >11.0 10^{9} /L, neutrophils >7.7 10^{9} /L, CRP >100 mg/L, albumin ≤35 g/L, creatinine >125 µmol/L, and eGFR ≤60 mL/min (Table 3).

Significant predictors of outcome from the multivariable regression model were age, CXR reported as classic appearance of COVID-19, SOB, WCC > 11.0 10^{9} /L, and eGFR ≤60 mL/min (Table 3).

3.3 | Predictors of ITU admission

In univariable logistic regression, age, white ethnicity, and other ethnicities were associated with decreased odds of ITU admission

TABLE 1 Demographic, clinical, laboratory, and radiographic findings of patients on admission

	Total (n $=$ 383)	Discharged (n $=$ 184)	non-survivors (n = 127)	P-value
Demographics				
Age, years	71 (54,82)	62.5 (48,79)	80 (72,85)	<.001
Comorbidities				
HTN	191 (49.9%)	85 (46.2%)	79 (62.2%)	<.001
Dementia	28 (7.3%)	10 (5.4%)	16 (12.6%)	.042
CCF	9 (2.3%)	2 (1.1%)	7 (5.5%)	.035
Symptoms				
Shortness of breath	277 (72.3%)	131 (71.2%)	91 (71.7%)	.013
Cough	242 (63.2%)	136 (73.9%)	60 (47.2%)	.016
Myalgia	58 (15.1%)	34 (18.5%)	9 (7.1%)	.038
Laboratory findings				
WCC, 10 9 /L				<.001
<4.0	40 (10.4%)	24 (13%)	9 (7.1%)	-
>11.0	82 (21.4%)	24 (13%)	39 (30.7%)	-
Neutrophils, 10 9 /L				.017
<1.8	7 (1.8%)	4 (2.2%)	2 (1.6%)	-
>7.7	108 (28.2%)	39 (21.2%)	45 (35.4%)	-
CRP, mg/L				.002
<8	15 (3.9%)	12 (6.5%)	2 (1.6%)	-
>100	205 (53.5%)	83 (45.1%)	81 (63.8%)	-
Albumin, g/L				.020
≤35	225 (58.7%)	109 (59.2%)	92 (72.4%)	-
Urea, mmol/L				<.001
>7.8	143 (37.3%)	45 (24.5%)	45 (35.4%)	-
Creatinine, umol/L				<.001
>125	76 (19.8%)	23 (12.5%)	44 (34.6%)	-
eGFR, mI/min				<.001
≤60	134 (35%)	47 (25.5%)	71 (55.9%)	-
Imaging				
Chest X-ray				.015
Classic	201 (52.5%)	79 (42.9%)	77 (60.6%)	-

Note: Detailed results are found in Table S1. Variables with greater than 20% missing data were excluded from the regression analysis and this table. Abbreviations: CCF, congestive heart failure; CRP, C-reactive protein; eGFR, estimated glomerular filtration rate; HTN, hypertension; WCC, white cell count.

(Table 4). Male sex was strongly associated with increased likelihood of ITU admission (Table 4). The presence of symptoms on admission such as SOB, fever, cough, and production of sputum were all significant predictors of admission to ITU (Table 4).

The admission blood tests significantly associated with increased odds of ITU admission in univariable logistic regression included ALT >45 U/L, LDH >250 U/L, d-dimer >500 μ g/L, and pH >7.45 on blood gas. On the other hand, eGFR ≤60 mL/min, PCO2 > 6.4 kPa, and HCO3 > 28 mmol/L on blood gas were significant predictors of decreased odds of ITU admission. Although raised LDH, d-dimer, PCO2, and HCO3 (increase and decrease) appear to be significantly associated with odds of ITU admission, missingness of data of more

than 20% meant that these markers could not be conclusively convincingly interpreted in logistic regression.

In the multivariable logistic regression model, we found that male sex, SOB, production of sputum, and ALT >45 U/L were strongly associated with increased likelihood of ITU admission (Table 4).

4 | DISCUSSION

We present a comprehensive analysis of the baseline characteristics and factors associated with short-term mortality and ITU admission in 383 patients over 18 years old presenting to a London district general

DpenAccess — WILEY 5 of 9

TABLE 2 Demographic, clinical, laboratory, and radiographic findings of patients admitted to ITU

Variables	Total (n = 295)	ITU Admission (n $=$ 55)	No ITU Admission (n $=$ 240)	P-value
Demographics				
Age, years	71.0 (54.5,82.0)	62 (54,67)	74.50 (56.8,84)	<.001
Sex				.001
Male	171 (58%)	43 (78%)	128 (53.3%)	-
Ethnicity				<.001
White	141 (47.8%)	13 (23.6%)	128 (53.3%)	-
All other ethnicities	154 (52.2%)	42 (76.4%)	112 (46.7%)	-
Comorbidities				
IHD	58 (19.7%)	4 (7.3%)	54 (22.5%)	.029
CKD	42 (14.2%)	1 (1.8%)	41 (17.1%)	.003
COPD	29 (9.8%)	0	29 (12.1%)	.007
Carcinoma	30 (10.2%)	0	30 (12.5%)	.002
CVA	15 (5.1%)	0	15 (6.3%)	.082
Dementia	22 (7.5%)	1 (1.8%)	21 (8.8%)	.091
Symptoms				
Shortness of breath	220 (74.6%)	47 (85.5%)	173 (72.1%)	.016
Fever	179 (60.7%)	38 (69.1%)	141 (58.8%)	.029
Cough	193 (65.4%)	40 (72.7%)	153 (63.8%)	.014
Sputum	18 (6.1%)	7 (12.7%)	11 (4.6%)	.017
Laboratory findings				
Hb, g/L	128.82 ± 20.36	132.35 ± 12.75	128 ± 21.68	.053
CRP, mg/L				.021
<8	11 (3.7%)	0	11 (4.6%)	-
>100	156 (52.9%)	38 (69.1%)	118 (49.2%)	-
ALT, U/L				.008
>45	62 (21%)	19 (34.5%)	43 (17.9%)	-
eGFR, mL/min				.029
≤60	98 (33.2%)	11 (20%)	87 (36.25%)	-
Imaging				
Chest X-ray				<.001
Classic	146 (49.5%)	42 (76.4%)	104 (43.3%)	-

Note: Detailed results are found in Table S2. Variables with greater than 20% missing data were excluded from the regression analysis and this table. Abbreviations: ALT, alanine transaminase; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CRP, C-reactive protein; CVA, cerebrovascular accident; eGFR, estimated glomerular filtration rate; Hb, hemoglobin; IHD, ischemic heart disease.

hospital over a four-week period with COVID-19 infection. Identified factors significantly associated with adverse outcomes may form the basis of a risk stratification tool for COVID-19 patients admitted to a secondary care setting.

The mortality rate at THH from COVID-19 amongst the cohort by the end of the study period was 40.8%. The demographics, symptomatology, and comorbidity profile of our study cohort are broadly consistent with other UK studies.^{9,10,16-18}

The factors significantly associated with increased odds of mortality are consistent with those found in multiple prior cohort studies, with older age^{10,17-21} presence of HTN,^{10,18-21} COPD,^{18,20} carcinoma,¹⁸ dementia,^{10,18} and CCF^{17,18}; presentation with SOB^{8,17,19,21}; laboratory findings of WCC >11 10⁹/L,^{5,8,10,19-21} neutrophils >7.7 10⁹/L,^{5,8,21} CRP >100 mg/L,^{5,17,19,21} albumin \leq 35 g/L,^{5,8,10,18,20} creatinine >125 µmol/L,^{17,19-22} eGFR \leq 60 mL/min,¹⁰ and classic CXR appearance^{17,20} all previously reported. The association between COVID-19 mortality and older age is well established and thought to be multifactorial in origin, with a heightened systemic inflammatory response to infection in the elderly a potential contributor.^{3,9,10,17-21} We hypothesize that the association of cough and myalgia at presentation with decreased mortality odds may result from those presenting with less severe disease placing emphasis on less burdensome symptoms rather than the overriding SOB experienced by those with severe disease. In support of this, an increased

TABLE 3 Survival logistic regression: risk factors associated with mortality

n = 311	Univariable OR (95% CI)	P-value	Multivariable OR (95% CI)	P-value		
Demographics	Demographics					
Age, years	1.06 (1.04-1.08)	<.001	1.07 (1.05-1.10)	<.001		
Imaging report findings (vs not classic)						
Classic	2.06 (1.29-3.30)	.002	2.23 (1.21-4.16)	.010		
Comorbidities (vs not present)						
HTN	2.35 (1.45-3.84)	.001	-	-		
COPD	2.00 (1.00-4.04)	.049	-	-		
Carcinoma	2.08 (1.04-4.22)	.039	-	-		
Dementia	2.51 (1.11-5.91)	.029	-	-		
CCF	5.31 (1.26-36.03)	.039	-	-		
Symptoms (vs not present)						
Shortness of breath	2.32 (1.25-4.50)	.010	3.37 (1.60-7.51)	.002		
Cough	0.51 (0.30-0.86)	.012	-	-		
Myalgia	0.44 (0.19-0.93)	.042	-	-		
Lab findings						
WCC, 10 9 /L (Intercept: 4.0-11.0))					
<4.0	0.64 (0.27-1.40)	.284	0.84 (0.29-2.28)	.732		
>11.0	2.78 (1.57-5.01)	.001	2.47 (1.20-5.22)	.016		
Neutrophils, 10 9 /L (Intercept: 1.	8-7.7)					
<1.8	0.88 (0.12-4.62)	.885	-	-		
>7.7	2.03 (1.22-3.40)	.006	-	-		
CRP, mg/L (Intercept: <8)						
8-100	2.90 (0.75-19.15)	.176	-	-		
>100	5.86 (1.53-38.39)	.023	-	-		
Albumin, g/L (Intercept: >35)						
<=35	1.88 (1.14-3.15)	.015	-	-		
Urea, mmol/L (Intercept: ≤7.8)						
>7.8	4.48 (2.76-7.36)	<.001	-	-		
Creatinine, umol/L (Intercept: ≤125)						
>125	3.71 (2.12-6.65)	<.001	-	-		
eGFR, ml/min (Intercept: >60)						
≤60	3.78 (2.34-6.17)	<.001	2.35 (1.29-4.32)	.005		

Note: Only significant results are shown above. Detailed results are found in Table S3. Variables with greater than 20% missing data were excluded from the regression analysis and this table.

Abbreviations: 95% CI, 95% confidence interval; CCF, congestive heart failure; COPD, chronic obstructive pulmonary disease; CRP, C-reactive protein; eGFR, estimated glomerular filtration rate; HTN, hypertension; WCC, white cell count.

proportion of myalgia reporting in patients who have been discharged vs those who have died in hospital has been previously noted.¹⁷ HTN has also repeatedly been found to be associated with increased odds of disease severity and mortality from COVID-19. There is debate as to whether this association might be confounded by the use of ACE inhibitors or angiotensin receptor blockers in the treatment of HTN, and whether such medications might worsen disease.^{22,23} Our study found no association between regular use of ACE inhibitor or ARB medication and mortality, suggesting that HTN may increase mortality risk independent of pharmacological treatment with such medications. Poor baseline renal function was another predictor of mortality

identified within our study. This is consistent with a recent metaanalysis of 1389 patients, which showed an association between CKD and enhanced risk of severe COVID-19 infection.²⁴ Postulated mechanisms for this increased risk include uremia-induced impairment in T and B lymphocyte function and increased cytokine production.^{25,26}

Regarding the cohort of patients admitted to ITU, characteristics overrepresented in this group and associated with ITU admission broadly paralleled those associated with increased likelihood of mortality, with the exception of age and patient comorbidities. The finding that male sex and BAME ethnicities were overrepresented in the ITU cohort is consistent with previous studies, which have demonstrated

-WILEY 7 of 9

TABLE 4 ITU logistic regression: risk factors associated with admission to ITU

n = 55	Univariable OR (95% CI)	P-value	Multivariable OR (95% CI)	P-value
Demographics				
Age, years	0.97 (0.96-0.99)	.002	-	-
Sex (vs Female)				
Male	3.14 (1.62-6.49)	.001	2.80 (1.29-6.56)	.012
Ethnicity (vs Asian)				
Black	1.93 (0.66-5.52)	.223	-	-
White	1.52 (0.69-3.44)	.305	-	-
Other	0.37 (0.16-0.85)	.019	-	-
Ethnicity (white vs everything else	e)			
White	0.27 (0.13-0.52)	<.001	-	-
Symptoms present (vs not present)				
Shortness of breath	3.21 (1.33-9.57)	.018	3.59 (1.32-12.73)	.024
Fever	2.40 (1.18-5.31)	.021	-	-
Cough	2.88 (1.30-7.28)	.015	-	
Sputum	3.56 (1.24-9.61)	.014	5.00 (1.58-15.47)	.005
Lab findings				
Platelets, 10 9 /L (Intercept: 140-	400)			
<140	1.55 (0.68-3.33)	.275	2.48 (0.91-6.36)	.064
>400	0.38 (0.02-1.98)	.352	0.57 (0.03-3.41)	.613
ALT, U/L (Intercept: ≤45)				
>45	2.54 (1.31-4.87)	.005	2.41 (1.12-5.15)	.023
eGFR, ml/min (Intercept: >60)				
≤60	0.43 (0.20-0.86)	.021	-	-
ABG				
pH (Intercept: 7.35-7.45)				
<7.35	0.74 (0.20-2.28)	.628	-	-
>7.45	2.02 (1.04-4.02)	.041	-	-
Missing	0.04 (0.00-0.20)	.002	-	-
PO2, kPa (Intercept: >11.1)				
≤11.1	1.74 (0.64-5.58)	.306	-	-
Missing	0.02 (0.00-0.16)	.001	-	-
PCO2, kPa (Intercept: 4.67-6.4)				
<4.67	0.79 (0.40-1.57)	.499	-	-
>6.4	0.19 (0.03-0.75)	.036	-	-
Missing	0.01 (0.00-0.06)	<.001	-	-
HCO3, mmol/L (Intercept 22-28)				
<22	0.42 (0.16-0.97)	.056	-	-
>28	0.17 (0.03-0.62)	.020	-	-
Missing	0.02 (0.00-0.10)	<.001	-	-
Lactate, mmol/L (Intercept: ≤1.6)				
>1.6	0.65 (0.29-1.34)	.261	-	-
Missing	0.03 (0.00-0.12)	<.001	-	-

Note: Only significant results are shown above. Detailed results are found in Table S4. Variables with greater than 20% missing data were excluded from the regression analysis and this table.

Abbreviations: 95% CI, 95% confidence interval; ALT, alanine transaminase; eGFR, estimated glomerular filtration rate.

that severity of COVID-19 is greater in this demographic,^{7,16} although younger age and increased proportion of males in the BAME group compared to white ethnicity may confound the association of BAME ethnicity with ITU admission. Younger age and lack of comorbidities in the ITU cohort is presumed to be a consequence of adherence to the NICE guidelines on admission to critical care, which encourage assessment of frailty to determine potential benefit from critical care organ support in severe disease.²⁴ This inevitably favors the admission of younger patients with fewer comorbidities, whereas older patients with multiple comorbidities may face a ward-based ceiling of care.²⁴ SOB, fever, and cough are all part of the case definition, and their overrepresentation in the ITU cohort and associated increased odds of ITU admission suggests that patients presenting with these classic symptoms are more likely to develop severe disease than those presenting less typically. Arterial blood gas results on admission in this cohort demonstrate a picture of hypoxemia and hyperventilation with respiratory alkalosis, as expected in severely ill patients.

The overrepresentation of BAME groups in terms of both hospital and ITU admission is consistent with recent UK-based studies, and its cause is a current focus of public health research.⁷ Postulated reasons include higher risk of COVID-19 infection or greater severity of infection amongst BAME groups.⁷ The significantly higher proportion of BAME patients than white patients requiring ITU, ventilation, or CPAP in our cohort lends credence to the latter possibility. There is an increased prevalence of comorbidities, urban living, overcrowded households, lower socioeconomic status, and proportion in key worker roles in BAME groups vs white ethnicity. all of which are potential contributing factors.²⁷⁻²⁹ The lack of association between ethnicity and odds of mortality in our study is consistent with the Imperial College Healthcare NHS Trust study.⁷ but contrary to the study of 17 million UK health records,¹⁸ which found increased mortality risk for all non-white ethnicities. It is possible that the effect size of the influence of ethnicity on mortality is too small to detect in single-center studies. The association of white ethnicity with increased length of hospital stay may be accounted for by the older mean age of this group leading to an increased complexity of care or delayed discharge due to social care planning.

The main limitation of our study is its single-center nature. We recognize missing laboratory results as a potential limitation of our multivariate regression model (eg, d-dimer, ferritin, troponin, and blood gases), although this was accounted for through use of a maximum cut-off of 20% missing data for each variable. We do recognize that body mass index data on admission was unavailable to the authors, and thus, this study was unable to assess its effect on primary outcomes or exclude its potential confounding nature. We acknowledge that due to adherence to the NICE guidelines on admission to critical care²⁴ favoring younger healthier patients, this potential confounder should be taken into consideration when assessing ITU regression analysis results. We also recognize the lack of inclusion of initial treatments given to our cohort of patients as a limitation, preventing our study from assessing the impact of treatment on mortality and disease severity.

5 | CONCLUSION

Our study provides comprehensive characterization of presenting clinical features and predictors of mortality and ITU admission for hospitalized COVID-19 patients within our ethnically diverse population. Our study shows that features, such as older age, classic COVID-19 chest X-ray, SOB, WCC > 11 10^{9} /L, and eGFR ≤60 mL/min, found on admission should prompt the clinician to be aware of an increased odds of mortality for those patients. The risk factors for poor clinical outcomes identified within our study broadly correlate with those previously identified in previous UK and international studies and should facilitate the development of risk stratification algorithms for COVID-19 secondary care management in future.

AUTHORS' CONTRIBUTIONS

Conceptualization: MA, MC and GK.

Data Curation: MA, MC, SYS, BC, LJ, AM, EM, and AZ.

Methodology: MN, JT, MA and MC.

Formal Analysis: MN.

Writing - original draft, review and editing: MA, MC, MN, JT, SYS, BC,

LJ, AM, EM and GK.

Supervision: GK.

All authors have read and approved the final version of the manuscript.

Dr Michel Alhilani had full access to all of the data in this study and takes complete responsibility for the integrity of the data and the accuracy of the data analysis.

TRANSPARENCY STATEMENT

Dr Michel Alhilani affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

DATA AVAILABILITY STATEMENT

The authors confirm that the data supporting the findings of this study are available within the article and its supplementary materials.

ORCID

Michel Alhilani D https://orcid.org/0000-0001-5391-6459

REFERENCES

- World Health Organization. WHO Director-General's Opening Remarks at the Media Briefing on COVID-19-11 March 2020. Geneva: World Health Organization; 2020. https://www.who.int/dg/ speeches/detail/who-director-general-s-opening-remarks-at-the-mediabriefing-on-covid-19–11-march-2020. Accessed June 18, 2020.
- 2. European Centre for Disease Prevention and Control. COVID-19 situation update worldwide, as of June 4, 2020. Stockholm: European Centre for Disease Prevention and Control, 2020. https://www.ecdc.europa.eu/en/cases-2019-ncov-eueea. Accessed June 18, 2020.
- Rodriguez-Morales AJ, Cardona-Ospina JA, Gutiérrez-Ocampo E, et al. Clinical, laboratory and imaging features of COVID-19: a systematic review and meta-analysis. *Travel Med Infect Dis.* 2020;34: 101623. https://doi.org/10.1016/j.tmaid.2020.101623

- Chan JF, Yuan S, Kok KH, et al. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. *Lancet.* 2020;395(10223): 514-523. https://doi.org/10.1016/S0140-6736(20)30154-9
- Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet*. 2020;395(10223):507-513. https://doi.org/10.1016/S0140-6736(20)30211-7
- Moss P, Barlow G, Easom N, Lillie P, Samson A. Lessons for managing high-consequence infections from first COVID-19 cases in the UK. *Lancet.* 2020;395(10227):e46. https://doi.org/10.1016/S0140-6736 (20)30463-3
- Public Health England. Disparities in the Risk and Outcomes of COVID-19. London: Public Health England; 2020.
- Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet*. 2020;395(10223): 497-506. https://doi.org/10.1016/S0140-6736(20)30183-5
- Richardson S, Hirsch JS, Narasimhan M, et al. Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York City area. JAMA. 2020;323:2052-2059. https://doi.org/10.1001/jama.2020.6775
- Perez-Guzman PN, Daunt A, Mukherjee S, et al. Report 17 Clinical Characteristics and Predictors of Outcomes of Hospitalised Patients with COVID-19 in a London NHS Trust: a Retrospective Cohort Study. London: Imperial College London; 2020. https://doi.org/10. 25561/78613
- 11. Grasselli G, Zangrillo A, Zanella A, et al. Baseline characteristics and outcomes of 1591 patients infected with SARS-CoV-2 admitted to ICUs of the Lombardy region, Italy. JAMA. 2020;323:1574-1581. https://doi.org/10.1001/jama.2020.53944
- 12. Office for National Statistics. *Ethnic Group, National Identity and Religion.* London: Office for National Statistics; 2016.
- Malatesha G, Singh NK, Bharija A, Rehani B, Goel A. Comparison of arterial and venous pH, bicarbonate, PCO2 and PO2 in initial emergency department assessment. *Emerg Med J.* 2007;24(8):569-571. https://doi.org/10.1136/emj.2007.046979
- Yadav R, Sahoo D, Graham R. Thoracic imaging in COVID-19. Cleve Clin J Med. 2020;87:469-476. https://doi.org/10.3949/ccjm.87a. ccc032
- Furnival GM, Wilson RW. Regressions by leaps and bounds. Dent Tech. 2000;42(1):69-79. https://doi.org/10.1080/00401706.2000.10485982
- Docherty AB, Harrison EM, Green CA, et al. Features of 16,749 hospitalised UK patients with COVID-19 using the ISARIC WHO clinical characterisation protocol. medRxiv. January 1, 2020. https://doi.org/ 10.1101/2020.04.23.20076042
- Tomlins J, Hamilton F, Gunning S, Sheehy C, Moran E, MacGowan A. Clinical features of 95 sequential hospitalised patients with novel coronavirus 2019 disease (COVID-19), the first UKcohort. J Infect. 2020;81:e59–e61. https://doi.org/10.1016/j.jinf.2020.04.020
- Williamson E, Walker AJ, Bhaskaran KJ, et al. OpenSAFELY: factors associated with COVID-19-related hospital death in the linked electronic health records of 17 million adult NHS patients. MedRxiv, January 1, 2020. https://doi.org/10.1101/2020.05.06.20092999

 Deng Y, Liu W, Liu K, et al. Clinical characteristics of fatal and recovered cases of coronavirus disease 2019 in Wuhan, China: a retrospective study. *Chin Med J.* 2020;133(11):1261-1267. https://doi.org/10. 1097/CM9.00000000000824

-WILEY-

- Zhou F, Yu T, Du R, 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(10229):1054-1062. https://doi.org/ 10.1016/S0140-6736(20)30566-3
- Du RH, Liang LR, Yang CQ, et al. Predictors of mortality for patients with COVID-19 pneumonia caused by SARS-CoV-2: a prospective cohort study. *Eur Respir J.* 2020;55(5):2000524. https://doi.org/10. 1183/13993003.00524-2020
- Schiffrin EL, Flack JM, Ito S, Muntner P, Webb RC. Hypertension and COVID-19. Am J Hypertens. 2020;33(5):373-374. https://doi.org/10. 1093/ajh/hpaa057
- Fang L, Karakiulakis G, Roth M. Are patients with hypertension and diabetes mellitus at increased risk for COVID-19 infection? *Lancet Respir Med.* 2020;8(4):e21. https://doi.org/10.1016/S2213-2600(20)30116-8
- 24. National Institute for Health and Care Excellence. *COVID-19 Rapid Guideline: Critical Care in Adults*. London: National Institute for Health and Care Excellence; 2020. Guideline: NG159.
- Fernández-Fresnedo G, Ramos MA, González-Pardo MC, de Francisco ALM, López-Hoyos M, Arias M. B lymphopenia in uremia is related to an accelerated in vitro apoptosis and dysregulation of Bcl-2. Nephrol Dial Transplant. 2000;15(4):502-510. https://doi.org/10. 1093/ndt/15.4.502
- 26. Stenvinkel P, Ketteler M, Johnson RJ, et al. IL-10, IL-6, and TNFalpha: central factors in the altered cytokine network of uremia-the good, the bad, and the ugly. *Kidney Int.* 2005;67(4):1216-1233. https://doi.org/10.1111/j.1523-1755.2005.00200.x
- 27. Office for National Statistics. *Ethnicity and National Identity in England and Wales: 2011.* London: Office for National Statistics; 2012.
- Farquharson C, Rasul I, Sibieta L. Key Workers: Key Facts and Questions. London: The Institute for Fiscal Studies; 2020. https://www.ifs. org.uk/publications/14763. Accessed June 18, 2020.
- Pareek M, Bangash MN, Pareek N, et al. Ethnicity and COVID-19: an urgent public health research priority. *Lancet.* 2020;395(10234): 1421-1422. https://doi.org/10.1016/S0140-6736(20)30922-3

SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

How to cite this article: Alhilani M, Cohn M, Nakhoul M, et al. Predictors of mortality and ITU admission for COVID-19 patients admitted to a London district general hospital: A retrospective cohort study. *Health Sci Rep.* 2021;4:e404. doi: 10.1002/hsr2.404