## ORIGINAL ARTICLE

## Infection

## End-stage kidney disease patients from ethnic minorities and mortality in coronavirus disease 2019

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## Abstract

**Introduction:** Coronavirus disease 2019 (COVID-19) adversely affects patients who are older, multimorbid, and from Black, Asian or minority ethnicities (BAME). We assessed whether being from BAME is independently associated with mortality in end-stage kidney disease (ESKD) patients with COVID-19.

**Methods:** Prospective observational study in a single UK renal center. A study was conducted between March 10, 2020 and April 30, 2020. Demographics, socioeconomic deprivation (index of multiple deprivation), co-morbidities (Charlson comorbidity index [CCI]), and frailty data (clinical frailty score) were collected. The primary outcome was all-cause mortality. Data were censored on the 1st June 2020.

**Findings:** Overall, 191 of our 3379 ESKD patients contracted COVID-19 in the 8-week observation period; 84% hemodialysis, 5% peritoneal dialysis, and 11% kidney transplant recipients (KTR). Of these, 57% were male and 67% were from BAME groups (43% Asian, 17% Black, 2% mixed race, and 5% other). Mean CCI was 7.45 (SD 2.11) and 3.90 (SD 2.10) for dialysis patients and KTR, respectively. In our cohort, 60% of patients lived in areas classified as being in the most deprived 20% in the United Kingdom, and of these, 77% of patients were from BAME groups. The case fatality rate was 29%. Multivariable cox regression demonstrated that BAME (hazard ratio [HR]: 2.37, 95% CI: 1.22–4.61) was associated with all-cause mortality after adjustment for age, deprivation, co-morbidities, and frailty. Associations with all-cause mortality persisted in sensitivity analyses in patients from South Asian (HR: 2.52, 95% CI: 1.24–5.12) and Black (HR: 2.43, 95% CI: 1.04–5.67) ethnic backgrounds.

**Discussion:** BAME ESKD patients with COVID-19 are just over twice as likely to die compared to White patients, despite adjustment for age, deprivation, comorbidity, and frailty. This study highlights the need to develop strategies to improve BAME patient outcomes in future outbreaks of COVID-19.

#### **KEYWORDS**

coronavirus disease 2019, end-stage kidney disease, ethnicity, health care inequality, renal replacement therapy

## INTRODUCTION

Coronavirus disease 2019 (COVID-19) has been a global concern since December 2019, presenting with asymptomatic infection to life-threatening multiorgan failure.<sup>1</sup> It is increasingly recognized that comorbidity, aging, obesity, and frailty are associated with mortality in COVID-19.<sup>2</sup> End-stage kidney disease (ESKD) patients are highly co-morbid<sup>3</sup> and have a high prevalence of frailty<sup>4</sup>—a well-established predictor of poor outcomes in acutely hospitalized patients.<sup>5</sup> These factors, along with the metabolic milieu seen in ESKD and the requirement to administer immunosuppressants in kidney transplant recipients (KTR), mean that ESKD patients are at high risk of mortality in COVID-19; a hypothesis supported by early reports in ESKD cohorts.<sup>6</sup> In addition, ESKD patients, and particularly those on hemodialysis (HD), are more likely to contract COVID-19 because they need to regularly attend dialysis units.<sup>7</sup>

Ethnicity is emerging as a risk factor for mortality in COVID-19 in different populations,<sup>8</sup> but the reasons behind this association remain unclear.<sup>8</sup> This is germane to the ESKD population, given the prevalence of Black, Asian and minority ethnicity (BAME) patients is twice that of the UK population<sup>9</sup> and given a recent systematic review demonstrated ESKD patients from some ethnic minorities have a paradoxical long-term survival advantage.<sup>10</sup> Given BAME patients are more likely to be socio-economically deprived,<sup>11</sup> multimorbid,<sup>12</sup> and frail,<sup>13</sup> it therefore remains unclear whether any association between mortality and BAME status in ESKD patients with COVID-19 is independent of these factors.

Given the ongoing outbreak of COVID-19 across the world, including with new variants, this study assessed in the ESKD population whether being from BAME groups is independently associated with mortality in COVID-19.

## MATERIALS AND METHODS

## Study design and population

A prospective study was conducted on adult ESKD at the University Hospitals of Birmingham (UHB). As of March 1, 2020, UHB had 3379 patients with ESKD: 1686 were kidney transplant recipients (KTR), 258 were on peritoneal dialysis (PD) and 1435 were on hemodialysis (HD). Patients were included if they had severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) RNA identified from nasopharyngeal swabs using the VIASURE qRT-PCR.<sup>14</sup> Patients were swabbed if they were admitted to UHB with suspected COVID-19 or they presented to dialysis units/transplant clinics COVID-19 symptoms. Patients were identified over 8-weeks (March 10, 2020 to April 30, 2020) from admissions lists, laboratory reports, and through the electronic health records (EHRs). Patients were followed up using the EHR until the June 01, 2020, giving a follow-up period ranging between 4 and 12 weeks. The primary outcome for our study was all-cause mortality.

## **Ethical approval for study**

This analysis was conducted in accordance with both national and international standards for ethical conduct involving human research participants, including the UK standards set out by both the National Health Service (NHS) guidance on clinical audit and service development and the National Institute for Clinical Excellence (NICE) best practices guidance. Furthermore, the principles outlined in the 1964 Helsinki declaration and its later amendments (the latest being in 2001) were adhered too throughout this study.<sup>15</sup> Specific institutional approval was sought prior to proceeding with this analysis-with approval being granted on the basis that patient data were anonymized on collection from the EHR (CARMS approval number 16092). We were, on this basis, additionally exempt from the requirement to obtain written informed consent to undertake this analysis.

## Data collection, ethnicity determination, Charlson comorbidity index, clinical frailty score, and index of multiple deprivation

Baseline demographics were extracted from the EHR. Ethnicity was classified into the following categories: White, Black, South Asian (also referred to as Indo-Asian or as Indian-Subcontinent), mixed, or other. For this study, we compared BAME (combined Black, South Asian, Mixed and Other) with White ethnicity. Body mass index (BMI; kg/m<sup>2</sup>) was categorized into three groups: normal (18.5–24.9 kg/m<sup>2</sup>), overweight (25–29.9 kg/m<sup>2</sup>), and

obese ( $\geq$ 30 kg/m<sup>2</sup>).<sup>16</sup> Ethnicity adjusted BMI cut offs were used for South Asian patients<sup>16</sup>: normal (18.5–22.9 kg/m<sup>2</sup>), overweight (23–24.9 kg/m<sup>2</sup>), and obese ( $\geq$ 25 kg/m<sup>2</sup>). Comorbidities were collected from the EHR and used to calculate the Charlson comorbidity index (CCI).<sup>17</sup> Clinical frailty scores (CFS) were collected from the EHR for all patients admitted to UHB,<sup>18</sup> and where no CFS was documented, retrospective analysis of physiotherapy assessments in the EHR was performed to estimate the CFS. The index of multiple deprivation (IMD) was used to assess socioeconomic deprivation for the whole dialysis population under the care of UHB using postcode data.<sup>19</sup>

## Statistical analyses

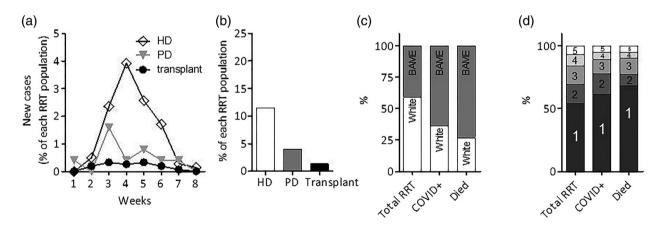
Normally distributed continuous variables were summarized using mean and standard deviation, with group comparisons being conducted using unpaired *t*-tests and one-way ANOVA. Non-normally distributed continuous variables were summarized using median and interquartile range (IQR), with comparisons being performed using Mann–Whitney-U tests. Categorical variables were summarized with counts and percentages, with comparisons being made using Chi-squared tests. A *p* value < 0.05 was used to designate statistical significance. Analyses were conducted on STATA SE 14.2.

Cox proportional hazards regression models were used for time-to-event analyses for all-cause mortality. Univariable cox regressions were conducted to assess all variables for associations with all-cause mortality, with an a-priori approach to the multivariable survival model being chosen given that socioeconomic deprivation, frailty, co-morbidity and age may affect this relationship. Sensitivity analyses were conducted to further assess this association in dialysis patients (excluding KTR) and when splitting ethnicity into White, Black, and Asian (>90% of BAME group). The Breslow method was used in the event of survival time ties and Schoenfeld residuals were used to ensure that there were no violation of the proportional hazards assumption in all cox regressions.

## RESULTS

# Case identification and evolution of the COVID-19 outbreak

A total 191 ESKD patients developed COVID-19 during the 8-week case ascertainment period (March 10 to April 30, 2020): 160 were on HD (83.8%), 10 on PD (5.2%) and 21 were a KTR (11.0%). The majority of COVID-19 cases were identified between Weeks 3 and 6 (March 24, 2020 to April 14, 2020; Figure 1(A)). The incidence of COVID-19 increased exponentially between Weeks 1 and 4 in the HD population; a pattern not replicated in the PD or KTR populations. During this period, 11% of the UHB HD, 4% of the PD, and 1% of the KTR UHB population contracted COVID-19 (Figure 1(B)).



**FIGURE 1** The evolution of the COVID-19 outbreak in the UHB ESKD population. (A) New confirmed COVID-19 cases stratified by RRT modality (HD—black square, PD—gray triangle, KTR—black circle). Cases expressed as weekly percentage of new cases within each RRT modality, with Week 1 commencing on the March 10, 2020. Denominator for each RRT modality populations within UHB fixed on the March 10, 2021. (B) Confirmed COVID-19 cases by RRT modality as a percentage of the total UHB RRT population. (C) Ethnicity of the UHB dialysis population, compared to the ethnicity of those who contracted COVID-19, compared to those that died from COVID-19. (D) IMD quintiles for the UHB dialysis population, compared to those that contracted COVID-19, compared to those that died. COVID-19, coronavirus disease 2019; HD, hemodialysis; IMD, index of multiple deprivation; KTR, kidney transplant recipient; PD, peritoneal dialysis; RRT, renal replacement therapy; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; UHB, University Hospitals Birmingham; UKRR, United Kingdom Renal Registry

#### **Patient characteristics**

Patient characteristics are reported according to ethnicity (Table 1). Overall, 66 (36%) of patients were White and 119 (64%) were from BAME groups (Figure 1(C)). This contrasts with the UHB dialysis cohort and the patients who died from COVID-19, with 41% and 73% of patients being from BAME groups respectively (Figure 1 (C)). South Asians were the commonest ethnic group in the BAME cohort (43%; Supplementary Table S1). BAME patients were younger and more likely to be in the most deprived IMD quintile. Additionally, BAME patients are more likely to be diabetic and less likely to have malignancy. When assessing co-morbidity burden using CCI scores, no statistically significant differences was observed between White and BAME patients.

Sixty percent of all cases were in the most deprived IMD quintile (Quintile 1) of the UK population. In contrast, 54% of the overall UHB dialysis cohort were from the most IMD quintile (Figure 1(D)). BAME patients in our cohort were much more likely to be in the most deprived quintile (70% vs. 39% in White ethnicity, p < 0.001; Table 1). When comparing dialysis and KTR patients in our cohort (Supplementary Table S2), dialysis patients were older, more likely to be frail and more likely to have greater degrees of comorbidity.

## Admissions to hospital in patients with COVID-19

During the study period, 12 patients acquired COVID-19 while already an inpatient and 128 were admitted with COVID-19, equating to a 67% admission rate for COVID-19. Most hospital admissions occurred between the third and sixth week of the study (March 24, 2020 to April 14, 2020), with over 50% of admissions occurring in the third and fourth week (March 24, 2020 to April 1, 2020).

## Factors associated with all-cause mortality

Overall, 56 patients (43 HD, 7 PD, and 6 KTR) died during the follow-up period (29.3% fatality rate; Table 2). Comparing survivors and those that died, patients who died were older, frailer and had higher mean CCI, with no differences in measures of socioeconomic deprivation or BMI being observed. Overall, 70% of PD patients died, compared with 27% of KTR and 29% of HD patients, respectively. The study follow-up period was 8.3 ( $\pm$ 1.2) weeks and no patients were lost to follow-up.

Univariable associations with all-cause mortality are shown in Table 3, with age, severe frailty (CFS 7-9),

comorbidity, and BAME being associated with all-cause mortality. BMI was not associated with mortality when treated as a categorical variable using standard and ethnicity-corrected BMI cut offs, nor when treated as a continuous variable.

Multivariable survival analysis demonstrated that BAME (HR: 2.37, 95% CI: 1.22–4.61) was associated with all-cause mortality (Table 3) despite adjustment for age, comorbidity, socioeconomic deprivation and frailty, including in sensitivity analysis in only dialysis patients (KTR excluded; HR: 2.14, 95% CI: 1.07–4.31; Supplementary Table S3). When Black and South Asian patients (>90% of BAME patients) were compared to White patients (Table 4), being South Asian (HR: 2.52, 95% CI: 1.24–5.12) or Black (HR: 2.43, 95% CI: 1.04–5.67) remained associated with all-cause mortality.

## DISCUSSION

Our study demonstrates that ESKD BAME patients in a large UK center are twice as likely to die after acquiring COVID-19 compared to their White counterparts. BAME status is associated with mortality despite adjustment for socioeconomic deprivation, age, comorbidity, and frailty—a critical observation given that our ESKD BAME patients were more likely to be deprived, diabetic and younger compared to their White counterparts. Our study demonstrates the urgent need to investigate this mortality inequality and highlights the critical need for renal services to protect high-risk patients from COVID-19 in future outbreaks.

Ethnicity is emerging as a predictor of poor outcomes in COVID-19.<sup>20</sup> The hypothesis is that BAME patients are more socioeconomically deprived, with poor access to housing, unemployment and overcrowding being known to be more prevalent in BAME populations.<sup>20</sup> Our study demonstrates that ethnicity remains associated with allcause mortality in ESKD patients with COVID-19 despite adjustment for socioeconomic deprivation when measured by IMD-a pattern replicated in patients from South Asian (Indian subcontinent) and Black ethnicities in sensitivity analysis. This is all the more remarkable given recent evidence summarized in a systematic review by Wilkinson et al. demonstrate a survival advantage for some ethnic minority groups with ESKD.<sup>10</sup> Shared sociocultural factors, not measured during IMD estimation, may explain our observation, including the prevalence of multi-generational housing<sup>21</sup>; different health beliefs about seeking professional help during the pandemic<sup>22</sup>; the effect of social stigmas associated with COVID-19 within different BAME communities<sup>20</sup> and lower levels of health literacy.<sup>23</sup> This demonstrates the complexity of TABLE 1 Baseline patient characteristics, comorbidity, and deprivation data in ESKD patients with COVID-19, according to their ethnicity

	White (n = 66)	Black, Asian and minority ethnicities $(n = 119)$	p values
Age (years; mean $\pm$ SD)	69.14 (±12.76)	62.81 (±13.53)	< 0.01
Male (%)	37 (56%)	68 (57%)	0.89
RRT modalities			
HD	55 (83%)	101 (85%)	0.78
PD	3 (5%)	7 (6%)	0.70
KTR	8 (12%)	11 (9%)	0.54
Body mass index <sup>a</sup>			
BMI (kg/m <sup>2</sup> ; mean $\pm$ SD)	29.15 (±5.43)	30.28 (±6.45)	0.34
% Normal BMI	10 (24%)	12 (16%)	0.31
% Overweight	15 (37%)	31 (41%)	0.62
% Obesity	16 (39%)	32 (43%)	0.69
CFS categories <sup>a</sup>			
CFS 1–3: nonfrail (%)	9 (18%)	25 (28%)	0.22
CFS 4–6: mild-moderate frailty (%)	34 (68%)	56 (62%)	0.56
CFS 7–9: severe frailty (%)	7 (14%)	9 (10%)	0.48
IMD deprivation <sup>a</sup>			
IMD quintile 1	24 (39%)	83 (70%)	< 0.01
IMD quintile 2	9 (15%)	21 (18%)	0.48
IMD quintile 3	10 (16%)	11 (9%)	0.23
IMD quintile 4	9 (15%)	2 (2%)	< 0.01
IMD quintile 5	9 (15%)	2 (2%)	< 0.01
CCI categories			
0–5 (%)	12 (18%)	30 (25%)	0.18
6–10 (%)	49 (74%)	82 (69%)	0.32
11–15 (%)	5 (8%)	7 (6%)	0.65
Mean CCI (± SD)	7.36 (±2.28)	6.89 (±2.35)	0.19
Comorbidities			
Diabetes mellitus (%)	23 (35%)	80 (67%)	< 0.01
Hypertension (%)	48 (74%)	95 (80%)	0.35
Ischemic heart disease (%)	19 (29%)	34 (29%)	0.98
Heart failure (%)	8 (12%)	14 (12%)	0.94
Peripheral vascular disease (%)	8 (12%)	13 (11%)	0.81
Previous stroke (%)	8 (12%)	19 (16%)	0.48
Dementia (%)	1 (2%)	2 (2%)	0.93
Chronic respiratory diseases (%)	10 (15%)	4 (3%)	< 0.01
Connective tissue diseases (%)	10 (15%)	9 (8%)	0.10
Peptic ulcer disease (%)	1 (2%)	3 (3%)	0.65
Chronic liver disease (%)	0 (0%)	4 (3%)	0.13
Malignancy (%)	11 (17%)	6 (5%)	< 0.01
Acquired immunodeficiency syndrome (%)	0 (0%)	0 (0%)	NA

Abbreviations: BAME, Black, Asian and minority ethnicities; BMI, body mass index; CCI, Charlson comorbidity index; CFS, Clinical frailty score;

HD, hemodialysis; HIV, human immunodeficiency virus; IMD, index of multiple deprivation; KTR, kidney transplant recipient; PD, peritoneal dialysis; SD, standard deviation.

<sup>a</sup>All percentages are calculated from patients with known values and does not account for missing values. Variables with missing data include BMI (72 patients), IMD (five patients) and CFS (from the admitted patients, four patients did not have a documented CFS).

investigating associations between ethnicity and mortality in COVID-19 and the critical need for cultural competence when developing healthcare guidance in future pandemic preparation. In addition to socio-cultural factors, heterogeneous biological responses to COVID-19 in BAME patients may explain the findings of our study, including different exposures to the Bacille-Camille-Guerin (BCG) vaccination, which has non-mycobacterial effects on cellular immunity,<sup>20</sup> and the variable prevalence of Vitamin D deficiency across different ethnicities<sup>24</sup>; a pertinent issue given Vitamin D deficiency is almost ubiquitous in ESKD patients and, itself, is associated with increased mortality.<sup>25</sup> It is notable that in a recently published London ESKD cohort that ethnicity was not associated with the risk of acquiring COVID-19.7 It can therefore be hypothesized that socio-cultural and biological factors may be associated more with the host response to COVID-19, given the critical nature of the viral load exposure in determining clinical outcomes,<sup>26</sup> rather than the risk of acquiring COVID-19 within the ESKD population.

Severe frailty is independently associated with mortality in this cohort, with the presence of severe frailty (CFS 7–9) being associated with approaching a threefold risk in mortality. The use of the Rockwood CFS<sup>18</sup> is recommended by the UK National Institute for Clinical Excellence (NICE) for assessment of whether patients who are over 65 with COVID-19 would benefit from escalation to critical care.<sup>27</sup> Our study supports the use of CFS in assessing the prognosis of ESKD patients with COVID-19 and lends support to the recently published work of Hewitt et al. who suggested that there was a fourfold increased association with mortality when comparing those with severe frailty (CFS 7–9) with those deemed not frail (CFS 1–2)<sup>28</sup>—findings replicated in our multivariable survival analysis in ESKD patients.

In contrast to reports that obesity is associated with increased mortality in the general population with COVID-19,29 obesity was not associated with all-cause mortality in our ESKD cohort, even when using ethnicity-specific BMI cut offs. ESKD patients who were overweight and obese appeared to be protected compared with those in the normal BMI group. These findings are consistent with the established obesity paradox in ESKD the population<sup>30</sup>: an observation likely explained by the higher fat and lean tissue mass content have when measured using dual energy X-ray absorptiometry (DEXA).<sup>31</sup> Subsequent observational studies have demonstrated that lean tissue mass losses are most strongly associated with poor outcomes in ESKD<sup>31</sup> and are associated with frailty,<sup>30</sup> relative overhydration and mortality.<sup>3</sup> It is therefore not surprising that 43% of severely frail patients in our cohort

were in the normal BMI category, compared with 18% in the non-frail and mild-moderate frail groups respectively. Furthermore, given the lower baseline mortality observed in the general population and earlier stages of CKD compared to the ESKD population,<sup>32</sup> the critical role obesity plays in the pathogenesis of acute respiratory distress syndrome (ARDS) during acute illness and given the additional armamentarium in dialysis patients of ultrafiltration in managing fluid overload in patients with ARDS,<sup>33,34</sup> it is not surprising that obesity has differential effects on mortality in the general/early CKD population in the context of acute respiratory failure precipitated by COVID-19.

Similarly, diabetes mellitus was not associated with mortality in our ESKD cohort with COVID-19 despite it being reported as being an important predictor of adverse outcomes in the general population. UK Renal Registry analyses in dialysis patients have demonstrated survival in diabetic and nondiabetic patients differs in younger patients, but in patients aged 65 years or over, 5-year survival between diabetics and non-diabetics is similar.<sup>35</sup> Given the mean age of our ESKD cohort is 65 years, and given 60% of our patients who died from COVID-19 were greater than 65 years, this likely explains our observation that diabetes mellitus was not associated with all-cause mortality in our study.

Our study has some strengths. First, cases were prospectively identified allowing for real time case ascertainment and data collection. Second, this is the first study to our knowledge that has sought to adjust for socioeconomic deprivation, comorbidity, and frailty on the association between ethnicity and mortality in COVID-19 in ESKD patients, providing a greater level of data granularity compared to the recent UK Renal Registry publication summarizing UK hemodialysis population outcomes with COVID-19.<sup>36</sup> This study also has limitations. The small number of KTR patients in our cohort mean that our findings should be applied to this population with caution. It is noteworthy, however, that our KTR patients with COVID-19 had a similar mortality rate to our dialysis patients (27% vs. 29%). The study is also relatively small with 191 ESKD patients. However, given UHB is the second largest renal center in the United Kingdom and is located in the second largest city in the United Kingdom, the findings from our study are applicable to similar innercity centers with similar patient demographics. Finally, the sensitivity of rtPCR testing for SARS-CoV-2 RNA is estimated to be approximately 70%, and there is emerging evidence that ESKD patients can asymptomatically seroconvert to form SARS-CoV-2 antibodies in the face of negative PCR tests.<sup>37</sup> Therefore, our findings, which are reported in symptomatic patients only, should be interpreted with caution and will be

**TABLE 2** Demographic, ethnicity, comorbidity, frailty, and socioeconomic deprivation data, comparing patients who survived and died with COVID-19

	Patients who survived (n = 135)	Patients who died $(n = 56)$	<i>p</i> valu
Age (years; mean $\pm$ SD)	63.08 (14.10)	69.86 (11.24)	< 0.01
Male (%)	74 (55%)	35 (63%)	0.33
Ethnicity <sup>a</sup>			
White (%)	52 (40%)	14 (25%)	0.07
Black (%)	22 (17%)	11 (20%)	0.58
South Asian (%)	50 (38%)	29 (53%)	0.06
Pakistani (%)	23 (18%)	15 (27%)	0.12
Indian (%)	14 (11%)	7 (13%)	0.67
Bangladeshi (%)	3 (2%)	1 (2%)	0.85
South Asian—Other (%)	10 (8%)	6 (11%)	0.45
Mixed race (%)	3 (2%)	0 (0%)	0.26
Other (%)	3 (2%)	1 (2%)	0.85
BAME (%)	78 (60%)	41 (75%)	0.06
RRT modality			
HD (%)	117 (87%)	43 (77%)	0.09
PD (%)	3 (2%)	7 (12%)	< 0.01
KTR (%)	15 (11%)	6 (11%)	0.94
Body mass index <sup>a</sup>			
BMI (kg/m <sup>2</sup> ; mean $\pm$ SD)	29.76 (0.61)	30.45 (1.23)	0.58
% Normal BMI	15 (17%)	7 (22%)	0.78
% Overweight	36 (41%)	11 (34%)	0.31
% Obese	36 (41%)	14 (44%)	0.81
CFS Categories <sup>a</sup>			
CFS 1–3: non frail (%)	28 (31%)	6 (12%)	0.10
CFS 4–6: Mild–moderate frailty (%)	57 (63%)	34 (65%)	0.02
CFS 7–9: Severe frailty (%)	5 (6%)	12 (23%)	< 0.01
Index of multiple deprivation <sup>a</sup>			
IMD quintile 1 (%)	73 (56%)	38 (68%)	0.08
IMD quintile 2 (%)	26 (20%)	5 (9%)	0.08
IMD quintile 3 (%)	14 (11%)	7 (13%)	0.67
IMD quintile 4 (%)	9 (7%)	3 (5%)	0.73
IMD quintile 5 (%)	8 (6%)	3 (5%)	0.88
CCI categories			
0-5 (%)	36 (27%)	8 (14%)	0.06
6–10 (%)	91 (67%)	43 (77%)	0.20
11–15 (%)	8 (6%)	5 (9%)	0.45
Mean CCI (95%CI)	6.77 (0.21)	7.75 (0.30)	< 0.01
Comorbidities	0 (0.22)		(0.01
Diabetes mellitus (%)	72 (53%)	34 (61%)	0.35
Hypertension (%)	101 (76%)	46 (82%)	0.35
Ischemic heart disease (%)	38 (28%)	40 (82 <i>%</i> ) 17 (30%)	0.35
Heart failure (%)	17 (13%)	5 (9%)	0.70

## TABLE 2 (Continued)

	Patients who survived (n = 135)	Patients who died ( $n = 56$ )	<i>p</i> value
Peripheral vascular disease (%)	13 (10%)	9 (16%)	0.20
Previous stroke (%)	20 (15%)	9 (16%)	0.83
Dementia (%)	2 (1%)	1 (2%)	0.88
Chronic respiratory diseases (%)	9 (7%)	6 (11%)	0.34
Connective tissue diseases (%)	15 (11%)	4 (7%)	0.40
Peptic ulcer disease (%)	4 (3%)	0 (0%)	0.19
Chronic liver disease (%)	3 (2%)	1 (2%)	0.84
Malignancy (%)	11 (8%)	7 (13%)	0.35
Acquired immunodeficiency syndrome (%)	0 (0%)	0 (0%)	

Abbreviations: BAME, Black, Asian and minority ethnicities; BMI, body mass index; CCI, Charlson comorbidity index; CFS, Clinical frailty score; HD, hemodialysis; HIV, human immunodeficiency virus; IMD, index of multiple deprivation; KTR, kidney transplant recipient; PD, peritoneal dialysis; SD, standard deviation.

<sup>a</sup>All percentages are calculated from patients with known values and does not account for missing values. Variables with missing data included ethnicity (five patients), BMI (72 patients), IMD (five patients) and CFS (from the admitted patients, four patients did not have a documented CFS).

	Univariable analysis (HR + 95% CI)	p value	Multivariable analysis (HR + 95% CI)	p value
Ethnicity				
White	1.00 (reference)			
BAME	2.02 (1.10-3.71)	p = 0.02	2.37 (1.22-4.61)	p = 0.01
Age	1.03 (1.01-1.06)	<i>p</i> < 0.01	1.02 (0.99–1.05)	p = 0.27
CFS categories				
1–3 (nonfrail)	1.00 (reference)		1.00 (reference)	
4–6 (mild-moderate)	2.30 (0.97-5.49)	p = 0.06	1.81 (0.68–4.84.	p = 0.24
7–9 (severe)	4.79 (1.80-12.79)	<i>p</i> = <0.01	4.08 (1.33-12.51)	<b>p</b> = 0.01
CCI continuous	1.16 (1.04–1.31)	p = 0.01	1.06 (0.88–1.29)	p = 0.55
IMD (quintiles; Q)				
Q1 (most deprived 20%)	1.00 (reference)		1.00 (reference)	
Q2-5 (remaining 80%)	0.64 (0.36–1.11)	p = 0.11	0.83 (0.44–1.55)	p = 0.55
Male	1.26 (0.73–2.16)	p = 0.41		
Diabetes mellitus	1.23 (0.93–1.64)	p = 0.15		
Hypertension	1.49 (0.75–2.96)	p = 0.25		
ACE or ARB use	0.90 (0.43-1.91)	p = 0.79		
Ethnicity-specific BMI categories				
Normal	1.00 (reference)			
Overweight	0.66 (0.26–1.72)	p = 0.40		
Obese	0.84 (0.34–2.09)	p = 0.71		

#### **TABLE 3** Univariable and multivariable associations with all-cause mortality in our cohort

Note: Bold values signify statistically significant hazard ratios (i.e. p < 0.05) from the multivariable Cox-regression.

Abbreviations: 95% CI, 95% confidence interval; ACEi, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; BAME, Black, Asian and minority ethnicities; BMI, body mass index; CCI, Charlson comorbidity index; CFS, clinical frailty score; IMD, index of multiple deprivation; HR, hazard ratio.

**TABLE 4** Univariable and multivariable associations with all-cause mortality in our patient cohort, splitting ethnicity into White, Black, and South Asian

	Univariable analysis (HR + 95% CI)	p value	Multivariable analysis (HR + 95% CI)	p value
BAME groups				
White	1.00 (reference)		1.00 (reference)	
Black	1.98 (0.90-4.37)	p = 0.09	2.43 (1.04-5.67)	<b>p</b> = 0.04
South Asian	2.20 (1.16-4.16)	p = 0.02	2.52 (1.24-5.12)	<b>p</b> = 0.01
Age	1.03 (1.01–1.05)	<i>p</i> < 0.01	1.02 (0.98–1.05)	<i>p</i> = 0.33
CFS categories				
1–3 (nonfrail)	1.00 (reference)		1.00 (reference)	
4–6 (mild-moderate)	2.30 (0.97-5.49)	p = 0.06	2.02 (0.72-5.65)	p = 0.18
7–9 (severe)	4.79 (1.80-12.79)	<b>p</b> = <0.01	4.26 (1.35-13.48)	<b>p</b> = 0.01
CCI continuous	1.16 (1.04–1.31)	p = 0.01	1.09 (0.90–1.31)	p = 0.38
IMD (quintiles; Q)				
Q1 (most deprived 20%)	1.00 (reference)		1.00 (reference)	
Q2-5 (remaining 80%)	0.64 (0.36-1.11)	p = 0.11	0.90 (0.47–1.72)	p = 0.75
Male	1.26 (0.73-2.16)	p = 0.41		
Diabetes mellitus	1.23 (0.93–1.64)	p = 0.15		
Hypertension	1.49 (0.75–2.96)	p = 0.25		
ACE or ARB use	0.90 (0.43-1.91)	p = 0.79		
BMI ethnicity-specific categories				
Normal	1.00 (reference)			
Overweight	0.66 (0.26–1.72)	p = 0.40		
Obese	0.84 (0.34–2.09)	p = 0.71		

*Note*: Bold values signify statistically significant hazard ratios (i.e. *p*<0.05) from the multivariable Cox-regression.

Abbreviations: 95%CI, 95% confidence interval; ACEi, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; BAME, Black, Asian and minority ethnicities; BMI, body mass index; CCI, Charlson comorbidity index; CFS, clinical frailty score; IMD, index of multiple deprivation; HR, hazard ratio.

further clarified once larger cohorts are published with access to SARS-CoV-2 serological testing.

## CONCLUSION

In conclusion, our study demonstrates that ESKD patients from BAME groups are twice as likely to die from COVID-19 when compared to their White counterparts, and this observation is not explained by age, socioeconomic deprivation, comorbidity or frailty. Our study also highlights the urgent need for renal centers to become culturally competent when disseminating guidance about COVID-19. Finally, our study highlights that ongoing issue that BAME ESKD patients suffer from health outcome inequality,<sup>38</sup> this time in the context of an infectious pandemic. The reasons for this, which are likely complex, need to be urgently investigated and tack-led if we want to ensure equality of health outcomes for patients from all ethnic backgrounds with ESKD in the United Kingdom.

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### **CONFLICT OF INTEREST**

Helen Eddington received an honorarium from the Vifor advisory board 2 years ago. All other authors have no disclosures.

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## REFERENCES

- den Bergh MFQK, Buiting AGM, Pas SD, Bentvelsen RG, van den Bijllaardt W, van Oudheusden AJG, et al. Prevalence and clinical presentation of health care workers with symptoms of coronavirus disease 2019 in 2 Dutch hospitals during an early phase of the pandemic. JAMA Netw Open. 2020 May 1;3(5): e209673–3.
- Guan W, Liang W, Zhao Y, Liang H, Chen Z, Li Y, et al. Comorbidity and its impact on 1590 patients with Covid-19 in China: a Nationwide analysis. Eur Respir J. 2020 Jan 1 [cited 2020 Jun 22];1–24. Available from: https://erj.ersjournals.com/ content/early/2020/03/17/13993003.00547-2020
- Tabinor M, Elphick E, Dudson M, Kwok CS, Lambie M, Davies SJ. Bioimpedance-defined overhydration predicts survival in end stage kidney failure (ESKF): systematic review and subgroup meta-analysis. Sci Rep. 2018;8(1):4441.
- 4. Anderson B, Correa G, Qasim M, Jackson T, Sharif A. P1436FRAILTY index and clinical frailty scale are superior to frailty phenotype and Edmonton Frail scale in mortality prediction: results from a large European haemodialysis cohort. Nephrol Dial Transplant [Internet]. 2020 Jun 1 [cited 2020 Jul 24];35(Supplement\_3):273. Available from: https://academic. oup.com/ndt/article/35/Supplement\_3/gfaa144.P1436/5853905
- Keeble E, Roberts HC, Williams CD, Van Oppen J, Conroy SP. Outcomes of hospital admissions among frail older people: a 2-year cohort study. Br J Gen Pract. 2019 Aug;69:e555–60.
- Bell S, Campbell J, McDonald J, O'Neill M, Watters C, Buck K, et al. COVID-19 in patients undergoing renal replacement therapy in Scotland: findings and experience from the Scottish renal registry. medRxiv. 2020:1–25.
- Corbett RW, Blakey S, Nitsch D, Loucaidou M, McLean A, Duncan N, et al. Epidemiology of COVID-19 in an urban dialysis center. J Am Soc Nephrol [Internet]. 2020 Jun 19 [cited 2020 Jul 11];1815–1823. Available from: https://jasn.asnjour nals.org/content/early/2020/06/18/ASN.2020040534
- Pan D, Sze S, Minhas JS, Bangash MN, Pareek N, Divall P, et al. The impact of ethnicity on clinical outcomes in COVID-19: a systematic review. EClinicalMedicine [Internet]. 2020 Jun [cited 2020 Jun 22]. Available from: https://www. thelancet.com/journals/eclinm/article/PIIS2589-5370(20)3014 8-6/abstract
- MacNeill SJ, Ford D, Evans K, Medcalf JF. Chapter 2 UK renal replacement therapy adult prevalence in 2016: national and Centre-specific analyses. Nephron. 2018;139(Suppl 1):47–74.
- Wilkinson E, Brettle A, Waqar M, Randhawa G. Inequalities and outcomes: end stage kidney disease in ethnic minorities. BMC Nephrol. 2019 Jun 26;20:234.
- Feng Z, Vlachantoni A, Falkingham J, Evandrou M. Ethnic differentials in health: the additional effect of ethnic density: ethnic density and health. Popul Space Place. 2017 May;23: e2030.1–16.

- Townsend MJ, Kyle TK, Stanford FC. Outcomes of COVID-19: disparities in obesity and by ethnicity/race. Int J Obes (Lond). 2020 Jul;9:1–3.
- Pradhananga S, Regmi K, Razzaq N, Ettefaghian A, Dey AB, Hewson D. Ethnic differences in the prevalence of frailty in the United Kingdom assessed using the electronic frailty index. AGING Med. 2019;2:168–73.
- Bosworth A, Whalley C, Poxon C, Wanigasooriya K, Pickles O, Aldera EL, et al. Rapid implementation and validation of a cold-chain free SARS-CoV-2 diagnostic testing workflow to support surge capacity. J Clin Virol. 2020 Jul;128:104469.
- World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. Bull World Health Organ. 2001;79 (4):373–4.
- Weir CB, Jan A. BMI classification percentile and cut off points. StatPearls [Internet]. Treasure Island, FL: StatPearls Publishing; 2020 [cited 2020 Aug 14]. Available from: http:// www.ncbi.nlm.nih.gov/books/NBK541070/
- Glasheen WP, Cordier T, Gumpina R, Haugh G, Davis J, Renda A. Charlson comorbidity index: ICD-9 update and ICD-10 translation. Am Health Drug Benefits. 2019 Jul;12: 188–97.
- Rockwood K, Song X, MacKnight C, Bergman H, Hogan DB, McDowell I, et al. A global clinical measure of fitness and frailty in elderly people. CMAJ Can Med Assoc J. 2005 Aug 30; 173(5):489–95.
- Heald A, Laing I, McLernon DJ, Donn R, Hartland AJ, Fryer AA, et al. Socioeconomic deprivation as measured by the index of multiple deprivation and its association with low sex hormone binding globulin in women. Open Biochem J. 2017 Mar 13;11:1–7.
- Khunti K, Singh AK, Pareek M, Hanif W. Is ethnicity linked to incidence or outcomes of Covid-19? BMJ [Internet]. 2020 Apr 20 [cited 2020 Jul 11];369:1–2. Available from: https://www. bmj.com/content/369/bmj.m1548
- Growing older in a South Asian family [Internet]. Centre for Ageing Better. [cited 2020 Aug 14]. Available from: https:// www.ageing-better.org.uk/blogs/growing-older-south-asianfamily
- 22. Sheikh S, Furnham A. A cross-cultural study of mental health beliefs and attitudes towards seeking professional help. Soc Psychiatry Psychiatr Epidemiol. 2000 Aug 1;35(7):326–34.
- Taylor DM, Bradley JA, Bradley C, Draper H, Johnson R, Metcalfe W, et al. Limited health literacy in advanced kidney disease. Kidney Int. 2016;90:685–95.
- Martineau AR, Jolliffe DA, Hooper RL, Greenberg L, Aloia JF, Bergman P, et al. Vitamin D supplementation to prevent acute respiratory tract infections: systematic review and metaanalysis of individual participant data. BMJ [Internet]. 2017 Feb 15 [cited 2020 Jul 11];356:1–14. Available from: https:// www.bmj.com/content/356/bmj.i6583
- 25. Wolf M, Shah A, Gutierrez O, Ankers E, Monroy M, Tamez H, et al. Vitamin D levels and early mortality among incident hemodialysis patients. Kidney Int. 2007 Oct 2;72:1004–13.
- Fajnzylber J, Regan J, Coxen K, Corry H, Wong C, Rosenthal A, et al. SARS-CoV-2 viral load is associated with increased disease severity and mortality. Nat Commun. 2020 Oct 30;11:5493.

- 27. Overview | COVID-19 rapid guideline: critical care in adults | Guidance | NICE [Internet]. [cited 2020 Jun 22]. Available from: https://www.nice.org.uk/guidance/ng159
- Hewitt J, Carter B, Vilches-Moraga A, Quinn TJ, Braude P, Verduri A, et al. The effect of frailty on survival in patients with COVID-19 (COPE): a multicentre, European, observational cohort study. Lancet Public Health [Internet]. 2020 Jun 30 [cited 2020 Jul 11];e444–e451. Available from: https://www. thelancet.com/journals/lanpub/article/PIIS2468-2667(20)30146-8/ abstract
- Anderson MR, Geleris J, Anderson DR, Zucker J, Nobel YR, Freedberg D, et al. Body mass index and risk for intubation or death in SARS-CoV-2 infection: a retrospective cohort study. Ann Intern Med [Internet]. 2020 Jul 29 [cited 2020 Sep 9]; 782–790. Available from: https://www.acpjournals.org
- Kalantar-Zadeh K, Rhee CM, Chou J, Ahmadi SF, Park J, Chen JLT, et al. The obesity paradox in kidney disease: how to reconcile it with obesity management. Kidney Int Rep. 2017 Feb 1;2(2):271–81.
- Pommer W. Preventive nephrology: the role of obesity in different stages of chronic kidney disease. Kidney Dis. 2018;4(4): 199–204.
- Go AS, Chertow GM, Fan D, McCulloch CE, Hsu C. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. N Engl J Med. 2004 Sep 23;351(13): 1296–305.
- Seitz KP, Caldwell ES, Hough CL. Fluid management in ARDS: an evaluation of current practice and the association between early diuretic use and hospital mortality. J Intensive Care. 2020 Dec;8(1):78.
- 34. van Mourik N, Metske HA, Hofstra JJ, Binnekade JM, Geerts BF, Schultz MJ, et al. Cumulative fluid balance predicts mortality and increases time on mechanical ventilation in

ARDS patients: an observational cohort study. PLoS One. 2019 Oct 30;14(10):e0224563.

- 35. Steenkamp R, Rao A, Roderick P. UK renal registry 17th annual report: chapter 5 survival and cause of death in UK adult patients on renal replacement therapy in 2013: national and Centre-specific analyses. Nephron. 2015;129(s1):99–129.
- 36. Savino M, Casula A, Santhakumaran S, Pitcher D, Wong E, Magadi W, et al. Sociodemographic features and mortality of individuals on haemodialysis treatment who test positive for SARS-CoV-2: a UKrenal registry data analysis. PLoS One. 2020 Oct 23;15:e0241263.
- Clarke C, Prendecki M, Dhutia A, Ali MA, Sajjad H, Shivakumar O, et al. High prevalence of asymptomatic COVID-19 infection in hemodialysis patients detected using serologic screening. J Am Soc Nephrol. 2020 Sep 1;31:1969–75.
- Caskey F, Dreyer G, Evans K, Methven S, Scott J. Kidney health inequalities in the UK- an agenda for change. Kidney Research UK; 2019;1–20.

#### SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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