Ethnicity and risk of death in patients hospitalised for COVID-19 infection in the UK: an observational cohort study in an urban catchment area

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ABSTRACT

Background Studies suggest that certain black and Asian minority ethnic groups experience poorer outcomes from COVID-19, but these studies have not provided insight into potential reasons for this. We hypothesised that outcomes would be poorer for those of South Asian ethnicity hospitalised from a confirmed SARS-CoV-2 infection, once confounding factors, health-seeking behaviours and community demographics were considered, and that this might reflect a more aggressive disease course in these patients.

Methods Patients with confirmed SARS-CoV-2 infection requiring admission to University Hospitals Birmingham NHS Foundation Trust (UHB) in Birmingham, UK between 10 March 2020 and 17 April 2020 were included. Standardised admission ratio (SAR) and standardised mortality ratio (SMR) were calculated using observed COVID-19 admissions/deaths and 2011 census data. Adjusted HR for mortality was estimated using Cox proportional hazard model adjusting and propensity score matching.

Results All patients admitted to UHB with COVID-19 during the study period were included (2217 in total). 58% were male, 69.5% were white and the majority (80.2%) had comorbidities. 18.5% were of South Asian ethnicity, and these patients were more likely to be younger and have no comorbidities, but twice the prevalence of diabetes than white patients. SAR and SMR suggested more admissions and deaths in South Asian patients than would be predicted and they were more likely to present with severe disease despite no delay in presentation since symptom onset. South Asian ethnicity was associated with an increased risk of death, both by Cox regression (HR 1.4, 95% CI 1.2 to 1.8), after adjusting for age, sex, deprivation and comorbidities, and by propensity score matching, matching for the same factors but categorising ethnicity into South Asian or not (HR 1.3, 95% CI 1.0 to 1.6).

Conclusions Those of South Asian ethnicity appear at risk of worse COVID-19 outcomes. Further studies need to establish the underlying mechanistic pathways.

TINTRODUCTION

COVID-19 was identified in January 2020 and given its designated name by the WHO in February 2020. Initial reports from China, Italy and the USA focused on risk factors which predisposed individuals to severe manifestations of infection such as viral pneumonia and adult respiratory distress syndrome (ARDS) requiring critical care support and death, including age, male sex and comorbidities.

A more recent report from the Centers for Disease Control and Prevention in the USA described an early sign of non-EU Hispanic, black people being disproportionately affected by COVID-19 hospitalisation. In the UK, Intensive Care National Audit and Research Centre reports described that a higher proportion of patients requiring critical care for COVID-19 were of Asian and black ethnicity compared with pre-COVID-19 historical data (2017–2019) for patients who required critical care for viral pneumonia. Since then, two studies, one from Office for National Statistics analysing over 10 000 deaths in UK and...
another examining around 5000 deaths from primary care records, concluded twofold to threefold high death rates in ethnic minority groups after accounting for important confounders. However, both studies reported mortality at a population level that could be a reflection of higher infection rates in these ethnic groups rather than a higher case fatality rate.

The West Midlands is experiencing a high incidence of COVID-19-associated hospitalisations. This is particularly marked in Birmingham, which has a higher than average percentage of minority ethnic groups, with the 2011 census reporting the following percentages: South Asian 23.4%, black 7.8%, mixed ethnicity 4.1%, others 1.8% and a lower than average white ethnic group at 63.12

University Hospitals Birmingham NHS Foundation Trust (UHB) is one of the largest National Health Service (NHS) Trusts in England, providing direct acute services and specialist care across four hospital sites, including 2.2 million patient episodes per year, with 2750 beds and an expanded ITU capacity of up to 250 beds during the COVID-19 pandemic. UHB constitutes four acute hospital sites following organisational merger in 2018. At present the Queen Elizabeth Hospital Birmingham (QEH) runs a fully electronic healthcare record (EHR) (PICS; Birmingham Systems, in place since 1999), while the other three sites currently run mixed electronic and paper healthcare records and a shared primary and secondary care record (Your Care Connected). UHB provides secondary care to a diverse population of 1.3 million in Birmingham and Solihull and provides a full range of tertiary services to the West Midlands region.

It was hypothesised that South Asian ethnicity would form a risk factor for the most severe respiratory manifestations of COVID-19 infection, even once age, sex, medical conditions and social deprivation were taken into account, and therefore:

▸ They have more admissions than would be expected given the proportion of different ethnic groups within the Birmingham Trust catchment area (based on the last census data).

▸ They have worse outcomes (death and/or admission to critical care) from hospitalised COVID-19 viral infection than white ethnic group, even once age, gender, deprivation and comorbidities were accounted for.

▸ They have more severe disease on presentation based on a severity score which could not be explained by duration of symptoms, compared with non-South Asian patients.

The study had the following aims:

▸ To identify all COVID-19 confirmed patients admitted to UHB hospital within a determined timeframe.

▸ To determine the expected and observed admission and death rates given the local population.

▸ To determine whether South Asian ethnicity was associated with poor outcomes following hospitalisation with confirmed COVID-19 infection, once potentially confounding factors were considered.

▸ To explore if disease presentation was more severe in patients of South Asian ethnicity and if there was any evidence of a delayed presentation to hospital.

METHODS

This retrospective cohort study, using prospectively collected data, was conducted in affiliation with PIONEER, the UK Health Data Research Hub in acute care.

Study population

All patients with a confirmed positive SARS-CoV-2 swab result between 09:00 on 10 March 2020 and 16:00 on 17 April 2020 and who were admitted to UHB at the time of or up to 2 weeks following their first positive SARS-CoV-2 swab test were included. COVID-19 cases were confirmed following a nasopharyngeal and oropharyngeal swab in all cases,15 which were processed in accordance with NHS guidance within UHB NHS laboratories.14 Mortality and (in those alive) patient admission status (discharged and alive, continued admission and alive) were assessed on 12 May 2020.

Data collection and variable definitions

Patient demographics and clinical data were collected from the EHR and from mandatory data sets within the Trust. Clinician-confirmed comorbidities were available from the EHR, the depth of which was enhanced by access to a summary primary care record (Your Care Connected) and further enriched with diagnostic codes derived from previous hospital episodes. The EHR encodes diagnoses using NHS Digital SNOMED CT browser15 alongside and mapped on to the International Classification of Diseases (ICD)-10 codes,16 allowing for the presentation and inclusion of historically entered ICD-10 codes. Comorbidities of interest were defined by those associated with poor outcomes from previous publications17 18 in order to determine the impact of multimorbidity.18 The most common clusters of diagnostic categories are listed in table 1. A simple count of comorbidities was undertaken to determine the impact of multimorbidity, as described.18 English Indices of Deprivation scores were calculated using postcodes from the current data provided by the UK’s Ministry of Housing, Communities and Local Government (2019) report.19 Seven main types of deprivation are considered in the Index of Multiple Deprivation 2019—income, employment, education, health, crime, access to housing and services, and living environment—and these are combined to form the overall measure of multiple deprivation.

Ethnicity was self-reported by the patient or their family members on admission to hospital. Where these data were missing, it was gathered from previous admissions and by reviewing primary and secondary medical records. If this was not available (as was the case in 91 patients), ethnicity was imputed from the modal ethnicity
Table 1  All patients with a confirmed positive SARS-CoV-2 swab during the study period

<table>
<thead>
<tr>
<th></th>
<th>All patients</th>
<th>White ethnicity</th>
<th>Asian ethnicity</th>
<th>Black ethnicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>2217</td>
<td>1540</td>
<td>410</td>
<td>134</td>
</tr>
<tr>
<td>Age in years, median (IQR)</td>
<td>73 (58–84)</td>
<td>77 (66–86)</td>
<td>61 (45–73)</td>
<td>62 (53–79)</td>
</tr>
<tr>
<td>Sex, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>927 (41.8)</td>
<td>639 (41.5)</td>
<td>170 (41.5)</td>
<td>59 (44.0)</td>
</tr>
<tr>
<td>Male</td>
<td>1290 (58.2)</td>
<td>901 (58.5)</td>
<td>240 (58.5)</td>
<td>75 (56.0)</td>
</tr>
<tr>
<td>Self-reported ethnicity, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>1540 (69.5)</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Mixed/multiple</td>
<td>18 (0.8)</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>South Asian/South Asian British</td>
<td>410 (18.5)</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Black/African/Caribbean/black British</td>
<td>134 (6.0)</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Other ethnic group</td>
<td>67 (3.0)</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Preferred not to say</td>
<td>22 (1.0)</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Not known</td>
<td>26 (1.2)</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Comorbidity count, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>439 (19.8)</td>
<td>255 (16.6)</td>
<td>114 (27.8)</td>
<td>25 (18.7)</td>
</tr>
<tr>
<td>1–2</td>
<td>888 (40.1)</td>
<td>620 (40.3)</td>
<td>155 (37.8)</td>
<td>61 (45.5)</td>
</tr>
<tr>
<td>3 or more</td>
<td>890 (40.1)</td>
<td>665 (43.2)</td>
<td>141 (34.4)</td>
<td>48 (35.8)</td>
</tr>
<tr>
<td>Morbidities, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>864 (39.0)</td>
<td>649 (42.1)</td>
<td>126 (30.7)</td>
<td>50 (37.3)</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>268 (12.1)</td>
<td>233 (15.1)</td>
<td>18 (4.4)</td>
<td>10 (7.5)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>464 (20.9)</td>
<td>404 (26.2)</td>
<td>26 (6.3)</td>
<td>20 (14.9)</td>
</tr>
<tr>
<td>Ischaemic heart disease, angina, myocardial infarct</td>
<td>546 (24.6)</td>
<td>404 (26.2)</td>
<td>100 (24.4)</td>
<td>24 (17.9)</td>
</tr>
<tr>
<td>Diabetes (type 1 and 2)</td>
<td>752 (33.9)</td>
<td>434 (28.2)</td>
<td>197 (48.0)</td>
<td>72 (53.7)</td>
</tr>
<tr>
<td>Asthma</td>
<td>439 (19.8)</td>
<td>290 (18.8)</td>
<td>91 (22.2)</td>
<td>34 (25.4)</td>
</tr>
<tr>
<td>COPD</td>
<td>376 (17.0)</td>
<td>333 (21.6)</td>
<td>20 (4.9)</td>
<td>14 (10.5)</td>
</tr>
<tr>
<td>Interstitial lung disease</td>
<td>49 (2.2)</td>
<td>40 (2.6)</td>
<td>4 (1.0)</td>
<td>2 (1.5)</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>511 (23.0)</td>
<td>338 (21.9)</td>
<td>111 (27.1)</td>
<td>42 (31.3)</td>
</tr>
<tr>
<td>Any active malignancy</td>
<td>152 (6.9)</td>
<td>124 (8.1)</td>
<td>12 (2.9)</td>
<td>7 (5.2)</td>
</tr>
<tr>
<td>Dementia (all types)</td>
<td>326 (14.7)</td>
<td>283 (18.4)</td>
<td>22 (5.4)</td>
<td>10 (7.5)</td>
</tr>
<tr>
<td>Obesity</td>
<td>267 (12.0)</td>
<td>174 (11.3)</td>
<td>60 (14.6)</td>
<td>12 (9.0)</td>
</tr>
<tr>
<td>English Indices of Deprivation, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (most deprived)</td>
<td>1003 (45.2)</td>
<td>554 (36.0)</td>
<td>276 (67.3)</td>
<td>89 (66.4)</td>
</tr>
<tr>
<td>2</td>
<td>416 (18.8)</td>
<td>320 (20.8)</td>
<td>50 (12.2)</td>
<td>26 (19.4)</td>
</tr>
<tr>
<td>3</td>
<td>311 (14.1)</td>
<td>263 (17.1)</td>
<td>29 (7.1)</td>
<td>11 (8.2)</td>
</tr>
<tr>
<td>4</td>
<td>230 (10.3)</td>
<td>195 (12.7)</td>
<td>18 (4.4)</td>
<td>4 (3.0)</td>
</tr>
<tr>
<td>5 (least deprived)</td>
<td>225 (10.1)</td>
<td>195 (12.7)</td>
<td>20 (4.9)</td>
<td>3 (2.2)</td>
</tr>
<tr>
<td>Missing, n (%)</td>
<td>32 (1.4)</td>
<td>13 (0.8)</td>
<td>17 (4.2)</td>
<td>1 (0.8)</td>
</tr>
<tr>
<td>Recovered and discharged, n (%)</td>
<td>1052 (47.5)</td>
<td>679 (44.1)</td>
<td>225 (54.9)</td>
<td>76 (56.7)</td>
</tr>
<tr>
<td>Remain admitted at point of data census, n (%)</td>
<td>554 (25.0)</td>
<td>411 (26.7)</td>
<td>79 (19.3)</td>
<td>26 (19.4)</td>
</tr>
<tr>
<td>Died, n (%)</td>
<td>611 (27.5)</td>
<td>450 (29.2)</td>
<td>106 (25.9)</td>
<td>32 (23.9)</td>
</tr>
<tr>
<td>Duration of symptoms prior to admission (in days), n where data were available (% of 567)</td>
<td>567</td>
<td>350 (61.7)</td>
<td>123 (21.7)</td>
<td>37 (6.5)</td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>7 (3–10)</td>
<td>6 (3–10)</td>
<td>7 (4–10)</td>
<td>7 (3.5–13.5)</td>
</tr>
</tbody>
</table>
of patients with the same surname in the EHR database where possible, as previously described, but remained unavailable in 48 patients (see table 1 for missing data). Ethnicity was grouped as per national guidelines.21

Severity of COVID-19 on admission
Physician-determined severity of COVID-19 on first admission was categorised using a pragmatic and locally developed score which made use of baseline physiological assessments and oxygen requirements to identify those on admission to hospital who were in need of urgent critical care assessments for respiratory support, and is as follows:

- Patients were considered to have severe respiratory manifestations of COVID-19 infection if COVID-19 was suspected and the patient required inspired oxygen ≥50% to maintain targeted oxygen saturations (>93% except in the presence of type 2 respiratory failure where the target saturations were 88%–92%) with respiratory pathology thought driven by COVID-19 illness.
- If not severe, patients were considered to have moderate severity respiratory manifestations of COVID-19 infection if COVID-19 was suspected and the patient required inspired oxygen of >4 L/min or inspired oxygen >28% to maintain target oxygen saturations.
- Patients were considered to have mild severity respiratory manifestations of COVID-19 infection if the patient had respiratory symptoms but did not meet the severe or moderate criteria as described above.

Baseline physiological assessments to determine severity of COVID-19 were considered to be those taken within 24 hours either side of the SARS-CoV-2 swab collection time, of which the earliest available measurement was used. Since not all patients were admitted within 24 hours of their SARS-CoV-2 swab test, and since these assessments are only routinely recorded in the EHR system for QEHB patients, baseline severity scores were only available for a subset of patients (736 of 2217).

To determine if disease severity on admission reflected duration of illness, medical clerking notes were reviewed to determine the duration of symptoms prior to admission. This was available in only a subset of patients (567 of 2217).

Outcomes
The primary outcome was death while in hospital or post discharge until 12 May 2020. For those patients discharged from hospital, primary care records were checked and any patients admitted to hospital with COVID-19 and discharged who had died in the community within the censor period were noted. Those with an ongoing admission were censored on the study end date.

Statistics
Baseline characteristics
Baseline characteristics for the total population and ethnic communities are presented as mean (SD) or median (IQR) for continuous variables and as frequency (percentage) for categorical variables. Ethnic groups were compared by age, sex, comorbidity and severity on presentation.

Table 1

<table>
<thead>
<tr>
<th>Documented, n</th>
<th>All patients</th>
<th>White ethnicity</th>
<th>Asian ethnicity</th>
<th>Black ethnicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild, n (%)</td>
<td>736</td>
<td>483</td>
<td>137</td>
<td>53</td>
</tr>
<tr>
<td>Moderate, n (%)</td>
<td>449 (61)</td>
<td>295 (61.1)</td>
<td>79 (57.7)</td>
<td>36 (67.9)</td>
</tr>
<tr>
<td>Severe, n (%)</td>
<td>185 (25.1)</td>
<td>134 (27.7)</td>
<td>24 (17.5)</td>
<td>10 (18.9)</td>
</tr>
<tr>
<td>Care escalation to ITU, n (%)</td>
<td>102 (13.9)</td>
<td>54 (11.2)</td>
<td>34 (24.8)</td>
<td>7 (13.2)</td>
</tr>
<tr>
<td>LOS in full days, median (IQR)</td>
<td>269 (12.1)</td>
<td>133 (8.6)</td>
<td>86 (21.0)</td>
<td>21 (15.7)</td>
</tr>
</tbody>
</table>

Data are number (percentage) unless otherwise stated. Ethnicity was self-reported or inferred (see the Methods section). Medical conditions were physician-confirmed and checked against admission and linked primary care notes. English Indices of Deprivation were calculated using postcode. Severity was determined by respiratory oxygen requirements (see the Methods section). Subgroup data are provided for those ethnicities which represented more than 5% of the whole population.

For English Indices of Deprivation, the quintiles were as follows: quintile 1=33.5–78.1; quintile 2=21.7–33.2; quintile 3=14.4–21.5; quintile 4=8.8–14.1; quintile 5=1.4–8.6.

COPD, chronic obstructive pulmonary disease; LOS, length of stay; N/A, not applicable.
Standardised admission rate and standardised mortality rate by ethnicity

Ethnicity data for the Birmingham and Solihull area from the 2011 census were used to estimate expected numbers of admissions and deaths for each ethnic category conditional on the observed numbers and sex-specific age distributions of COVID-19 admissions and deaths in UHB. The ratios of observed to expected numbers were calculated to provide standardised admission ratio (SAR) and standardised mortality ratio (SMR) for each ethnic category, and 95%, 99% and 99.9% CIs were obtained using the mid-p exact test.22

Predictors of mortality

The overall effects of age, sex, ethnicity, comorbidities and admission severity on mortality were tested by univariable analysis. The effect of ethnicity on mortality was then considered adjusting for age, sex, comorbidity counts and deprivation in a multivariable analysis. Cox model was used to derive adjusted HR (aHR) for mortality, defined as death from any cause after COVID-19. Survival time was calculated as the time between the collection of a sample on clinical suspicion to the date of death or study end date and was used for Kaplan-Meier estimates. Multiple parameterisations were tested for patient age, including linear fit, square-root transformation, categorical groupings and natural cubic splines. Categorical variables were fitted for sex, ethnicity, deprivation score quintiles and number of clinically assessed comorbidities. The proportional hazards assumption was tested through correlation of the scaled Schoenfeld residuals with survival time, with hypothesis tests for independence.23 Models were then tested using propensity score matching,24 where age, sex, social deprivation index and comorbidities were matched and ethnicity was treated as a dichotomous variable. Models were fitted in R V.3.6.3 using the survival package and twang package in ‘r’ (www.r-project.org).25 All p values are reported exactly and no corrections were made for multiple comparisons unless stated.

Patient and public involvement

Three hundred and two patients and public members were consulted as to the use of health data to improve the care for people with acute, unplanned illness. A group of patients recovering from COVID-19 specifically were asked and supported the use of routinely collected health data to investigate the relationship between poor outcomes and ethnicity. A working group of staff and patients from black and Asian minority ethnic groups discussed the results and how they should be disseminated.

RESULTS

The study analysed 2217 consecutive patients admitted to UHB with a swab-proven diagnosis of COVID-19. A modified Consolidated Standards of Reporting Trials diagram (online supplementary figure S1) and a summary of the demographic and clinical characteristics on admission (table 1) are shown. Most patients (n=2132) had a Birmingham postcode. The majority of patients were male (1290 of 2217; 58.2%) and white (1540 of 2217; 69.5%). High levels of comorbidity were identified across all ethnic groups (with 40.1% of patients having three or more comorbidities).

Of note, up to 50% had missing morbidity data and 30% had missing ethnicity data using the secondary care records for the COVID-19-related admission alone, but >96% of ethnicity data and all available morbidity data were resolved through review of primary and secondary care records.

Comparison of baseline characteristics between ethnicities

South Asian patients, when compared with white patients, were younger (median age 61 years vs 77 years, p<0.001), had a higher prevalence of diabetes mellitus (48.1% vs 28.2%, p<0.001) but lower prevalence of dementia (5.4% vs 18.9%), chronic obstructive pulmonary disease (COPD) (4.9% vs 21.6%), atrial fibrillation (6.3% vs 26.2%) and cerebrovascular disease (4.4% vs 15.1%) (p<0.0001 for all). Similar to the South Asian patients, black ethnic population were younger (median age 62 years), had a higher prevalence of diabetes mellitus (53.7%) but lower prevalence of other key comorbidities than the white population. Two-thirds of the South Asian and black ethnicity came from the most deprived quintile of deprivation compared with 36% from the white patients.

Across the course of data collection, the proportion of patients presenting from different ethnic groups was relatively stable (online supplementary figure S2), suggesting no differential transmission related to ethnic group within the location and timeframe studied.

SAR in different ethnicities

Age and sex SAR (95% CI) for South Asian women was 74% higher (SAR 1.7, 95% CI 1.5 to 2.0) and for South Asian men 63% higher (SAR 1.6, 95% CI 1.4 to 1.9) than the standard population (see online supplementary table S1). In contrast white patients were less likely to be admitted in comparison with the standard population (white women: 0.8 (0.8–0.9); white men: 0.9 (0.8–0.9)). Admission rates were similar to expected rates of the standard population for black ethnicity.

Severity of COVID-19 at presentation in different ethnicities

In 736 patients admitted directly to the QEH site, the severity of COVID-19 recorded on admission identified 185 (25.1%) classified as moderate and 102 (13.9%) classified as severe. In this data set a higher proportion of South Asians than whites were assessed to have severe disease on presentation (34 of 137 (24.8%) vs 54 of 483 (11.2%), p<0.0001) online supplementary table
### Table 2: Comparison of demographics of patients who met the primary endpoint of death up to and including 12 May 2020

<table>
<thead>
<tr>
<th></th>
<th>Patients currently alive (admitted or discharged)</th>
<th>Patients discharged and alive</th>
<th>Patients still admitted/receiving inpatient care and alive</th>
<th>Patients who died</th>
<th>P value comparing all alive patients and patients who died</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>1448</td>
<td>1372</td>
<td>76</td>
<td>769</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age, IQR and range</td>
<td>68 (52–80)</td>
<td>68 (52–80)</td>
<td>66 (54–76)</td>
<td>80 (71–887)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Sex, n (%) (female)</td>
<td>637 (44.0)</td>
<td>616 (44.9)</td>
<td>21 (27.6)</td>
<td>290 (37.7)</td>
<td>0.004</td>
</tr>
<tr>
<td>Self-reported ethnicity, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>White</td>
<td>958 (66.2)</td>
<td>906 (66.0)</td>
<td>52 (68.4)</td>
<td>582 (75.7)</td>
<td></td>
</tr>
<tr>
<td>Mixed/multiple</td>
<td>10 (0.7)</td>
<td>10 (0.7)</td>
<td>0 (0.0)</td>
<td>8 (1.0)</td>
<td></td>
</tr>
<tr>
<td>South Asian/South Asian British</td>
<td>290 (20.0)</td>
<td>275 (20.0)</td>
<td>15 (19.7)</td>
<td>120 (15.6)</td>
<td></td>
</tr>
<tr>
<td>Black/African/Caribbean/black British</td>
<td>94 (6.5)</td>
<td>92 (6.7)</td>
<td>2 (2.6)</td>
<td>40 (5.2)</td>
<td></td>
</tr>
<tr>
<td>Other ethnic group</td>
<td>60 (4.1)</td>
<td>53 (3.9)</td>
<td>7 (9.2)</td>
<td>7 (0.9)</td>
<td></td>
</tr>
<tr>
<td>Preferred not to say</td>
<td>16 (1.1)</td>
<td>16 (1.2)</td>
<td>0 (0.0)</td>
<td>6 (0.8)</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>20 (1.4)</td>
<td>20 (1.5)</td>
<td>0 (0.0)</td>
<td>6 (0.8)</td>
<td></td>
</tr>
<tr>
<td>Comorbidity count, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>None</td>
<td>377 (26.0)</td>
<td>362 (26.4)</td>
<td>15 (19.7)</td>
<td>62 (8.1)</td>
<td></td>
</tr>
<tr>
<td>1 or 2</td>
<td>593 (41.0)</td>
<td>555 (40.5)</td>
<td>38 (50.0)</td>
<td>295 (38.4)</td>
<td></td>
</tr>
<tr>
<td>3 or more</td>
<td>478 (33.0)</td>
<td>455 (33.2)</td>
<td>23 (30.3)</td>
<td>412 (53.6)*</td>
<td></td>
</tr>
<tr>
<td>Morbidities</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>490 (33.8)</td>
<td>457 (33.3)</td>
<td>33 (43.4)</td>
<td>374 (48.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>128 (8.8)</td>
<td>125 (9.1)</td>
<td>3 (3.9)</td>
<td>140 (18.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>236 (16.3)</td>
<td>228 (16.6)</td>
<td>8 (10.5)</td>
<td>228 (29.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Ischaemic heart disease, angina, myocardial infarct</td>
<td>286 (19.8)</td>
<td>276 (20.1)</td>
<td>10 (13.2)</td>
<td>260 (33.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diabetes (type 1 and 2)</td>
<td>459 (31.7)</td>
<td>431 (31.4)</td>
<td>28 (36.8)</td>
<td>293 (38.1)</td>
<td>0.002</td>
</tr>
<tr>
<td>Asthma</td>
<td>296 (20.4)</td>
<td>280 (20.4)</td>
<td>16 (21.1)</td>
<td>143 (18.6)</td>
<td>0.299</td>
</tr>
<tr>
<td>COPD</td>
<td>202 (14.0)</td>
<td>194 (14.1)</td>
<td>8 (10.5)</td>
<td>174 (22.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Interstitial lung disease</td>
<td>24 (1.7)</td>
<td>23 (1.7)</td>
<td>1 (1.3)</td>
<td>25 (3.3)</td>
<td>0.015</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>267 (18.4)</td>
<td>253 (18.4)</td>
<td>14 (18.4)</td>
<td>244 (31.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Any active malignancy</td>
<td>87 (6.0)</td>
<td>84 (6.1)</td>
<td>3 (3.9)</td>
<td>65 (8.5)</td>
<td>0.030</td>
</tr>
<tr>
<td>Dementia (all types)</td>
<td>131 (9.0)</td>
<td>129 (9.4)</td>
<td>2 (2.6)</td>
<td>195 (25.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Obesity</td>
<td>176 (12.2)</td>
<td>163 (11.9)</td>
<td>13 (17.1)</td>
<td>91 (11.8)</td>
<td>0.825</td>
</tr>
<tr>
<td>English Indices of Deprivation, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.848</td>
</tr>
<tr>
<td>1</td>
<td>667 (46.1)</td>
<td>633 (46.1)</td>
<td>34 (44.7)</td>
<td>336 (43.7)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>271 (18.7)</td>
<td>253 (18.4)</td>
<td>18 (23.7)</td>
<td>145 (18.9)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>200 (13.8)</td>
<td>191 (13.9)</td>
<td>9 (11.6)</td>
<td>111 (14.4)</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>150 (10.4)</td>
<td>146 (10.6)</td>
<td>4 (5.3)</td>
<td>80 (10.4)</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>139 (9.6)</td>
<td>128 (9.3)</td>
<td>11 (14.5)</td>
<td>86 (11.2)</td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>21 (1.5)</td>
<td>21 (1.5)</td>
<td>0 (0.0)</td>
<td>11 (1.4)</td>
<td></td>
</tr>
<tr>
<td>Duration of symptoms prior to admission (n days), n where data were available (%)</td>
<td>245 (16.9)</td>
<td>223 (16.3)</td>
<td>22 (28.9)</td>
<td>110 (14.3)</td>
<td></td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>9 (2–16)</td>
<td>9 (3–16)</td>
<td>7 (5–12)</td>
<td>7 (3–15)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Severity of COVID-19 on admission, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>348 (71.2)</td>
<td>338 (74.6)</td>
<td>10 (27.8)</td>
<td>101 (40.8)</td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>91 (18.6)</td>
<td>81 (17.8)</td>
<td>10 (27.8)</td>
<td>94 (38.1)</td>
<td></td>
</tr>
<tr>
<td>Severe</td>
<td>50 (10.2)</td>
<td>34 (7.5)</td>
<td>16 (44.4)</td>
<td>52 (21.1)†</td>
<td></td>
</tr>
</tbody>
</table>

Data are number (percentage) unless otherwise stated. Medical conditions were self-reported and checked against admission and linked primary care notes. Groups are compared using χ² analysis, except for pregnancy where Fisher’s exact test was used, and age distribution where Kruskal-Wallis was used. Of note, p values compared all patients currently alive (in patients or discharged) versus those who had died. For English Indices of Deprivation, the quintiles were as follows: quintile 1=33.5–78.1; quintile 2=21.7–33.2; quintile 3=14.4–21.5; quintile 4=8.8–14.1; quintile 5=1.4–8.6. *Increased deaths with 3 or more (p<0.0001) comorbidities on post-hoc analysis. †Increased deaths in moderate and severe cases versus mild cases on post-hoc analysis (p<0.0001) for comparisons with patients discharged alive and currently alive. COPD, chronic obstructive pulmonary disease.
Characteristics of patients who died

On 12 May 2020, 769 of 2217 (34.6%) patients had died in hospital or following discharge. These patients were older, more likely to be male, white, have multiple comorbidities, and in the 736 patients admitted directly to the QEHB site, in whom data were available, more likely to have moderate or severe disease on admission, in comparison with all other groups of patients (table 2).

In those in whom data were available, people who died had a shorter duration of symptoms prior to admission compared with those who were still alive (median 7 days (3–36) vs 9 (5–36) days). In all in whom data were available, the duration of symptoms prior to admission did not relate to disease severity on admission (p=0.46). The relationships between survival from diagnosis and age, gender and number of comorbidities are further illustrated in figure 1.

Ethnic group outcome analysis

SMR between different ethnic groups

In comparison with the expected number of deaths based on Birmingham and Solihull 2011 census data and sex structure, there were significantly more South Asian women and men who died with a positive COVID-19 swab than would be expected: SMR (95% CI): Asian women 1.9 (1.4 to 2.6) and Asian men 1.7 (1.4 to 2.1). In contrast fewer white women and men died than would be expected: SMR (95% CI): white women 0.9 (0.8 to 1.0) and white men 0.9 (0.8 to 1.0) (see online supplementary table S1). For those of black ethnicity, death rates were not different from the expected rates in the standard population.

Survival curves for mortality in different ethnicities

An age-adjusted Kaplan-Meier showed that although there were no differences in age-adjusted survival in white and black ethnicities, patients from Asian ethnic groups were less likely to survive (see figure 2).

Multivariable analysis

In a multivariable Cox regression model adjusted for age, sex, comorbidity counts and deprivation, South Asian ethnicity (aHR 1.4, 95% CI 1.2 to 1.8) was associated with
a significantly higher risk of death. Within the limits of the power of the study, there was absence of a significant difference in survival for black ethnicity compared with the white population (aHR 1.1, 95% CI 0.8 to 1.5). In addition to this we found age z-score (aHR 2.4, 95% CI 1.8 to 3.2) and comorbidities (1–2 comorbidities, aHR 1.7, 95% CI 1.3 to 2.2; 3 or more comorbidities, aHR 2.3, 95% CI 1.7 to 3.0) as significant predictors. We also found a significant effect of sex (aHR for male sex, 1.3, 95% CI 1.1 to 1.5), with the interaction between age and sex suggesting an amplified risk in men with increasing age (table 3). The main effects of age and multiple comorbidities were modified by an interaction (aHR for age interaction with 1–2 comorbidities, 0.9, 95% CI 0.7 to 1.2; age interaction with 3+ comorbidities, 0.7, 95% CI 0.5 to 0.9) that attenuated the relative impact of increasing comorbidity at advanced age. Of note, the HR of 1.4 (1.2–1.8) did not change (1.4, 1.2–1.8) if the interactions were removed from the model.

To further test the assumption that South Asian ethnicity was associated with worse outcomes even when comorbidities, age and sex were considered, propensity score matching was conducted, matching for the same factors in the Cox regression but categorising ethnicity into South Asian or not. With propensity score matching the HR for risk of death was 1.3 (1.0–1.6) for South Asian patients compared with non-South Asian patients. When comorbidities were added independently (rather than as a count) using propensity score matching, South Asian ethnicity was still associated with a significantly higher risk of death (HR 1.4, 95% CI 1.1 to 1.7).

**DISCUSSION**

This is the first study to specifically describe the impact of South Asian ethnicity on the outcome of COVID-19 infection using highly characterised and accurate primary and secondary data from patients admitted to hospital in the UK. South Asians were significantly younger and twice likely to have diabetes than white patients, and when accounted for the age structure of the local population had a high admission and death rate. South Asians...
increased risk of death, with similar effect size with the
2020;
:e000644. doi:10.1136/bmjresp-2020-000644
et al
Sapey E, BMJ Open Resp Res
studies10 11 where South Asians were found to be at
42% higher.
eties, the effect of South Asian ethnicity on mortality was
adjusting for age, deprivation and multiple comorbidities
was exchanged for the presence of specific comorbidities
including diabetes mellitus and hypertension. To place
this in context, the effect of South Asian on mortality is
significantly less than the effect of one or more comorbi-
dities (present in 80.2% of all admitted patients) and
approximates to the effect of ageing 10 years in the
white population. In this study we did not observe an
independent signal related to higher deprivation levels26
and poor outcomes in contrast to the population-based
study,11 suggesting deprivation is likely to be related to
high infection rates and thereby high mortality, rather
than high rates of severe infection leading to increased
mortality.

It is notable that in the subanalysis of patients admitted
to QEHB, where we were able to immediately integrate a
COVID-19-specific assessment into our EHR, South Asian
patients appear to present with more severe disease, but
there was no difference in the duration of symptoms
prior to admission, suggesting disease severity was not
caused simply by delayed presentation to medical services
or differences in health service utilisation (although this
cannot be fully excluded, given the unknown burden of
COVID-19 in the community). Indeed, when comparing
those still alive and those who had died at the end of the
study, the patients who had died had a shorter history
of symptoms prior to admission, suggesting a different
disease course.

Our study is in line with two population-based studies10 11 where South Asians were found to be at
increased risk of death, with similar effect size with the
study11 that considered similar covariates for adjusting
(aHR 1.4 (1.2–1.8) vs 1.6 (1.4–1.8)). However, the find-
ing of the two population-based studies could reflect
infection rates rather than case fatality rates, and there-
fore differentiating this is important from a public health
and research perspective. If increased deaths in South
Asian patients reflected high infection rates, then our
focus should be on looking at barriers and emphasising
the need for adherence to current social distancing
guidelines. If this reflects an increased susceptibility to
poorer outcomes from SARS-CoV-2 infection, we need to
urgently understand the reasons for severity of infection
and mitigate risk or develop targeted treatments. While
no firm conclusion can be drawn from the current data
set, our study potentially supports the latter, with South
Asian patients more likely to be admitted, more likely
to present with severe symptoms and have an increased
risk of mortality. This supports the call by the govern-
ment and research community for urgent research on
the reasons underpinning these observations. Our study
was not sufficiently powered to report on other ethnic
groups, particularly those of black ethnicity, and there-
fore the findings among these ethnic groups should be
interpreted cautiously.

The excess age-adjusted mortality in COVID-19 is not
solely attributable to a range of cardiovascular and meta-
\( \text{Table 3 Adjusted HR of risk factors for mortality} \)

<table>
<thead>
<tr>
<th>Predictors</th>
<th>Estimates</th>
<th>CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (z-score)</td>
<td>2.4</td>
<td>1.8 to 3.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>White</td>
<td>Reference</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>1.4</td>
<td>1.2 to 1.8</td>
<td>0.001</td>
</tr>
<tr>
<td>Black</td>
<td>1.1</td>
<td>0.8 to 1.5</td>
<td>0.536</td>
</tr>
<tr>
<td>Mixed</td>
<td>1.9</td>
<td>0.9 to 3.9</td>
<td>0.072</td>
</tr>
<tr>
<td>Unknown</td>
<td>0.8</td>
<td>0.4 to 1.9</td>
<td>0.676</td>
</tr>
<tr>
<td>Other</td>
<td>0.6</td>
<td>0.3 to 1.3</td>
<td>0.226</td>
</tr>
<tr>
<td>Not stated</td>
<td>1.2</td>
<td>0.6 to 2.8</td>
<td>0.603</td>
</tr>
<tr>
<td>Female</td>
<td>Reference</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>1.3</td>
<td>1.1 to 1.5</td>
<td>0.014</td>
</tr>
<tr>
<td>Deprivation quintile 1</td>
<td>Reference</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Deprivation quintile 2</td>
<td>0.9</td>
<td>0.7 to 1.0</td>
<td>0.126</td>
</tr>
<tr>
<td>Deprivation quintile 3</td>
<td>0.9</td>
<td>0.7 to 1.1</td>
<td>0.439</td>
</tr>
<tr>
<td>Deprivation quintile 4</td>
<td>0.8</td>
<td>0.7 to 1.1</td>
<td>0.183</td>
</tr>
<tr>
<td>Deprivation quintile 5</td>
<td>0.9</td>
<td>0.7 to 1.2</td>
<td>0.593</td>
</tr>
<tr>
<td>Deprivation quintile missing</td>
<td>1.0</td>
<td>0.5 to 1.8</td>
<td>0.930</td>
</tr>
<tr>
<td>No comorbidity</td>
<td>Reference</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Comorbidity group 1–2</td>
<td>1.7</td>
<td>1.3 to 2.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Comorbidity group 3+</td>
<td>2.3</td>
<td>1.7 to 3.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age (z-score) × sex (male)</td>
<td>1.2</td>
<td>1.0 to 1.5</td>
<td>0.055</td>
</tr>
<tr>
<td>Age (z-score) × comorbidity group 1–2</td>
<td>0.9</td>
<td>0.7 to 1.2</td>
<td>0.529</td>
</tr>
<tr>
<td>Age (z-score) × comorbidity group 3+</td>
<td>0.7</td>
<td>0.5 to 0.9</td>
<td>0.015</td>
</tr>
</tbody>
</table>

Multivariable Cox regression model including age (z-score),
ethnicity, sex and comorbidity count as covariates.
Adjusted HRs along with their CI are presented.

were also more likely to present with severe symptoms,
but with no difference in the duration of symptoms and
more likely to be admitted to ITU. Importantly, after
adjusting for age, deprivation and multiple comorbid-
ties, the effect of South Asian ethnicity on mortality was
42% higher.

The limitations in our overall analysis need to be consid-
ered, specifically that 5% of patients remain in hospital at
the time of the data lock and more patients have been
admitted, so our findings will evolve. Since the propor-
tion of patients presenting from different ethnic groups
was stable across the course of data collection, any conse-
quence for our main conclusion on the mortality risk in
South Asians admitted to hospital is likely to be small.
Data on the admission severity scoring did not include
all patients, which is a limitation. This limitation reflects
the real-world response within a global pandemic which
includes designing a score to inform care escalation deci-
sions and updating the UHB electronic health record to
capture this information during the first wave of patient
admissions. However, these data suggest further explora-
tion of severity of disease at presentation is warranted.

It is also important to acknowledge that standardised
admission and mortality ratios from Birmingham and
Solihull use the most recent census data, but that these
are from 2011. Estimates of the contemporary age struc-
ture do not however suggest a need to significantly qualify
these findings. The UK has not undertaken widespread
screening or diagnosis of patients in the community, and
we are therefore unable to comment on the natural history
of COVID-19 prior to admission to secondary care, irre-
respectively of ethnic group. This testing regimen is likely
to evolve with the development of capacity and methodology
and will provide a more complete picture of COVID-19.
A description of disease in the community will help build
a clearer understanding of the apparent excess mortality
following admission, for which there remain a number of
possible explanations. A limitation of this study (and,
arguably, of any observational study) is that it cannot
exclude the possibility that another, unmeasured variable
could account for the ethnicity effect described here. The
assessment of comorbidities does not reflect the degree of
severity of the condition, nor disease treatment or control,
and the assessment of social deprivation might impact on
chronic disorders. There is also the possibility that differ-
ences in work or home living arrangements might impact
on potential transmission and this may be different across
ethnic communities. However, a real strength has been
the ability to study a highly curated and complete data set,
without the inherent issues of significant undercoding seen
with morbidity and ethnicity data when using a secondary
care data set.

The biological basis of any difference in outcome can
only be speculated on at present. There are reported differ-
ences in outcomes for non-white ethnic groups from
ARDS even after adjusting for sex, age, disease severity, type
of hospital and median household income.27 28 The worst
clinical manifestations of COVID-19 appear to be associ-
ated with a cytokine storm syndrome. Here a hypercyto-
kinaemia is seen,4 with predictors of mortality reflecting a
viraically induced inflammatory state which can be assessed
using a scoring system including validated clinical labora-
tory tests.29 Candidate genes associated with ARDS have
been identified in bioinformatic analyses, with a strong
predominance of inflammatory pathways, including reac-
tive oxygen species, innate immunity-related inflammation
and endothelial vascular signalling pathways.30 Ethnicity
may influence cytokine gene polymorphisms and inflam-
matory profiles following specific challenges,31 with some
ethnic groups more prone to a heightened inflamma-
tory response. Of note, socioeconomic factors might also
impact on inflammatory pathways and gene expression.32

These factors remain poorly understood, and were a
priority for our patient and public involvement group who
were consulted for this study, and there is an urgent need
to understand the genomic and associated phenomic and
socioeconomic characteristics of patients who are suscep-
tible or resistant to the severe manifestations of COVID-19
to understand this further.

Although our study includes only one NHS Founda-
tion Trust, it covers an ethnically diverse contiguous
population of 1.3 million people for which it is the
sole provider of adult acute secondary care across four
hospital sites. This provides for continuity of data, clin-
ical protocols and access to therapy. The immediate
availability of access to an electronic representation of
a primary care record to support the care of admitted
patients also supports the integrity of data collection,
the quality of which might otherwise be more limited.33

Our findings, which describe and quantify the risk of
COVID-19 in the South Asian population, are relevant
to national policy and to understanding the under-
lying biological mechanisms in ‘at risk’ populations.
Future studies will extend our observations and explore
underlying epidemiology and biological mechanisms,
to improve interventions based in the community, the
emergency department, ward and ITU. Perhaps most
importantly our findings inform the UK’s national discus-
sion on at ‘at risk’ groups and the ensuing fear arising
from uncertainty.

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12HDR-UK Midlands Physical Site, University Hospitals Birmingham,
Birmingham, UK

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Khaled ElFandi, Rifat Rashid and Paul Cockwell.

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ences in outcomes for non-white ethnic groups from
ARDS even after adjusting for sex, age, disease severity, type
of hospital and median household income.27 28 The worst
clinical manifestations of COVID-19 appear to be associ-
ated with a cytokine storm syndrome. Here a hypercyto-
kinaemia is seen,4 with predictors of mortality reflecting a
viraically induced inflammatory state which can be assessed
using a scoring system including validated clinical labora-
tory tests.29 Candidate genes associated with ARDS have
been identified in bioinformatic analyses, with a strong
predominance of inflammatory pathways, including reac-
tive oxygen species, innate immunity-related inflammation
and endothelial vascular signalling pathways.30 Ethnicity
may influence cytokine gene polymorphisms and inflam-
matory profiles following specific challenges,31 with some

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