Biochemical abnormalities in COVID-19: a comparison of white versus ethnic minority populations in the UK

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Abstract

Aims Public Health England has identified that in COVID-19, death rates among ethnic minorities far exceed that of the white population. While the increase in ethnic minorities is likely to be multifactorial, to date, no studies have looked to see whether values for routine clinical biochemistry parameters differ between ethnic minority and white individuals.

Methods Baseline biochemical data for 22 common tests from 311 SARS-CoV-2 positive patients presenting to hospital in April 2020 in whom ethnicity data were available was retrospectively collected and evaluated. Data comparisons between ethnic minority and white groups were made for all patient data and for the subset of patients subsequently admitted to intensive care.

Results When all patient data were considered, the ethnic minority population had statistically significant higher concentrations of C reactive protein (CRP), aspartate aminotransferase and gamma-glutamyl transferase, while troponin T was higher in the white group. A greater proportion of ethnic minority patients were subsequently admitted to intensive care, but when the presenting biochemistry of this subset of patients was compared, no significant differences were observed between ethnic minority and white groups.

Conclusion Our data show for the first time that routine biochemistry at hospital presentation in COVID-19 differs between ethnic minority and white groups. Among the markers identified, CRP was significantly higher in the ethnic minority group pointing towards an increased tendency for severe inflammation in this group.

Introduction

In December 2019, a new highly infectious disease, COVID-19, was first reported in Wuhan, Hubei Province, China.1,2 The causative agent of COVID-19, SARS-CoV-2, has since spread worldwide resulting in 88 387 352 cases and 1 919 204 deaths as of 10 January 2021, according to a weekly epidemiological update from the WHO.1

Severe or fatal COVID-19 infection has been associated with gross changes in clinical biochemistry parameters. To date, common findings include increases of markers of tissue damage (creatinine kinase (CK), lactate dehydrogenase (LDH), myoglobin and troponin), inflammation (C reactive protein (CRP), ferritin and procalcitonin), renal impairment (increased creatinine and urea) and liver dysfunction (increases of aminotransferases and bilirubin and decreased albumin).3,4 Severe COVID-19 infection has also been associated with low serum sodium, potassium and calcium.5 Biochemical data can be predictive in COVID-19; parameters that are predictive of death include increased CRP, LDH, aspartate aminotransferase (AST), troponin I, creatinine and low albumin.3,5–10

In a review by Public Health England, death rates among Asian, and other minority ethnicities COVID-19 positive people were shown to be significantly higher than in white British people.11 Death rates in those of Bangladeshi background were twice as high and for other ethnic minority groups between 10% and 50% higher, after taking into account age, sex, deprivation and region. The cause of these discrepancies is unclear but likely to be multifactorial. We have previously assessed differences in cardiac markers at hospital presentation in ethnic minority and white groups in COVID-19,12 but to date, no study has investigated whether more broad routine biochemistry profiles differ in this setting, nor whether any differences provide prognostic value. To address these questions, we retrospectively reviewed admission biochemistry for a cohort of COVID-19 positive patients in whom ethnicity data were available. We compared all data between ethnic minority and white groups and in a subset of patients who were subsequently admitted to an intensive care unit (ITU).

Methods

This retrospective observational study was conducted at King’s College Hospital National Health Service Foundation Trust, a busy teaching hospital located in South London. Patients with baseline biochemistry data were included in the analysis if they were admitted between 1 and 28 April 2020 (the period of peak admission rates in London during the first wave of the pandemic), had positive (RT-PCR) SARS-CoV-2 serology and if ethnicity data were available. The first available result after hospital admission for the following 22 biochemical tests were obtained for each patient: albumin, alkaline phosphatase (ALP), alanine aminotransferase (ALT), AST, total bilirubin, adjusted calcium, CK, creatinine, CRP, estimated glomerular filtration rate (eGFR), ferritin, gamma-glutamyl transferase (GGT), LDH, magnesium, sodium, N-terminal prohormone of brain natriuretic peptide (NT-proBNP), procalcitonin, phosphate, potassium, troponin T, total protein and urea. Inclusion of admission biochemical data in
the ITU analyses was made if the individual was subsequently transferred to ITU within 28 days of admission. Electronic patient records were accessed for body mass index (BMI) data and to assess for the presence of pre-existing common comorbidities in each patient at baseline (defined as histories of diabetes mellitus, cardiovascular disease (CVD), chronic kidney disease (CKD), hypertension and chronic obstructive pulmonary disease (COPD) or asthma). Patients were classified as ‘white’ or ‘ethnic minority’ using the Office for National Statistics list of ethnic groups. All biochemical data were generated using Roche c-702 and e-801 analytical platforms (Roche, Burgess Hill, UK), using blood samples collected into serum separator tubes (Greiner Bio-One Ltd, Stonehouse, UK). All tests are accredited by the United Kingdom Accreditation Service to iso15189. The methods used for ALT and AST included pyridoxal phosphate, with the LDH assay being measured in the L-lactate to pyruvate direction. Test requests on samples for which haemolysis, icteric or lipaemic indices exceeded the manufacturer’s limits for that particular test were cancelled and not included in analyses. Biochemical test data were tested for normality using the Kolmogorov-Smirnov test, and with the exception of albumin, adjusted calcium, globulin, LDH, magnesium, potassium and total protein, were found to be not normally distributed so group comparisons of biochemical data were made using a two-tailed Mann-Whitney U test. Data are reported as median (interquartile range (IQR)). Values of p<0.05 were taken as statistically significant. The proportion of abnormal results for each test studied was compared using a $\chi^2$ test. Data comparisons were made using R V.3.6.2 (R Foundation for Statistical Computing, Vienna, Austria).  

**RESULTS**

Ethnic minority patients presenting in April 2020 with COVID-19, in comparison with those from white ethnic groups, were younger (median age 65 vs 75 years) and predominantly male (64% vs 52%, table 1). Ethnic minority individuals were more likely to subsequently require ITU admission (19% patients vs 13% white patients, table 1). A history of diabetes mellitus was more common in the ethnic minority group, while CVD history was more common in the white group. Frequencies of hypertension, CKD and respiratory disorders (COPD or asthma) were similar in ethnic minority and white groups (table 1). BMI data were incomplete across the two groups. Of available data (151/211 ethnic minority patients and 70/100 white patients), BMI was similar in the two groups. Median BMI (IQR) in the ethnic minority group was 28.8 kg/m$^2$ (24.7–33.5) and in the white group 28.7 kg/m$^2$ (23.3–32.0).

Review of baseline biochemistry data for all patients revealed statistically significant differences between the two groups for a number of common analytes (table 2). Of these results, 86% were obtained on hospital admission day, with 97% of test results being acquired within the first 3 days of the patients hospital stay. The majority of patients in the study had abnormal CRP results; however, CRP concentrations were higher in the ethnic minority group (median value 111.2 mg/L, IQR 66.5–181.1) than in the white group (48.1 mg/L, 22.1–112.9). Increase of this inflammatory marker was not reflected by ethnicity-related differences in procalcitonin, nor ferritin concentration; almost all patients had elevated ferritin. The median cardiac troponin T was higher, and a greater proportion of patients had abnormal results, in the white group than in the ethnic minority group. Median NT-proBNP concentration was also higher in the white group, although this association did not reach statistical significance. Of markers of liver function, AST and GGT were higher in the ethnic minority group but ALP lower. A greater proportion of the ethnic minority population also had AST concentrations falling outside the reference interval. ALT, albumin and total bilirubin were not different between the two groups. No differences between ethnic minority and white groups were noted for sodium, potassium, adjusted calcium or phosphate, nor for markers of renal function (creatinine, eGFR and urea). The tissue damage markers, LDH and CK also showed no ethnicity-specific differences at presentation, with the majority of patients having abnormal values.

When baseline biochemistry data for ethnic minority and white patients that were subsequently admitted to ITU were compared, no statistically significant differences between these groups were observed for any of the analytes studied (table 3).

**DISCUSSION**

For the first time, we have shown that there are significant differences at hospital presentation between ethnic minority and white populations in results for a number of routine biochemistry tests. The results of this study are therefore important because they may contribute towards a greater understanding of why ethnic minority individuals are at increased risk of death due to COVID-19. The most striking finding from our study is the increase at presentation of CRP in ethnic minority individuals versus white individuals. CRP measurement is now well established as a marker of disease severity in COVID-19. Zhang et al showed that in 140 hospitalised patients with confirmed SARS-CoV-2 infection, in non-severe disease, CRP concentrations ranged from 9.5 to 52.1 mg/L, while in severe disease, values ranged from 20.6 to 87.1 mg/L. In another study, 56.4% of patients with non-severe COVID-19 had CRP above the reference interval, which rose to 81.5% in those with severe disease. Around 20% of patients infected with SARS-CoV-2 progress to having associated life-threatening complications involving acute inflammation associated with a cytokine storm, coagulopathy, septic shock and multiple organ failure. Increased concentrations of interleukin-6 (IL-6) are associated with severe COVID-19 and positively correlate with adverse outcomes. The increased concentrations of IL-6 directly result in the liver increasing synthesis of CRP. The results from this study raise the interesting possibility that the higher concentrations of CRP in ethnic

Table 1  Demographic data in ethnic minority and white groups

| Ethnic minority | White |
|-----------------|-------|
| **All patient data** | | |
| Number | 211 | 100 |
| Age (years) | 65 (55–78) | 75 (66–84) |
| Male/female (%) | 64/36 | 52/48 |
| **Pre-existing comorbidities (%)** | | |
| Diabetes | 54 | 31 |
| CVD | 25 | 50 |
| CKD | 31 | 28 |
| Hypertension | 49 | 49 |
| COPD/asthma | 30 | 27 |
| **Patients subsequently admitted to intensive care** | | |
| Number (% total) | 39 (18) | 13 (13) |
| Age (years) | 59 (52–65) | 65 (57–71) |
| Male/female (%) | 77/23 | 77/23 |
| Age data presented as median (IQR). CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CVD, cardiovascular disease.
minority patients at hospital presentation may mark an increased susceptibility to severe inflammation during their COVID-19 disease course. These differences appear not to be accounted for by a genetic predisposition of ethnic minority individuals to higher CRP levels; median value of CRP in blacks was 3.0 mg/L versus 2.3 mg/L in whites in one study of healthy individuals. The absence of differences between the ethnic minority and white groups for the two other markers of inflammation studied (procalcitonin and ferritin) supports the hypothesis of a specific white groups for the two other markers of inflammation studied (procalcitonin and ferritin) supports the hypothesis of a specific

Table 2 Biochemistry at presentation (all patient data)

| Test                        | Number of results | Test result (median (IQR)) | Abnormal results (%) | P value |
|-----------------------------|-------------------|----------------------------|----------------------|---------|
|                            | Ethnic minority   | White                      |                      |         |
|                            |                   | (median (IQR))             |                      |         |
| Albumin (g/L)              | 211               | 3.70 (3.40–3.95)           |                      | 0.247   |
|                            | 100               | 3.75 (3.40–4.10)           |                      | 0.33    |
| ALP (IU/L)                 | 209               | 74.0 (57.0–98.0)           |                      | 0.059   |
|                            | 100               | 84.0 (63.0–102.5)          |                      | 0.11    |
| ALT (IU/L)                 | 104               | 41.0 (27.8–58.0)           |                      | 0.076   |
|                            | 33                | 32.0 (17.0–70.0)           |                      | 0.27    |
| AST (IU/L)                 | 206               | 52.0 (35.2–76.0)           |                      | 0.004   |
|                            | 99                | 40.0 (28.0–71.5)           |                      | 0.56    |
| Total bilirubin (µmol/L)   | 211               | 9.0 (6.5–13.0)             |                      | 0.617   |
|                            | 100               | 9.0 (6.0–14.0)             |                      | 0.6    |
| Adjusted calcium (mmol/L)  | 183               | 2.3 (2.2–2.4)              |                      | 0.537   |
|                            | 83                | 2.3 (2.2–2.4)              |                      | 0.6    |
| CK (IU/L)                  | 63                | 270.0 (111.5–1139.0)       |                      | 0.447   |
|                            | 31                | 163.0 (63.5–725.0)         |                      | 0.57    |
| Creatinine (µmol/L)        | 211               | 106.0 (80.0–159.5)         |                      | 0.208   |
|                            | 100               | 100.0 (76.8–138.5)         |                      | 0.35    |
| CRP (mg/L)                 | 209               | 111.2 (66.5–181.1)         |                      | <0.001  |
|                            | 98                | 48.1 (22.1–112.9)          |                      | 0.93    |
| eGFR (mL/min/1.73 m²)      | 210               | 58.0 (34.0–78.8)           |                      | 0.447   |
|                            | 99                | 55.0 (38.5–86.0)           |                      | 0.65    |
| Ferritin (µg/L)            | 91                | 916.0 (579.0–1815.5)       |                      | 0.208   |
|                            | 35                | 1046.0 (3865.8–1859.0)     |                      | 0.86    |
| GGT (IU/L)                 | 209               | 57.0 (32.0–99.0)           |                      | 0.030   |
|                            | 100               | 41.0 (23.0–83.2)           |                      | 0.51    |
| LDH (IU/L)                 | 48                | 467.0 (351.2–631.2)        |                      | 0.432   |
|                            | 8                 | 505.3 (457.5–634.0)        |                      | 0.92    |
| Magnesium (mmol/L)         | 183               | 0.9 (0.8–1.0)              |                      | 0.028   |
|                            | 81                | 0.8 (0.8–1.0)              |                      | 0.32    |
| Sodium (mmol/L)            | 211               | 137.0 (130.0–140.0)        |                      | 0.521   |
|                            | 100               | 137.0 (130.0–140.30)       |                      | 0.35    |
| NT-proBNP (ng/L)           | 34                | 2215 (90.0–1077.5)         |                      | 0.274   |
|                            | 13                | 427.0 (140.0–1678.0)       |                      | 0.77    |
| Procalcitonin (µg/L)       | 28                | 1.2 (0.4–1.14)             |                      | 0.594   |
|                            | 8                 | 0.7 (0.3–2.5)              |                      | 0.100   |
| Phosphate (mmol/L)         | 181               | 1.0 (0.8–1.2)              |                      | 0.145   |
|                            | 81                | 1.0 (0.9–1.2)              |                      | 0.30    |
| Potassium (mmol/L)         | 208               | 4.2 (3.8–4.7)              |                      | 0.215   |
|                            | 98                | 4.3 (3.9–4.8)              |                      | 0.19    |
| Troponin T (ng/L)          | 122               | 19.0 (8.2–52.2)            |                      | 0.023   |
|                            | 45                | 35.0 (16.0–74.0)           |                      | 0.82    |
| Total protein (g/L)        | 210               | 71.0 (67.0–74.0)           |                      | <0.001  |
|                            | 100               | 68.5 (64.0–71.2)           |                      | 0.13    |
| Urea (mmol/L)              | 211               | 7.0 (4.6–14.3)             |                      | 0.059   |
|                            | 99                | 8.7 (5.9–13.9)             |                      | 0.64    |

P values <0.05 were taken as statistically significant. N/A: test was not applicable to data where only abnormal results were recorded.

ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CK, creatine kinase; CRP, C reactive protein; eGFR, estimated glomerular filtration rate; GGT, gamma-glutamyl transferase; LDH, lactate dehydrogenase; NT-proBNP, N-terminal prohormone of brain natriuretic peptide.

Minority population, this difference is likely related to known ethnic differences in this marker. We have previously reported higher troponin T and NT-ProBNP in the white population than in ethnic minorities, although the latter association did not reach statistical significance. Likely contributory factors to these findings are that the white population were older with a higher prevalence of CVD. Elevated troponin has been associated with worse outcomes in COVID-19.

In our cohort, although non-white ethnicity and male gender were predictive of ITU admission, no statistically significant differences in biochemistry at presentation were noted for those who were subsequently admitted to ITU compared with the white population, including for CRP. This may suggest that there is no difference in the pathological mechanisms underlying severe COVID-19 that are reflected by routine biochemistry, but that ethnic minority subjects are at an increased risk of developing them. Of course, the association between ethnic minority and severe COVID-19 disease is likely to be complex and incorporate multiple demographic and socioeconomic factors not already captured in this study. In one study, Raisi-Estabragh et al suggested that both the sex and ethnic patterns of COVID-19 are not adequately explained by variation in cardiometabolic factors, 25(OH)-vitamin D concentrations or socioeconomic factors; clearly, there is a need for more research required to define the mechanism of increased ethnic minority risk.

This study has some limitations. Although the facts that 86% of total test results were obtained on admission day and 97% within 3 days of admission would argue against the possibility of differences in care between ethnic groups while in hospital, we cannot exclude the possibility that biochemical differences...
are not contributed to by variance in the disease stage at which different ethnic groups accessed hospital care. In the patients who were admitted to ITU during their hospital stay, the number of results for some tests may be too low to identify true differences between the two groups. The outcomes of ITU patients (requirement for mechanical ventilation/continuous positive airway pressure support and morbidity/mortality) were also not different between the two groups. The outcomes of ITU patients not otherwise determined by BMJ. The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors. None declared.

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In conclusion, the major finding of this study is that ethnic minority patients have higher CRP concentrations at presentation, indicating a more severe acute inflammation. This may augment existing comorbidities characterised by chronic inflammation that may be more prevalent in the ethnic minority population such as diabetes, pointing towards an increased tendency for severe inflammation in this group.

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Table 3  Biochemistry at hospital presentation in patients subsequently admitted to intensive care

| Test                      | Number of results | Test result (Median (IQR)) | Abnormal results (%) | P value |
|---------------------------|-------------------|-----------------------------|----------------------|---------|
|                           | Ethnic minority   | White                       |                      |         |
|                           |                   | Ethnic minority             | White                |         |
| Albumin (g/L)             | 39 13             | 38.0 (34.0–39.0)            | 35.0 (32.0–37.0)     | 0.167   |
| ALP (IU/L)                | 39 13             | 81.0 (57.0–107.0)           | 83.0 (74.0–132.0)    | 0.459   |
| ALT (IU/L)                | 36 10             | 44.5 (30.0–68.5)            | 76.0 (41.0–154.5)    | 0.432   |
| AST (IU/L)                | 39 13             | 68.0 (48.5–136.0)           | 65.0 (44.0–183.0)    | 0.966   |
| Total bilirubin (µmol/L)  | 39 13             | 8.0 (7.0–13.0)              | 11.0 (8.0–18.0)      | 0.203   |
| Adjusted calcium (mmol/L) | 39 13             | 2.3 (2.2–2.4)               | 2.3 (2.2–2.3)        | 0.958   |
| CK (IU/L)                 | 29 10             | 632.0 (161.0–1687.0)        | 142.5 (83.2–1174.2)  | 0.311   |
| Creatinine (µmol/L)       | 39 13             | 110.0 (81.0–211.0)          | 130.0 (110.0–182.0)  | 0.310   |
| CRP (mg/L)                | 39 13             | 157.0 (111.4–257.1)         | 168.4 (40.9–251.8)   | 0.616   |
| eGFR (mL/min/1.73 m²)     | 39 13             | 59.0 (28.0–83.0)            | 39.0 (32.0–58.0)     | 0.295   |
| Ferritin (µg/L)           | 34 10             | 1054.5 (718.0–1981.0)       | 1822.0 (1018.2–2507.5) | 0.245   |
| GGT (IU/L)                | 39 13             | 91.0 (46.0–136.0)           | 66.0 (48.0–100.0)    | 0.512   |
| LDH (IU/L)                | 28 6              | 522.5 (399.8–687.0)         | 500.5 (402.2–672.2)  | 0.878   |
| Magnesium (mmol/L)        | 39 13             | 0.9 (0.9–1.0)               | 1.0 (0.8–1.1)        | 0.657   |
| Sodium (mmol/L)           | 39 13             | 136.0 (134.0–139.0)         | 137.0 (136.0–138.0)  | 0.367   |
| NT-proBNP (ng/L)          | 23 5              | 400.0 (164.5–1867.0)        | 427.0 (126.0–3916.0) | 0.676   |
| Procalcitonin (µg/L)      | 22 8              | 1.6 (0.5–11.8)              | 0.7 (0.3–2.5)        | 0.241   |
| Phosphate (mmol/L)        | 39 13             | 1.1 (0.8–1.5)               | 1.2 (1.0–1.7)        | 0.336   |
| Potassium (mmol/L)        | 39 13             | 4.4 (4.0–4.9)               | 4.7 (3.8–5.4)        | 0.695   |
| Troponin T (ng/L)         | 35 12             | 24.0 (14.5–54.0)            | 32.0 (16.0–90.2)     | 0.472   |
| Total protein (g/L)       | 39 13             | 72.0 (67.0–73.0)            | 66.0 (60.0–71.0)     | 0.044   |
| Urea (mmol/L)             | 39 13             | 8.6 (5.0–15.2)              | 17.6 (9.9–19.1)      | 0.076   |

P values <0.05 were taken as statistically significant.

N/A=z test was not applicable to data where only abnormal results were recorded.

ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CK, creatine kinase; CRP, C reactive protein; eGFR, estimated glomerular filtration rate; GGT, gamma-glutamyl transferase; LDH, lactate dehydrogenase; NT-proBNP, N-terminal prohormone of brain natriuretic peptide.

In the UK, it has been shown that ethnic minorities have poorer outcomes in COVID-19 relative to those of the white population, including an increased risk of death.

In this study, we show that there are significant differences between ethnic minority and white populations in routine clinical biochemistry parameters at presentation to hospital with COVID-19.

Among the markers identified, C reactive protein was significantly higher in the ethnic minority group, pointing towards an increased tendency for severe inflammation in this group, which may contribute towards the poorer outcomes in this group reported previously.
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