Maximal temperature varies by sex and ethnic group in hospital in-patients with Covid-19 infection

Colin J Crooks[1,3,4] , PhD, Associate Professor in Clinical Epidemiology,

Joe West[2,3,4,6] , PhD, Professor of Epidemiology

Tasso Gazis[4] , DM, Clinical Director for Urgent and Emergency Care

Mark Simmonds[4] , MBBS, Divisional Director, Medicine

Dominick Shaw [4,5] , DM, Professor of Respiratory Medicine

Timothy R Card[2,3,4] , PhD, Associate Professor in Clinical Epidemiology

Andrew W Fogarty[2,3,4], DM, Reader in Clinical Epidemiology

1. **Nottingham Digestive Diseases Centre, School of Medicine, University of Nottingham, NG7 2UH**
2. **Population and Lifespan Sciences, School of Medicine, University of Nottingham, NG5 1PB**
3. **NIHR Nottingham Biomedical Research Centre (BRC), Nottingham University Hospitals NHS Trust and the University of Nottingham, NG7 2UH**
4. **Nottingham University Hospitals NHS Trust, NG7 2UH**
5. **Division of Respiratory Medicine, School of Medicine, University of Nottingham, NG5 1PB**
6. **East Midlands Academic Health Science Network, University of Nottingham, Nottingham, NG7 2TU**

Corresponding Author: andrew.fogarty@nottingham.ac.uk

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Dear Editor,

Both ethnicity and sex may modify the host response to infection, and hence clinical outcomes. Individuals from ethnic groups that originated outside the UK have a higher mortality from Covid-19 infection; age standardised mortality rates demonstrated an excess risk of 2.7-fold and 1.9-fold higher mortality from Covid-19 infection for males and females of Bangladeshi origin respectively when compared to their white British counterparts [1]. During the first wave of Covid-19 infection before effective treatments or vaccinations were available, the age standardised mortality ratio was approximately two-fold higher in men compared with women for COVID-19–related deaths [1].

We tested the hypothesis that there is a differential host response of maximum temperature recorded during infection with Covid-19 virus in individuals from both sexes and different ethnic groups.

Data were available for all adult patients admitted to Nottingham University Hospitals NHS trust with a diagnosis of Covid-19 infection from June 2020 to December 2021 [2]. The association between the maximal temperature recorded during each admission with both sex and ethnicity were explored using routinely collected data for all eligible adult patients. Temperature was measured using Welch Allyn Sure Temp Thermometers.

Mixed effect linear models were fitted predicting the maximum temperature during a hospital admission episode by ethnicity and sex using patient as a random intercept adjusted for age.

Approval for this work was granted via an NUH Clinical Effectiveness Team audit (reference: reference: 21-294C) and IRAS (REC: 20/WM/0142, project ID: 282490, amendment No. SA02 20/07/21).

Data were available from 7,749 individuals with 15,155 admissions. Maximum temperature ($p<0.0001$, ANOVA) varied by ethnicity. After adjustment for age and sex (Table), the maximum temperature for each admission episode, those labelled as from South-East Asia and as Black/mixed ethnic groups had higher maximum temperatures with Covid-19 infection compared to individuals with white skin, with differences of +0.10 °C (95% CI: +0.03 to +0.16) and +0.17 °C 95% CI: +0.10 to +0.24) respectively.

Males had higher maximum temperatures for each admission episode than females, with a difference of +0.12 °C (95% CI: +0.09 to +0.15). These observations were not qualitatively changed by further adjustment for maximum serum C-reactive protein CRP.

Maximum temperature in response to Covid-19 infection varies across ethnic groups and also by sex. This is consistent with a more vigorous host response, which could be contributing to the higher morbidity and mortality observed from Covid-19 infection in both males and also individuals with non-white skin.

The strength of this analysis is that data were collected on an unselected population of all patients admitted with Covid-19 infection, with no awareness of the hypothesis to be tested, thus reducing the risk of bias. By using the maximum temperature recorded for each admission, the analysis could utilise peak values attained in response to the same viral infection. Addition of maximal serum CRP to the model allowed adjustment for a proxy measure of infection severity.

It is important to clarify that this analysis does not demonstrate a cause for these differences in peak temperature observed between males and females and different ethnic groups. Thus, it is possible that differences in the intensity of infection or time-course of the infection prior to presentation to the health services could potentially impact on the peak temperatures recorded after admission to hospital. One determinant of this could be ability to access health care services easily. Alternatively, environmental, lifestyle or medical co-morbidities may also potentially impact on the host response to Covid-19, and hence the peak temperatures observed.

These data are consistent with the perception that males experience more symptoms from common viral infections than females; a phenomenon described as ‘man flu’ [3]. While healthy black women have been reported as having higher baseline temperatures than white women [4], this is the first report of maximal temperature attained in the context of a single infection in black skinned individuals compared to white-skinned individuals.

These differences may contribute to different clinical responses and outcomes observed between different ethnic groups and between the sexes [5] in patients with Covid-19 infection.

Author Contributions: Dr Crook had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Concept and design: Crooks, Fogarty, Shaw, Gazis.

Acquisition, analysis, or interpretation of data: West, Card, Simmonds, Crooks.

Drafting of the manuscript: Crooks, Fogarty.

Critical revision of the manuscript for important intellectual content: Gazis, Simmonds, Shaw, Card, West.

Statistical analysis: Crooks.

Conflict of Interest Disclosures: No conflicts of interest declared.

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Data availability statement: We are unable to share these data due to UK data governance law.

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Table. Association between ethnic group and sex with maximum temperature per admission

	Admissions N	Max Temperature per admission (95% CI)	p value	Max Temperature per admission (adjusted for maximum CRP in admission)	p value
Mean age, years sd	65.4 years (19.9 years)	0.000 (-0.001 to +0.001)	0.706	-0.002 (-0.003 to -0.001)	**<0.001**
Male (%)	7574 (50.0%)	*Reference*	-	*Reference*	-
Female (%)	7581 (50.0%)	-0.124 (-0.153 to -0.094)	**<0.001**	-0.050 (-0.078 to -0.023)	**<0.001**
White (%)	11240 (74.2%)	*Reference*		*Reference*	
Indian/Pakistani (%)	858 (5.7%)	+0.098 (+0.033 to +0.163)	**0.003**	+0.104 (+0.045 to +0.163)	**0.001**
Black/Mixed (%)	613 (4.0%)	+0.171 (+0.096 to +0.245)	**<0.001**	+0.143 (+0.075 to +0.211)	**<0.001**
Other (%)	322 (2.1%)	+0.095 (-0.005 to +0.196)	0.064	+0.072 (-0.020 to +0.164)	0.124
Unknown (%)	2122 (14.0%)	+0.134 (+0.094 to +0.175)	**<0.001**	+0.092 (+0.055 to +0.129)	**<0.001**
Max CRP during admission	-	-		+0.003 (+0.003 to +0.003)	**<0.001**
N of patients	7749	7749		7749	
N of admissions	15155	15155		15155	

CI Confidence intervals