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COVID-19: Unique public health issues facing Black, Asian and minority ethnic communities

Eyad Abuelgasima, Li Jing Sawb, Manasi Shirkec, Mohamed Zeinah, MD, FRCS CThd, and Amer Harky, MScb,d*

From the a Faculty of Medicine, Imperial College London, London, United Kingdom, b University of Liverpool School of Medicine, Liverpool, United Kingdom, c Queen’s University Belfast School of Medicine, Belfast, United Kingdom and d Department of Cardiothoracic Surgery, Liverpool Heart and Chest Hospital, Liverpool, United Kingdom.

Abstract: The 2019 coronavirus disease is a serious public health emergency, with serious adverse implications for populations, healthcare systems, and economies globally. Recently, concerns have been raised about possible association between ethnicity, incidence and outcomes of COVID-19 arisen from early government data. In this review, we will explore the possible association using both recent COVID-19 studies and studies of previous pandemics. We call for data on ethnicity to be routinely collected by governments, as part of an international collaboration, alongside other patient demographics and further research to robustly determine the magnitude of association. Moreover, governments must learn from previous pandemics and recommended strategies to mitigate risks on minority ethnicities due to socioeconomic disadvantages. (Curr Probl Cardiol 2020;45:100621.)

Introduction

The 2019 coronavirus disease (COVID-19), caused by severe acute respiratory syndrome coronavirus SARS-CoV-2, is a public health emergency with serious adverse implications for
populations, healthcare systems, and economies globally. Systematic reviews of ethnically homogenous cohorts from China suggest that the key risk factors for hospital admission include age, male sex, and comorbidities such as cardiovascular disease, hypertension, and diabetes.\textsuperscript{1} Governments have been warning vulnerable adults at high risk to be particularly stringent in observing social distancing measures.\textsuperscript{2}

Recently, concerns have been raised about possible association between ethnicity, incidence and outcomes of COVID-19 following observational data released from the Intensive Care National Audit and Research Centre, published on 10 April 2020.\textsuperscript{3} The data showed that of 3883 patients with confirmed COVID-19, 14\% (486) were Asian and 12\% (402) were Black. This is double the 13\% ethnic minority population of the UK at the time of the last census in 2011.\textsuperscript{4} Moreover, of 2249 patients admitted to 201 critical care units in England, 64.8\% were White, 13.8\% were Asian, 13.6\% were Black, and 7.8\% were from other or mixed ethnic groups.\textsuperscript{3} The UK is the first country in the COVID-19 pandemic with an ethnically diverse population and universal healthcare.

In this review, we will explore the possible association between ethnicity, incidence and outcomes of COVID-19 using both recent COVID-19 studies and studies of previous pandemics. The higher incidence and severity in ethnic minority groups may be associated with socioeconomic, cultural, or lifestyle factors, genetic predisposition, or pathophysiological differences in susceptibility or response to infection.

**Biological factors**

*Ethnic disparities in lung function*  
Multiple studies have investigated the disparities of lung function in different ethnic groups and showed an association between those of minority ethnic descent and lower lung function, compared to their Caucasian counterparts.\textsuperscript{5–8} The systematic review by Braun et al. noted that the definition of race/ethnicities were lacking in most studies, and a proportion did not include socio-economic circumstances.\textsuperscript{9} It was suggested that past research should be analysed and to attempt to view the definitions of race from a less Anglo-American point of view, which highlights the need for this correlation to be further addressed.
Genetic polymorphisms

The angiotensin-converting enzyme-2 (ACE2) receptor serves as an entry point for SARS-CoV-2. Previous studies have shown that higher expressions of ACE2 receptor increases susceptibility to SARS-CoV in vitro. Cao et al. systematically analysed coding-region variants in ACE2 and expression quantitative trait loci (eQTLs). It was found that East Asians populations have higher allele frequencies of eQTL variants associated with a higher expressions of ACE2 levels compared to Caucasians. While there is limited research available on ACE2 gene polymorphisms and its effect on COVID-19’s outcome, a study conducted by Chiu et al. on SARS-CoV does not support an association between its genetic variants and disease outcome. No significant difference was observed in the allele distributions between female and male controls, between SARS cases and controls, between SARS cases with poor outcomes and controls, between the male SARS patients with poor outcome and the male controls and between the female SARS patients and female controls. However, as both viruses share ACE2 receptor as their entry point, it should be explored to see if the same stands true for COVID-19 as well.

A possible association between Glucose-6-phosphate dehydrogenase (G6PD) deficiency and COVID-19 has recently been recently suggested. G6PD deficiency has a high prevalence in persons of African, Asian, and Mediterranean descent. Accumulating evidence suggests that G6PD deficiency may increase viral replication and susceptibility to viral infections due to its cellular redox state. In a study conducted on Human Coronavirus HCoV 229E, it was found that antioxidant treatment may protect against viral infection. Oxidative stress increases susceptibility to viral infections and successfully shown that it can be attenuated by pre-treating these deficient cells with lipoic acid (antioxidant). Considering that it is the most common enzymatic deficiency worldwide and in light of COVID-19, this provides a strong rationale for future studies.

Pathophysiological factors

The observed disproportionate impact of COVID-19 on ethnic minorities maybe due to BCG vaccination policy in their country of birth and immune effects. It has been shown that countries with a BCG vaccination policy has a reduced morbidity and mortality rate for COVID-19 due to its non-specific immunity. It has been found that middle to high-income countries with a universal BCG policy have a lower mortality rate (0.78/million) of COVID-19 compared to those with the same income but without a BCG policy (16.39/million). Moreover, within countries that had
a universal BCG policy, those with a more established policy have lower mortality rates.\textsuperscript{18}

However, such data is observational and may have confounding factors, such as limited testing and reporting in many countries, difference in government policies regarding safety precautions etc. It may be the case that BCG may not be have a direct result on COVID-19 but on associated co-occurring infections or sepsis. Further studies are needed to address these factors.

Another possible prevention strategy has been linked to Vitamin D deficiency. Vitamin D deficiency is common amongst minority ethnic groups in the UK. For instance, one study found that 42.2\% of South Asians and 12.5\% of Black African-Caribbeans had severe Vitamin D deficiency.\textsuperscript{19} Observational studies have demonstrated that there is a correlation with low serum of Vitamin D and the incidence of acute respiratory tract infections (ARTIs).\textsuperscript{20,21} In an extensive review conducted by Grant et al., it was suggested that Vitamin D supplementation may have a role in reducing the risk of COVID-19 infections.\textsuperscript{20}

The role of vitamin D in the modulation of the innate and adaptive immune responses is well documented in literature. Vitamin D helps maintain tight junctions, enhances cellular innate immunity via induction of antimicrobial peptides and reduces production of pro-inflammatory cytokines.\textsuperscript{22}

However, there is a lack of agreement between observational studies and RCT in the role of Vitamin D in reducing incidence and severity of ARTIs.\textsuperscript{21} More clinical studies are needed to substantiate the benefits of micronutrient supplementation against COVID-19 infection.

\textbf{Underlying health conditions}

Black, Asian and Minority Ethnics (BAME) communities are prone to higher rates of cardiovascular disease (CVD) such as hypertension, diabetes and are subject to adverse healthcare disparities than their white counterparts. Multiple studies have confirmed that the most common comorbidities associated with severe cases of COVID-19 are hypertension, diabetes and cardiovascular disease (CVD).\textsuperscript{23,24}

It is still unclear if uncontrolled hypertension is a risk factor for contracting COVID-19, though it is undisputed that good blood pressure control would relieve the disease burden. In those of African-Caribbean descent, their hypertension is likely to be more severe and treatment resistant compared to their white counterparts.\textsuperscript{25} Moreover, south Asians have a higher incidence of coronary heart disease,\textsuperscript{26} which is considered a high-risk group for COVID-19.
It is well documented that ethnic minorities have a higher prevalence of diabetes than non-minority individuals. In previous pandemics, diabetes was an independent risk factor for complications and mortality.\textsuperscript{27} The presence of diabetes tripled the risk of hospitalization and quadrupled the risk of ICU admission during the H1N1 outbreak in 2009.\textsuperscript{28} Hyperglycaemia and insulin resistance promotes a pro-inflammatory response, which may lead to a higher propensity to infections.\textsuperscript{39} This metabolic inflammatory state also predisposes them to an enhanced release of cytokines, which is implicated with multi-organ failure in severe COVID-19 cases.\textsuperscript{30} Patients with poorly controlled diabetes also have a compromised immune response,\textsuperscript{29,30} which may prolong the recovery and impair the healing process.

The relationship between ethnicity and renal disease has been studied extensively. In the US, ethnic minorities are 1.5-4 times more at greater risk of end stage renal failure at rates than those of their white counterparts.\textsuperscript{31} Chronic Kidney Disease (CKD) is a common complication of both diabetes and hypertension, therefore it is important to consider its implications with COVID-19. Pooled data of 4 studies found CKD to be a significant clinical predictor of severe COVID-19.\textsuperscript{32} These patients have a pro-inflammatory state with functional defects in their immune system that leaves them at a higher risk for URTIs and Pneumonia.\textsuperscript{32,33}

Patients with pre-existing CKD will be at increased risk of AKI, which is associated with an increased risk of in-hospital mortality.\textsuperscript{33} AKI in COVID-19 appears to be accompanied with multi-organ failure and shock. Patients with elevated baseline serum creatinine on admission had a higher risk of deterioration and mortality, therefore careful monitoring of kidney function should be emphasized.\textsuperscript{33}

**Cultural and socioeconomic factors**

Evidence published from past pandemics proves that ethnic minorities are disproportionately affected, and experience worse health outcomes compared to other groups. Poor health outcomes may be due to limited access to healthcare, poor living conditions, and educational and linguistic obstacles in adopting preventative measures.\textsuperscript{34}

The English House Survey published by the UK government shows that overcrowding affects 11% of Asian households, including 30% of Bangladeshi households, and 15% Black African households, compared with 2% of white households in the UK.\textsuperscript{35} Whereas, white British households are the least likely to be overcrowded, in comparison to all other ethnic groups. The culture of multi-generational living within some Black, Asian and minority ethnic (BAME) communities’ results in
overcrowding, thereby placing the elderly and those with comorbidities at risk. These disadvantages collectively make it more challenging for COVID-19 social distancing measures to work.

Moreover, Africans are at a higher risk of receiving later and more indigent healthcare compared to other ethnic groups. A pandemic at the magnitude of COVID-19, with severe economic crises, can further hamper the delivery and availability of healthcare. Studies from A/H1N1 influenza suggest that despite people from ethnic minorities express greater intention to make behavioural changes in response to recommendations and adopt protective behaviours, barriers exist which prevent this from translating into health-seeking action.

Ethnic minority communities are also more likely to be socioeconomically disadvantaged than white communities. Evidence from the 2009 A/H1N1 influenza pandemic showed poor antiviral uptake in areas with higher levels of deprivation, hence following the inverse care law. This seemed to have contributed to the disproportionately high morbidity in minority groups.

A large proportion of BAME communities rank poorly in socioeconomic indicators of poverty and deprivation. Reasons attributed may be long-standing structural inequalities, institutional racism relating to housing, immigration and social welfare support. These members living under the federal poverty line are at risk due to inability to stockpile food, pay for utilities, shelter, and transportation. Furthermore, their financial conditions worsen if they are unable to work while complying with isolation measures.

The lack of financial resources, diversity of belief, distrust of medical professionals, research, lack of tailored and culturally appropriate education and limited inclusion of minorities while planning for a pandemic prove disadvantageous to people belonging to BAME groups. Non-native English speakers in hospitals face linguistic disparities due to lack of assistance in translation usually provided by family members, further leading to feelings of anxiety and stress. A vast majority of ethnic minorities work in the service-sector and rely on public transport for their travel. Studies conducted in the US have shown that minorities account for 63% of public transport users, making this a possible source of disparity in exposure.

Studies suggest that in order to reduce the occurrence of such discrepancies, culturally competent and low literacy pre-pandemic educational and communication materials should be made available with useful messages.
Future direction

Further research is needed to better understand the disproportionate impact that coronavirus has on BAME communities. Data on the ethnicity and outcomes of patients diagnosed with COVID-19 needs to be routinely collected by governments as part of an international data set alongside other patient demographics. Clear evidence on association between ethnicity and outcome in COVID-19 is important for regions where the pandemic is at an earlier stage and can help with implementation of appropriate public health policies to mitigate adverse outcomes following risk-analysis.

Moreover, future and ongoing genome and association analysis studies, to identify protective or susceptible DNA variants, need to record ethnicity of participants. This is important to determine the strength of any genetic predisposition to the susceptibility of serious cases of coronavirus on BAME communities. Moreover, further research is needed to determine if vitamin D deficiency factors in COVID-19 susceptibility, incidence progression and outcomes. Results of such studies can be factored into governments’ COVID-19 forward planning policies, such as vitamin D supplementation for at risk groups.

Governments must ensure they now learn from previous pandemics and undertake suggested measures to protect ethnic minority communities and mitigate the socioeconomic, cultural, educational, and linguistic barriers to adoption of pandemic interventions. Governments and policy makers should consistently engage with ethnic minority populations, their service providers, and trusted community leaders to effectively communicate information about pandemic status, affected communities, risks and recommended actions.

Conclusion

We call for data on ethnicity to be routinely collected by governments, as part of international collaboration, alongside other patient demographics and further research to robustly determine magnitude of association. Moreover, governments must learn from previous pandemics and recommended strategies to mitigate risks on minority ethnicities due to socioeconomic disadvantages.

REFERENCES

1. Li B, Yang J, Zhao F, Zhi L, Wang X, Liu L, Bi Z, Zhao Y. Prevalence and impact of cardiovascular metabolic diseases on COVID-19 in china. Clin Res Cardiol 2020 May;109(5):531–8.
2. Public Health England. Guidance on social distancing for everyone in the UK. Available from: https://www.gov.uk/government/publications/covid-19-guidance-on-social-distancing-and-for-vulnerable-people/guidance-on-social-distancing-for-everyone-in-the-uk-and-protecting-older-people-and-vulnerable-adults.

3. Intensive Care National Audit and Research Centre. Covid-19 study case mix programme. 2020.

4. Office of National Statistics. 2011 census. 2011.

5. Menezes AMB, Wehrmeister FC, Hartwig FP, Perez-Padilla R, Gigante DP, Barros FC, Oliveira IO, Ferreira GD, Horta BL. African ancestry, lung function and the effect of genetics. *Eur Respir J* 2015 Jun;45(6):1582–9.

6. Korotzer B, Ong S, Hansen JE. Ethnic differences in pulmonary function in healthy nonsmoking asian-americans and european-americans. *Am J Respir Crit Care Med* 2000 Apr;161(4 Pt 1):1101–8.

7. Saad NJ, Patel J, Minelli C, Burney PGJ. Explaining ethnic disparities in lung function among young adults: A pilot investigation. *PLoS ONE* 2017;12(6):e0178962.

8. Stocks J, Sonnappa S, Lum S. Lung function testing in children: Importance of race and ethnic-specific reference equations. *Expert Rev Respir Med* 2014 Oct;8(5):527–31.

9. Braun L, Wolfgang M, Dickersin K. Defining race/ethnicity and explaining difference in research studies on lung function. *Eur Respir J* 2013 Jun;41(6):1362–70.

10. Khan IH, Zahra SA, Zaim S, Harky A. At the heart of COVID-19. *J Card Surg* 2020 May 5. https://doi.org/10.1111/jocs.14596.

11. Li W, Sui J, Huang I-, Kuhn JH, Radoshitzky SR, Marasco WA, Choe H, Farzan M. The S proteins of human coronavirus NL63 and severe acute respiratory syndrome coronavirus bind overlapping regions of ACE2. *Virology* 2007 Oct 25;367(2):367–74.

12. Hofmann H, Geier M, Marzi A, Krumbiegel M, Peipp M, Fey GH, Gramberg T, Pöhlmann S. Susceptibility to SARS coronavirus S protein-driven infection correlates with expression of angiotensin converting enzyme 2 and infection can be blocked by soluble receptor. *Biochem Biophys Res Commun* 2004 Jul 09;319(4):1216–21.

13. Khashkhusha TR, Chan JSK, Harky A. ACE inhibitors and COVID-19: We don’t know yet. *J Card Surg* 2020 Apr 27. https://doi.org/10.1111/jocs.14582.

14. Chiu RWK, Tang NLS, Hui DSC, Chung GTY, Chim SSC, Chan KCA, Sung Y, Chan LYS, Tong Y, Lee W, Chan PKS, Lo YMD. ACE2 gene polymorphisms do not affect outcome of severe acute respiratory syndrome. *Clin Chem* 2004 Sep;50 (9):1683–6.

15. Al-Abdi S, Al-Aamri M. G6PD deficiency in the COVID-19 pandemic: Ghost within Ghost. *Hematol Oncol Stem Cell Ther* 2020 Apr 18. S1658-3876(20)30044-3.

16. Nkhoma ET, Poole C, Vannappagari V, Hall SA, Beutler E. The global prevalence of glucose-6-phosphate dehydrogenase deficiency: A systematic review and meta-analysis. *Blood Cells Mol Dis* 2009 May-Jun;42(3):267–78.

17. Wu Y, Tseng C, Cheng M, Ho H, Shih S, Chiu DT. Glucose-6-phosphate dehydrogenase deficiency enhances human coronavirus 229E infection. *J Infect Dis* 2008 Mar 15;197(6):812–6.

18. Miller A, Reandelar M, Fasciglione K, Roumenova V, Li Y, Otazu G. Correlation between universal BCG vaccination policy and reduced morbidity and mortality for
COVID-19: An epidemiological study. *MedRxiv* 2020. [Preprint.][cited 2020 April 26]. Available from: https://www.medrxiv.org/content/10.1101/2020.03.24.20042937v1.

19. Patel JV, Chackathayil J, Hughes EA, Webster C, Lip GYH, Gill PS. Vitamin D deficiency amongst minority ethnic groups in the UK: A cross sectional study. *Int J Cardiol* 2013 Sep 01;167(5):2172–6.

20. Grant WB, Lahore H, McDonnell SL, Baggerly CA, French CB, Aliano JL, et al. Evidence that vitamin D supplementation could reduce risk of influenza and COVID-19 infections and deaths. *Nutrients* 2020 Apr 02;12(4).

21. Martineau AR, Jolliffe DA, Hooper RL, Greenberg L, Aloia JF, Bergman P, Dubnov-Raz G, et al. Vitamin D supplementation to prevent acute respiratory tract infections: Systematic review and meta-analysis of individual participant data. *BMJ* 2017 Feb 15;356:i6583.

22. Aranow C. Vitamin D and the immune system. *J Investig Med* 2011 Aug;59(6):881–6.

23. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in wuhan, china. *Lancet* 2020 Feb 15;395 (10223):497–506.

24. Wu C, Chen X, Cai Y, Xia J, Zhou X, Xu S, et al. Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in wuhan, china. *JAMA Intern Med* 2020 Mar 13.

25. Khan JM, Beevers DG. Management of hypertension in ethnic minorities. *Heart* 2005 Aug;91(8):1105–9.

26. Schiffrin EL, Flack J, Ito S, Munter P, Webb C. Hypertension and COVID-19. *Am J Hypertens. Epub* 2020 Apr 06.

27. Yang JK, Feng Y, Yuan MY, Yuan SY, Fu HJ, Wu BY, Sun GZ, Yang GR, Zhang XL, Wang L, Xu X, Xu XP, Chan JCN. Plasma glucose levels and diabetes are independent predictors for mortality and morbidity in patients with SARS. *Diabet Med* 2006 Jun;23(6):623–8.

28. Allard R, Leclerc P, Tremblay C, Tannenbaum T. Diabetes and the severity of pandemic influenza A (H1N1) infection. *Diabetes Care* 2010 Jul;33(7):1491–3.

29. Knapp S. Diabetes and infection: Is there a link?—A mini-review. *Gerontology* 2013;59(2):99–104.

30. Bornstein SR, Dalan R, Hopkins D, Mingrone G, Boehm BO. Endocrine and metabolic link to coronavirus infection. *Nat Rev Endocrinol. Epub* 2020 Apr 02.

31. Harawa NT, Norris KC. The role of ethnic variation and CKD. *Clin J Am Soc Nephrol* 2015 Oct 07;10(10):1708–10.

32. Henry BM, Lippi G. Chronic kidney disease is associated with severe coronavirus disease 2019 (COVID-19) infection. *Int Urol Nephrol. Epub* 2020 Mar 28.

33. Zaim S, Chong JH, Sankaranarayanan S, Harky A. COVID-19 and Multi-Organ Response. *Curr Probl Cardio. Epub* 2020 April 28. https://doi.org/10.1016/j.cpcardiol.2020.100618.

34. Sachedinah N, Donaldson LJ. Paediatric mortality related to pandemic influenza A H1N1 infection in england: An observational population-based study. *Lancet [Internet]* 2010 Nov 27:376(9755):1846–52.

35. UK government. Overcrowded households. Available from:https://www.ethnicity-facts-figures.service.gov.uk/housing/housing-conditions/overcrowded-households/2.2.
36. Quinn SC, Kumar S, Freimuth VS, Musa D, Casteneda-Angarita N, Kidwell K. Racial disparities in exposure, susceptibility, and access to health care in the US H1N1 influenza pandemic. *Am J Public Health* 2011 Feb;101(2):285–93.

37. Rubin GJ, Amlot R, Page L, Wessely S. Public perceptions, anxiety, and behaviour change in relation to the swine flu outbreak: Cross sectional telephone survey. *BMJ* 2009 Jul 02;339:b2651.

38. Haroon SMM, Barbosa GP, Saunders PJ. The determinants of health-seeking behaviour during the A/H1N1 influenza pandemic: An ecological study. *J Public Health (Oxf)* 2011 Dec;33(4):503–10.

39. Blendon RJ, Koonin LM, Benson JM, Cetron MS, Pollard WE, Mitchell EW, Weldon KJ, Herrmann MJ. Public response to community mitigation measures for pandemic influenza. *Emerging Infect Dis* 2008 May;14(5):778–86.

40. Hutchins SS, Fiscella K, Levine RS, Ompad DC, McDonald M. Protection of racial/ethnic minority populations during an influenza pandemic. *Am J Public Health* 2009 Oct;99(Suppl 2):261.

41. Harky A, Chiu CM, Yau THL, Lai SHD. Cancer Patient Care during COVID-19 [published online ahead of print, 2020 May 14]. *Cancer Cell* 2020. https://doi.org/10.1016/j.ccell.2020.05.006.

42. Kermali M, Khalsa RK, Pillai K, Ismail Z, Harky A. The role of biomarkers in diagnosis of COVID-19 - A systematic review [published online ahead of print, 2020 May 13]. *Life Sci* 2020. https://doi.org/10.1016/j.lfs.2020.117788.