ANATOL J FAMILY MED
The Anatolian Journal of Family Medicine

Short Communication

DOI: 10.5505/anatoljfm.2020.84756
Anatol J Family Med 2020;3(2):173–178

A Clinical View on the COVID-19 Racial Disparity in the United States and the United Kingdom

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ABSTRACT

COVID-19 that was originating from Wuhan in China has then evolved into various variants, which are specific to regions. Interestingly, COVID-19 highlights that the first strain travelled majorly to the Western Region and was possibly transforming during endemic transmission. There are approximately 93 mutations acquired by the novel virus, and the multiple strains are now grouped into three different clusters. This outbreak has led to a global pandemic never seen for more than a century. This viewpoint is focused on mutation hotspots, case fatalities in most affected nations, impacts of a cytokine storm, and influencing factors that may have amplified the pandemic, to culminate with a racial disparity in both the United States and the United Kingdom Leadership at the highest level of government is important to quickly averting the worst outcome of this pandemic as evident from other countries. Science is the key toresolving many problems; however, that may be professionally used by society and governments as to tackle the difficulty and challenges posed by COVID-19.

Keywords: COVID-19 pandemic, chemotactic cytokines, DNA mutational analysis, healthcare disparity, pathogenesis

Please cite this article as: Herbert E, Fournier D. A Clinical View on the COVID-19 Racial Disparity in the United State and the United State. Anatol J Family Med 2020;3(2):173–178.

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Received Date: 02.06.2020
Accepted Date: 18.06.2020
Published online: 21.08.2020

INTRODUCTION

Symptoms associated with SARS-CoV-2 actually began among patients in Wuhan already in November 2019, when affected patients presented various degrees of a respiratory distress syndrome with unknown aetiology. As it became apparent that most cases had a shared history of exposure to the Huanan Seafood Wholesale Market (the so-called "wet market"), the local health authority in Wuhan issued an epidemiological alert on December 30, 2019, which resulted in its closing.[1]

The origin of COVID-19 is not completely understood. Assuming this virus is artificial, it is important afterwards to reflect back to 45 years ago when scientists met to discuss potential biohazards and regulation of biotechnology and banned some potentially dangerous experiments, including cloning of recombinant DNA during Asilomar Conference (California, U.S.) on rDNA held in 1975.[2] If the virus is of natural origin, then it is necessary to understand how novel coronaviruses are transmitted from animal reservoirs to humans and reduce the likelihood of person coming into contact with them.[3]

On a global level to date, there are over 4.5M+ infected with COVID-19 and approximately 312.000+ deaths recorded as of May 18, 2020, and the number is increasing by the day.[4] The COVID-19 is infecting and killing in a disproportionate way African Americans across much of the south of the U.S. just in the same way as ethnic minorities in the U.K. are also dying

from it at a higher rate.[5] Louisiana, a major U.S. hotspot, was the first Southern state to categorize COVID-19 deaths by race and recorded a shocking 70% were among African Americans.[6,7] In Georgia, an incomplete-data picture still show African Americans who are making up 33% of the state's population, compared with 60% for whites are being hit disproportionately hard by the virus.[8] In Alabama, a similar story is playing out where the data released from the state's department of public health showed that black Alabamians are being infected and killed by the virus at a disproportionate rate (Table 1).[9]

The unprecedented nature of this crisis is a complete shock to the healthcare system in particular. The rapid influx of ailing patients outpaced the inadequate supplies of Personal Protective Equipment (PPE) even to healthcare workers.[10] The economic collapse is beyond imagination and continues to unfold. While the virus does not discriminate, history of discrimination notably in the U.S., likewise in the U.K., creates potential long-term scenarios that reflect in this pandemic. The reckless actions from governments that did not take earlier precautionary measures to mitigate the spread of disease led to disparities among people of colour. This is going to be overlaid on top of the existing racial inequalities. COVID-19's disproportionate impact on communities of colour has been partially of structural factors. Ethnic minority populations are making up "essential workers", such as hospitals, retail/grocery workers, public transit employees, health/social care professionals and custodial staff. These frontline workers, disproportionately black and brown, are typically segregated communities. The health disparities were already in existence before COVID-19.[10]

Table 1. Fatalities per 100.000 populations in the U.S. and the U.K.

Ethnicity	**Fatality rate per 100.000 (U.S.)**
Asian	10.1
Black	25.5
Latino	10.6
White	9.4
All Americans (in these places)	15.4
Ethnicity	**Fatality rate/100.000 (U.K.)**
White British	23
Indian	30
Pakistani	26
Bangladeshi	20
Any other Asians	27
Total Asians	27
Caribbean	69
African	27
Any other Blacks	47

Undocumented Latino communities in the U.S. working in rural industries, such as farming, poultry, and meat production often have no health insurance and stand no chance of being treated when infected with COVID-19, adding to the disparity.[11]

COVID-19 Mutation Hotspots

A phylogenetic network of 160 complete SARS-CoV-2 genomes has been reported in which three core variants distinguished by amino acid changes are named as A, B, and C, with A being the ancestral type according to the bat outgroup coronavirus.[12]

Notably, some evidence has emerged recently supporting that COVID-19 mortality can differ significantly depending on geographical location. Baud et al. reported that the mortality rate was three times higher out of China in comparison to 5.6% in the country.[13] There are various factors influencing the rate of a viral infection, such as diversenational approaches applied to people's movement restrictions, isolation, quarantine, mass screening, adequate PPE from the onset and herd immunity in different genetic populations. The differences in mortality could be understood, but viral mutations and evolutionary capability over time may be vital.[14]

Mutations in 2891, 3036, 14408, 23403 and 28881 positions are predominantly in Europe, while mutations located at positions 17746, 17857 and 18060 are exclusively dominant in North America.[15] For the first time, a silent mutation in the RdRp gene has been discovered in England (U.K.) on February 9, 2020, while in Lombardy (Italy), a different mutation in the same gene changing amino acid composition was identified on February 20, 2020.[15] Although there are varying strains of COVID-19 identified and evolving in Europe, North America and Asia, they may co-exist with each of them characterized by a different mutation pattern. Among these hotspots, one mutation in position 14408 is located within the RdRp protein and is linked with an overall rate.[14]

There were no mutations identified in the Asian genomes analyzed in December.[14] In North American patients, a distinct pattern of hotspot mutations is detected from March 2020, when the outbreak of positive cases was reported in the U.S. and Canada.[14] Interestingly, viral genomes present in North American patients carrying RdRp mutations (14%) do not carry any of Europe's specific ones. There are 93 mutations revealed via a nucleotide sequence alignment over the entire genome of SARS-CoV-2 (Table 2).[16]

Table 2. List of mutations found in the entire genome of SARS-CoV-2 strains

Genomic region	Missense mutation	Country where strain detected
ORF1ab polyprotein	A→T	USA/CA3/2020/EPI_ISL_408008
		USA/CA4/2020/EPI_ISL_408009
	P→S	France/IDF0515/2020/EPI_ISL_408430
	S→N	USA/CA1/2020/EPI_ISL_406034
	T→I	USA/CA5/2020/EPI_ISL_408010
	A→V	Japan/TY-WK-012/2020/EPI_ISL_408665
	L→F	Korea/KCDC03/2020/EPI_ISL_407193
	I→V	USA/CA3/2020/EPI_ISL_408008
		USA/CA4/2020/EPI_ISL_408009
	M→T	Shenzhen/SZTH-004/2020/EPI_ISL_406595
	L→I	Wuhan/WHO1/2019/EPI_ISL_406798
	I→T	Wuhan/IPBCAMS-WH-03/2019/EPI_ISL_403930
	G→S	Wuhan/WIV05/2019/EPI_ISL_402128
	A→V	Shandong/IVDC-SD-001/2020/EPI_ISL_408482
	G→V	Wuhan/IPBCAMS-WH-05/2020/EPI_ISL_403928
	D→A	Wuhan/WIV07/2019/EPI_ISL_402130
	N→S	Wuhan/IPBCAMS-WH-01/2019/EPI_ISL_402123
	F→I	Wuhan/IPBCAMS-WH-01/2019/EPI_ISL_402123
	T→I	France/IDF0515/2020/EPI_ISL_408430
	S→L	Shenzhen/HKU-SZ-005/2020/EPI_ISL_405839
	L→F	Yunnan/IVDC-YN-003/2020/EPI_ISL_408480
		Shandong/IVDC-SD-001/2020/EPI_ISL_408482
		Chongqing/IVDC-CQ-001/2020/EPI_ISL_408481
		Singapore/3/2020/EPI_ISL_407988
		France/IDF0515/2020/EPI_ISL_408430
		USA/AZI/2020/EPI_ISL_406223
	E→D	Japan/KY-V-029/2020/EPI_ISL_408669
	N→K	Wuhan/WHO1/2019/EPI_ISL_406798
	W→C	Taiwan/2/2020/EPI_ISL_406031
	T→I	USA/CA2/2020/EPI_ISL_406036
	I→T	England/02/2020/EPI_ISL_407073
		England/01/2020/EPI_ISL_407071
	P→L	Japan/AI/I-004/2020/EPI_ISL_407084
	F→Y	Sichuan/IVDC-SC-001/2020/EPI_ISL_408484
	E→D	Shenzhen/SZTH-004/2020/EPI_ISL_406595
	K→R	Wuhan/WIV05/2019/EPI_ISL_402128
	D→N	Wuhan/WIV02/2019/EPI_ISL_402127
Spike glycoprotein	F→I	Wuhan/HBCDC-HB-01/2019/EPI_ISL_402132
	H→Y	Guangdong/20SF174/2020/EPI_ISL_406531
		Guangdong/20SF040/2020/EPI_ISL_403937
		Guangdong/20SF028/2020/EPI_ISL_403936
	S→R	Australia/VIC01/2020/EPI_ISL_406844
	N→D	Shenzhen/SZTH-004/2020/EPI_ISL_406595
	D→Y	Shenzhen/SZTH-004/2020/EPI_ISL_406595
	V→F	France/IDF0372/2020/EPI_ISL_406596
		France/IDF0373/2020/EPI_ISL_406597
	D→G	Germany/BavPat1/2020/EPI_ISL_406862

Table 2. CONT.

Genomic region	Missense mutation	Country where strain detected
	P→L	Australia/QLD02/2020/EPI_ISL_407896
Matrix protein	D→H	Singapore/2/2020/EPI_ISL_407987
Nucleocapsid protein	T→I	Shenzhen/SZTH-004/2020/EPI_ISL_406595
	S→L	Shenzhen/SZTH-003/2020/EPI_ISL_406594
		Foshan/20SF207/2020/EPI_ISL_406534
		USA/CA3/2020/EPI_ISL_408008
		USA/CA4/2020/EPI_ISL_408009
	S→N	Australia/QLD02/2020/EPI_ISL_407896
	P→S	Guangzhou/20SF206/2020/EPI_ISL_406533

Nations with the Highest Fatalities associated with COVID-19

The spread of COVID-19 has spanned over 200 countries globally with the worst affected mortality recorded in the U.S., the U.K., Italy, Spain, France and Brazil of late (Table 3).[17, 18] Certainly, differences in demographics may play a role in case fatalities. Italy has one of the oldest populations in the world, with an average age of 45–46, and given that mean age of COVID-19 is 81, it would be understandable for the high incidence of deaths among the elderly population.[18] Interestingly, Italy, as a developed nation, has an excellent healthcare system based on world comparisons; however, intensive care unit beds were at 90% capacity before the surge of COVID-19 in the Northern Region of the country.[19] Unfortunately, the advancement in the treatment of cardiovascular diseases, over the past two decades, created a fertile ground for SARS-CoV-2 infection and COVID-19 severity in Italy. Over 90% of the deaths over there had at least one underlying illness and cardiovascular disease was found in greater than 70% of patients.[20] Here is the COVID-19 situation in the World Health Organization European Region data as of March 29, 2020, at 10:00 CET.[21]

On April 8, 2020, the Centers for Disease Control and Prevention published surveillance data of laboratory-confirmed COVID-19 associated hospitalizations in 14 states within the U.S.[22] Although 18% of people in the catchment population were African Americans, among people with data on race/ethnicity, 33.1% were belonging to this ethnic group, suggesting that they may be disproportionately affected by COVID-19.[22] These data are corresponding with government statistics from cities in the U.S. demonstrating similar racial disparities. In Chicago, more than 50% of COVID-19 cases and approximately 70% of deaths involve black individuals, although they make up only 30% of the population.[6] Incidentally, these deaths are concentrated mostly in just five neighbourhoods on the city's south side. In Louisiana, 70.5% of deaths have occurred among blacks, who represent 32.2% of the state's population, as reported by the Associated Press on April 7, 2020.[23] As for Michigan, 33% of COVID-19 cases and 40% have affected black people, representing 14% of the population.[24] In New York City, which has become the epicenter, this disproportionate burden is validated again in under represented minorities, particularly blacks and Hispanics, who have accounted for 28% and 34% of deaths, respectively (respective population representation: 22% and 29%).[25]

Table 3. List of the countries with COVID-19 highest mortality worldwide (up to May 29, 2020) [17, 18]

Country	Confirmed cases	Recovered	Mortality
U.S.	1,772,355	499,113	103,418
U.K.	269,127	N/A	37,837
Italy	231,732	150,604	33,142
Spain	284,986	196,958	27,119
France	186,238	67,191	28,662
Brazil	438,812	193,181	26,764
Germany	182,710	164,100	8,577

The pandemic reached Latin America later than other continents. The first case recorded in Brazil was on February 25, 2020, but this country had the most cases of deaths in Latin America (465,166 cases and 27,878 deaths as of May 29).[26,27]

The Pathogenesis of Cytokine Storm and Fatal Contribution to COVID-19

The pathogenesis of COVID-19, caused by SARS-CoV-2, is likely to be dependent on the severe disruption of immune and inflammatory processes.[28] The pathophysiology of SARS-CoV-2 induced acute respiratory distress syndrome, which has similarities to that of severe community-acquired

pneumonia caused by other viruses or bacteria.[29,30] Overproduction of early response pro-inflammatory cytokines (tumor necrosis factor, IL-6 and IL-1β) results in what has been termed as a cytokine storm, leading to an increased risk of vascular hyper-permeability, multiple organ failure, and eventually death when the high cytokine concentrations unabated over time.[31,32]

Activation of coagulation pathways during the immune response to COVID-19 infection results in the overproduction of pro-inflammatory cytokines leading to multiple organ injury.[28] Although the major function of thrombin is to promote clot formation by activating platelets and by converting fibrinogen to fibrin, it is also known to exert multiple cellular effects and can further increase inflammation via proteinase-activated receptors.[33] The three regulatory mechanisms associated with the thrombin generation are antithrombin III, tissue factor pathway inhibitor and protein C system.[28] A defective balance between pro-coagulants and anticoagulants predisposes to the development of micro-thrombosis, disseminated intravascular coagulation, and multi-organ failure as evidenced in severe COVID-19 pneumonia with raised D-Dimer levels being a poor prognostic feature common in non-survivors.[34,35]

CONCLUSION

The comorbidities are not mainly attributed to blacks or people of colour, but rather the global dilemma before the COVID-19 outbreak, which has been amplified during this pandemic. There are concerns that go beyond these comorbidities. Where and how black individuals live matters, assuming race per se could be drawn into this pandemic, it is because, in so many communities, race determines home. COVID-19 has become the heralded event that now fully exposes the deep-rooted and chronic wounds both in the U.S. and U.K. communities. Lack of precautionary measures and slow reactions of the U.K. government from the pandemic onset contributed to the chaos and brink of the NHS. COVID-19 does not discriminate based on race or ethnic background, especially when there is no biological link but leadership style, political decisions and inherent structural inequalities will, resulting in the disparity.

Disclosures

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

Authorship Contributions: Concept – E.H., D.F.; Design – E.H., D.F.; Supervision – E.H., D.F.; Materials – E.H., D.F.; Data collection &/or processing – E.H., D.F.; Analysis and/or interpretation – E.H., D.F.; Literature search – E.H., D.F.; Writing – E.H., D.F.; Critical review – E.H., D.F.

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