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Letter to the editor

Analysis of clinical and demographic heterogeneity of patients dying from COVID-19 in Brazil versus China and Italy

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Dear Editor,

As the outbreak of Coronavirus disease 2019 (COVID-19) has already spread around the world,[1] many countries have found themselves mostly unprepared to deal with this new disease, which has now escalated to global pandemic.[2] While there is urgent need for development of appropriate treatments and interventions, understanding the factors associated with mortality are needed to better inform clinical guidelines and public health interventions.[3,4] Interestingly, there is a notable difference in the rate of COVID-19 mortality across countries, which merits the consideration of epidemiologists and clinicians. It should be acknowledged that actual mortality rates may vary from reported cases in each country, and though reporting practices vary, it is likely reported cases are an underestimation of true mortality. Nonetheless, in the most recent report by the World Health Organization (WHO), there is significant variability in case fatality rates (CFR) between Brazil (6.98%), China (5.50%), and Italy (13.60%).[2]

The reason for such differences in CFR remains mostly undefined. It has generally been accepted that age, sex, and burden of comorbidities (i.e., lung and heart diseases, hypertension, obesity, diabetes, renal and liver failure) may have an impact on the outcome of COVID-19 disease[5] and likely influence CFR. As understanding the differences between such populations can better enable effective public health interventions, in this article we aimed to compare the clinical characteristics and patient demographics of patients dying from COVID-19 in Brazil compared to China and Italy.

Clinical and demographic data on COVID-19 mortality in Brazil, China, and Italy were extracted from the most recent official reports from each country: Brazilian Ministry of Health,[6] China Center for Disease Control and Prevention,[7] and Italian National Institute of Health,[8] respectively. To adjust for differences in age between populations, estimates of population age distribution was obtained from the United

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Table 1 – Odds ratios (OR) and prevalence ratios (PR) comparing clinical and demographic characteristics of patients who died in Brazil vs China and Italy.

Characteristic	Brazil vs China					Brazil vs Italy				
	Proportion of Brazilian Deceased	Proportion of Chinese Deceased	OR (95% CI)	PR (95% CI)	Chi Square p-value	Proportion of Brazilian Deceased	Proportion of Italian Deceased	OR (95% CI)	PR (95% CI)	Chi Square p-value
Male Sex	59.30%	62.10%	0.83 (0.72, 0.95)	0.93 (0.88, 0.98)	0.009	59.30%	63.30%	0.84 (0.79, 0.91)	0.94 (0.91, 0.96)	<0.001
Younger than 60 years	30.50%	19.00%	1.87 (1.58, 2.23)	1.61 (1.4, 1.84)	<0.001	30.50%	4.80%	8.63 (7.87, 9.47)	6.31 (5.85, 6.8)	<0.001
Older than 60 years	69.50%	81.00%	0.53 (0.45, 0.63)	0.86 (0.83, 0.89)	<0.001	69.50%	95.20%	0.12 (0.11, 0.13)	0.73 (0.71, 0.75)	<0.001
No comorbidities	33.00%	32.80%	1.01 (0.81, 1.26)	1.01 (0.87, 1.17)	0.92	33.00%	3.60%	13.1 (10.28, 16.69)	9.1 (7.25, 11.44)	<0.001
1 or more comorbidities	67.00%	67.20%	0.99 (0.79, 1.23)	1 (0.93, 1.07)	0.92	67.00%	96.40%	0.08 (0.06, 0.1)	0.7 (0.68, 0.71)	<0.001
Diabetes	33.90%	19.70%	2.09 (1.62, 2.69)	1.72 (1.41, 2.1)	<0.001	33.90%	31.70%	1.1 (0.98, 1.24)	1.07 (0.99, 1.16)	0.1
Cardiovascular Disease	43.40%	22.70%	2.61 (2.05, 3.33)	1.91 (1.59, 2.30)	<0.001	43.40%	65.70%	0.40 (0.36, 0.45)	0.66 (0.63, 0.69)	<0.001
Respiratory Disease	7.70%	7.90%	0.98 (0.67, 1.43)	0.98 (0.69, 1.39)	0.91	7.70%	22.50%	0.29 (0.25, 0.34)	0.34 (0.3, 0.39)	<0.001
Neurologic Disease	–	–	–	–	–	7.30%	26.20%	0.22 (0.19, 0.26)	0.28 (0.24, 0.32)	<0.001
Renal Disease	–	–	–	–	–	8.20%	23.20%	0.3 (0.25, 0.35)	0.35 (0.31, 0.4)	<0.001
Immunodeficiency	–	–	–	–	–	4.70%	4.00%	1.19 (0.91, 1.56)	1.18 (0.91, 1.53)	0.21
Obesity	–	–	–	–	–	4.60%	12.20%	0.34 (0.28, 0.42)	0.37 (0.31, 0.45)	<0.001

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Nations (UN) World Population Ageing 2017 Report.[9] Available data described only fatal cases, therefore making it impossible to estimate risk or odds of death. This study aims to compare the main characteristics of the deceased population of each country, estimating prevalence ratios (PR) and odds ratios (OR) with their respective 95% confidence interval (95% CI), as well as associated frequency distribution (by chi-square test). A PR represents the ratio between the proportions of a specific characteristic of two samples. It can be used to indicate how different the prevalence of a variable/outcome is in one group of subjects compared to another. Statistical analysis was conducted using the R software for statistical computing (version 6.3.2)[10] and the package epiR: Tool for the Analysis of Epidemiological Data (version 1.0–14).[11] The study was carried out in accordance with the Declaration of Helsinki, under the terms of relevant local legislation.

A total of 3611 fatal COVID-19 cases from Brazil, 1023 from China, and 23,188 from Italy were finally included in our analysis (Table 1). Compared to China, Brazil reported 60% higher proportion of patients dying under the age of 60 years (30.5% vs. 19.0%; PR 1.61, 95% CI 1.40–1.84, $p < 0.001$). No significant difference in prevalence of comorbidity (PR 1.00, 95% CI 0.93–1.07, $p = 0.92$) was observed among COVID-19 deaths in each country. When considering individual comorbidities as factors, diabetes (PR 1.72, 95% CI 1.41–2.10, $p < 0.001$) and cardiovascular disease (PR 1.91, 95% CI 1.59–2.30, $p < 0.001$) were more commonly found in individuals dying in Brazil compared to China.

When compared to Italy, those dying from COVID-19 in Brazil had over 6-fold higher prevalence of age<60 years (30.5% vs. 4.8%; PR 6.31, 95% CI 5.85–6.80, $p < 0.001$) and over 9-fold higher prevalence of patients with no comorbidities (33.0% vs. 3.6%; PR 9.10, 95% CI 7.25–11.44, $p < 0.001$). Analysis of specific comorbidities showed no significant difference in prevalence of diabetes (PR 1.07, 95% CI 0.99–1.16, $p = 0.10$) and immunodeficiency (PR 1.18, 95% CI 0.91–1.53, $p = 0.21$), whist decreased prevalence of cardiovascular disease (PR 0.66, 95% CI 0.63−0.69, $p < 0.001$), respiratory disease (PR 0.34, 95% CI 0.30−0.39, $p < 0.001$), neurologic disease (PR 0.28, 95% CI 0.24−0.32, $p < 0.001$), renal disease (PR 0.35, 95% CI 0.31−0.40, $p < 0.001$), and obesity (PR 0.37, 95% CI 0.31−0.45, $p < 0.001$) can be found among those dying from COVID-19 in Brazil. Compared to both Italy (male PR: 0.94, 95% CI 0.91−0.96, $p < 0.001$) and China (male PR: 0.93, 95% CI: 0.88−0.98, p-value = 0.009), a slightly higher prevalence of females can be noted among those dead in Brazil.

To account for difference in populations in each country with respect to age, we calculated the PR for Brazil:China and Brazil:Italy for the percentage of population under age 60 years. Using UN data,[9] the percentage of population under 60 years in each country was 87.4% in Brazil, 83.8% in China, 70.6% in Italy, with PR of 1.04 for Brazil:China and 1.24 for Brazil:Italy. After taking into consideration population differences with age (PR COVID-19 death/PR population age), a 55% higher prevalence of young patients in Brazil vs. China was still noted for COVID-19 deaths (1.61/1.04). After adjusting for population difference between Brazil and Italy, a over 5-fold higher prevalence of young patients among the COVID-19 deaths can be noted in Brazil (6.31/1.24). This confirms that patients dying in Brazil are younger compared to Italy and China.

While we continue to make progress in understanding the pathogenesis of COVID-19, the results of our concise analysis help elucidating a gap in our understanding of difference in mortality rates between countries.[2] Contrary to the reports of increased risk of severe COVID-19 in older patients and in those with comorbidities,[5] our results demonstrate that the deceased population in Brazil is younger and has less comorbidities, which cannot be explained by differences in population demographics alone. A potential explanation could be differences in testing and reporting by countries, as well as discrepancies in local policies, medical care access and infrastructures between young and older patients. However, a more serious implication could also be related to infection by different viral strains, as varying virulence SARS-CoV-2 is now characterized by a considerable genetic diversity which might strongly influence its interplay with human body.[12] These findings should help providing improved public health guidance and intervention. While more studies are required to make further conclusions, we urge clinicians to not be too quick to dismiss the seriousness of COVID-19 in young (<60 years old) and otherwise healthy patients.

Declarations of interest

None.

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