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Research Article

Covid-19 High Attack Rate Can Lead to High Case Fatality Rate -

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ABSTRACT

Background: We conduct this study to identify the relationships among the Attack Rate (AR), the Mortality Rate (MR), and the Case Fatality Rate (CFR).

Material and Methods: Thirty countries and territories with > 500 Covid-19 reported cases per 10,000 population inhabitants were selected on March 10, 2021. One-sample Kolmogorov-Smirnov (K-S), one-way ANOVA, Levene, Least Significant Different (LSD), and matched paired-samples T-tests were used in this study.

Results: There was a highly significant difference concerning AR and CFR mean values. Countries with MR ≥ 15 death / 10^4 inhabitants recorded the highest level of crude mean CFR and AR values, and recorded the highest gap with leftover groups. There were independence 95% confidence intervals of mean CFR and AR values between countries with ≥ 15 death / 10^4 MR and those with MR of <10 death /10^4. There was a significant difference between countries with MR ≥ 15 death / 10^4 inhabitants and countries with MR of <10 death / 10^4 inhabitants through least significant difference (LSD) test for CFR (0.042 p- value) and Games Howell (GH) test for AR/10^4 (0.000 p-value).

Conclusions: Total and mean AR and CFR are higher in high MR countries and vice versa.

Keywords: Case fatality rate; Mortality rate; Attack rate; Covid-19

INTRODUCTION

During the coronavirus disease 2019 (COVID-19) pandemic, mortality rates were heterogeneous, with some countries being hit very hard, others had a much lower death rate [1]. Many factors have been proposed as determining this heterogeneity, including demographics & social factors, comorbidities, and environmental factors (such as temperature, humidity, and air pollution the age, smoking habits, hosting of big public events, socializing habits, or the capacity of the health care system [2].

Of the many driving factors of the strong transmissibility, cluster infections play critical roles in the widespread of disease and exponentially increases the number of cases [3]. It is thought that super-spreaders of COVID-19 play a role in transmission within these clusters since they are partially contributing to the high transmission risk of SARS-CoV-2 [3].

High fatality rates were also reported within these SARS-CoV-2 cluster infections [4].

The Case Fatality Rate (CFR) sometimes called case fatality risk is used to define the probability that a case dies from the infection [5].

At country levels, CFR was seen to be different in different places and seen to be not a constant finding. Furthermore, it can decrease or increase over time [6].

Studies have reported multiple factors for variances in COVID-19 CFR among countries, these include demographics & social factors, comorbidities, and environmental factors (such as temperature, humidity, and air pollution) [2]. Although high AR was studied in small clusters and small locations its relation to MR or CFR was not identified. High mortalities during waves' peaks were attributed to system failure to cope with the increase in disease burden.

However, although the number of cases has been extensively discussed, the number of cases/population at risk i.e. AR, and its relation to MR and CFR with data at the population (country) level have not been verified.

The current paper aimed to identify the statistical correlations between AR and CFR with MR because of the COVID-19 outbreak and its difference among countries, with data at the population (country) level.

From a global health perspective, there is evidence of a research knowledge gap in this field aspect.

MATERIAL AND METHODS

Materials

Thirty countries and territories were chosen. Inclusion criterion was > 500 Covid-19 reported cases per 10,000 population inhabitants. Data on covid-19 cases and deaths was selected as it was on March 10, 2021. Countries and territories were classified into three group groups: group I: countries with mortality rate ≥ 15 death/10^4 population inhabitants; group II: ≥ 10-15 death/10^4 population inhabitants; and group III <10 death/10^4 population inhabitants.

A supplementary document attached file contains original data, computed data, and references for data sources.

Definitions

The detected AR for a given country was calculated as the total number of reported cases divided by the estimated population of that country.

Crude COVID-19 CFR was calculated as the total number of COVID-19 deaths divided by the number of total COVID-19 confirmed cases by March 10, 2021 multiplied by 100.

METHODS

The following statistical data analysis approaches were used under the application of the statistical package (SPSS) *ver.* (22.0):

Descriptive data analysis: Mean value, standard deviation, standard error, (95%) confidence interval, and graphical presentation by using Bar Charts. Mean values and the two extremes values (min. and max.) were computed assuming that data followed normal distribution function.

Inferential data analysis: These were used to accept or reject the statistical hypotheses, which included the following:

a- The One-Sample Kolmogorov-Smirnov (K-S) test. This is a goodness-of-fit test whether the observations could reasonably have come from the specified distribution.

b- The One-Way ANOVA procedure to test the hypothesis that several means are equal. In addition to that, we applied

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after rejecting the statistical hypotheses, the Least Significant Difference (LSD) test requiring equal variances was assumed, and the Games Howell test not requiring equal variances was assumed.

c- Levene test: was used to test homogeneity of variances for equality of variances of two and several independent groups.

d- Matched paired-samples T-Test procedure was used to compare the means of two variables for a single group. It computes the differences between values of the two variables for each case and tests whether the average differs from zero.

RESULTS

Table 1 represents a one-sample "Kolmogorov-Smirnov" test procedure comparing the observed cumulative distribution function for studied data with a specified theoretical distribution, which proposed normal shape (i.e. bell shape), for the studied markers.

The results showed that the test's distribution was normal for the studied reading's markers since no significant levels were accounted for (p-value >0.05). This enabled us of applying conventional two methods of statistics: the descriptive methods of estimations (points and intervals), and the inferential statistics.

In the table 2 results showed group I countries with higher total attack rate and higher total CFR % than group III countries. Group II countries showed the lowest test coverage among the three groups. The CFR % marker recorded a high level of mean value in group I countries with a high gap concerning leftover groups, especially to group III, which accounted for the lowest level among all markers. In addition to that, first and third groups recorded an independent or non-interferer of 95% confidence interval for mean values for each other. Furthermore, group III recorded an independent (non-interferer) of 95% confidence interval for mean values concerning other groups.

Regarding the (AR/10^4) marker, results showed that group I recorded a high level of mean value, and a high gap concerning leftover groups, especially to group III, which accounted for the lowest level for preceding markers. In addition to that, first and third groups recorded independent or non-interferer of 95% confidence interval for mean values.

Table 1: Normal distribution function test (Goodness of fit test) for studied markers.

One-Sample Kolmogorov-Smirnov Test				
Markers	Statistics	Groups (**)		
		I	II	III
CFR %	No.	12	12	16
	Kolmogorov-Smirnov Z	0.589	0.481	0.509
	Asymptotic Sig. (2-tailed)	0.878	0.975	0.958
	C.S. (*)	NS	NS	NS
AR X 10^4	No.	12	12	16
	Kolmogorov-Smirnov Z	0.591	0.848	0.739
	Asymptotic Sig. (2-tailed)	0.876	0.468	0.646
	C.S. (*)	NS	NS	NS
Statistical Hypothesis: Ho: Markers are followed normal distribution function				
Test distribution is Normal.				

(*) NS: Non Sig. at p > 0.05.
(**) Country mortality rate groups: group I: ≥ 15 death/10^4 population inhabitants; group II: ≥10-15 death/10^4 population inhabitants; and group III <10 death/10^4 population inhabitants.
CFR: Case Fatality Rate; AR: Attack Rate.

Concerning testing the compound statistical hypothesis, which says that studied group's concerning (CFR%, and AR/10^4) readings were thrown from the same population, and that should be proved according to of testing equal variances were assumed, as well as equal mean values were assumed through "Levene and one-way ANOVA" tests respectively, and as illustrated in the table 3.

Concerning testing equal variances of CFR% marker, the Levene test showed that no significant differences were accounted at $p > 0.05$ among studied groups and a highly significant result (0.006 p-value) concerning AR. ANOVA test showed a significant difference at $p <$ 0.01 among all studied groups concerning AR and CFR mean values.

The alternative statistical hypothesis says that at least two groups are not equal due to their mean values. This was tested through the LSD test for CFR% marker, and Games Howell (GH) test for AR/10^4 marker (Table 4).

Results in the table 4 showed that no significant difference between groups I, and II regarding both studied markers, and no significant difference between groups II and III regarding the AR marker. There were significant differences among the leftover comparisons in at least at $p < 0.05$ for each of the studied markers. There was a significant difference between the I and III groups in both two tests.

DISCUSSION

Main findings of this study

The results of the current study suggest that the high total and mean attack rates were found in high mortality rates countries. CFRs were also higher in these countries (Table 2 and Figure 1).

It was thought that CFR is used as a measure of disease severity and is often used for predicting disease course or outcome rather than (as in our study) that CFR reflects the level of disease burden among the community.

What is already known on this topic

Commentators may consider CFR as if it's a steady and unchanging number confined to a specific disease in general and Covid-19 in particular.

Studies have reported multiple factors for variances in COVID-19 CFR among countries, these include demographics & social factors, comorbidities, and environmental factors as early mentioned [2].

Previous literature usually attributes an increase in CFR to low estimates due to low testing. Another cause of high CFR in certain places is usually attributed to unknown or yet not yet proved causes. There is evidence suggested by recent literature that CFR is positively related to MR [7,8].

What this study adds

Our significant findings of a highly significant association between AR and CFR is supported by the following previous observations: (1) available data about South Americans and Asian countries that took the strictest measures, and they also had relatively lower COVID-19 CFR [9,10], (2) it has been noticed that in European countries that have had both large numbers of cases and deaths , the average of country-specific CFR was at 0.7%-1.3% at early times of pandemic raised to about 2%-3.31% thereafter [9], this increase in Covid-19

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Table 2: Summary statistics concerning studied markers and total tests/million among different groups of countries.

Markers	Group	No.	Total	Mean	Std. D.	Std. E.	95% C.I. for Mean		Min.	Max.	Total MR	Total tests/million
							L.b.	U.b.				
CFR %	I	12	2.082	2.271	0.598	0.173	1.891	2.651	1.351	3.261	16.377	1,069,856.523
	II	12	2.296	1.880	0.458	0.132	1.589	2.171	1.012	2.465	12.762	335,599.494
	III	16	1.024	0.872	0.464	0.116	0.624	1.119	0.157	1.827	6.763	658,743
AR X 10^4	I	12	786.473	881.7	294.9	85.1	694.3	1069.0	510.2	1286.6	16.377	1,069,856.523
	II	12	555.616	734.1	242.5	70.0	580.0	888.2	517.5	1430.9	12.762	335,599.494
	III	16	659.951	637.7	105.3	26.3	581.6	693.8	513.3	923.3	6.763	658,743

Country mortality rate groups: group I: ≥ 15 death/10^4 population inhabitants; group II: ≥10-15 death/10^4 population inhabitants; and group III <10 death /10^4 population inhabitants.
CFR: Case Fatality Rate; AR: Attack Rate; MR: Mortality Rate.

Table 3: Testing equal variances and equal mean values for studied markers concerning different groups of countries classified according to different mortality rates /10^4 population inhabitants.

Marker	Testing Homogeneity of Variances		ANOVA- Testing Equality of Means	
	Levene Statistic	Sig. (*)	F-test	Sig. (*)
CFR%	0.888	0.420 (NS)	28.936	0.000 (HS)
AR/10^4	5.968	0.006 (HS)	4.273	0.021 (S)

(*) HS: Highly Sig. at $p < 0.01$; S: Sig. at $p < 0.05$; NS: Non Sig. at $p > 0.05$.
CFR: Case Fatality Rate; AR: Attack Rate

Table 4: Multiple Comparisons using (LSD) and (GH) tests for studied markers among studied groups of countries.

Marker	(I) Group	(J) Group	Mean Diff. (I-J)	Sig.	C.S. (*)
CFR%	I	II	0.391	0.066	NS
		III	1.399	0.000	HS
	II	III	1.008	0.000	HS
AR/10^4	I	II	147.6	0.390	NS
		III	244.0	0.042	S
	II	III	96.4	0.424	NS

(*) HS: Highly Sig. at $p < 0.01$; S: Sig. at $p < 0.05$; Non Sig. at $p > 0.05$; Testing based on GH test.

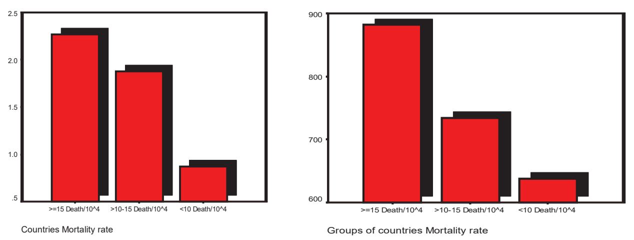

Figure 1: Represent graphically plotting of bar chart regarding mean values studied marker's readings distributed in different groups of countries regarding mortality rates.
Country mortality rate groups: group I: ≥ 15 death /104 population inhabitants; group II: ≥10-15 death / 104 population inhabitants; and group III <10 death /104 population inhabitants.
CFR: Case Fatality Rate; AR: Attack Rate

CFR possibly goes in parallel with an increase in the number of cases, (3) in general, the CFR of COVID-19 differs by location, and has changed during the period of the outbreak [2,4], (4) small clusters of fatal COVID-19 infections were reported previously with high CFR within these clusters (families, tourists , long-term care hospitals and facilities, etc.) [12-16]. There were also identified "vulnerable" clusters of counties in USA with high mortality incidence ratio [17]. In UK A few areas saw COVID-19 mortality more than seven times the expected level compared with the rest of the country [18], (5) there was a positive association between population size and COVID-19 CFR [6], and (6) our findings were in concordance with recent studies which founded very high positive significant correlation between total deaths/1 million and the total number of cases / million inhabitants and a very high positive influence of the COVID-19 MR on the CFR [7,8]. Another study suggested that the crucial factor for the different death rates because of the COVID-19 outbreak is the fast implementation of public events ban [1].

We suggest that AR plays an important role in explaining variances.

The underlying cause for increased CFR with increased AR is possibly related to high viral overload as it was observed in clustering infections a phenomenon already described before that is characterized by high mortality and fatality rates.

During a disease outbreak, estimation of the (CFR) is usually used as an indication of its severity, and is used for planning and determining the intensity of a response to an outbreak as a guide to plan public health strategies [5,19,20]. As CFR value reflects the density of infection, we suggest herein, to study CFR in the context of AR rather than the CFR alone.

As far as the epidemiology concerns with the virulence of the disease in addition to the transmissibility of infectious disease [21], our finding of the significant role of AR will add an important factor explaining various virulence of epidemics in different places and times.

This study will help in the development of prevention and intervention measures to fight against this global public health crisis.

Limitations of this study

The CFR has been consistently being subjected to underestimation and overestimation [22].

Overestimate of CFR is largely due to underestimation [22] of cases especially encountered in an infection with a range of manifestations from relatively mild to severe [5].

Testing capacity, which is associated with the availability of resources and manpower, is the single most important factor that can tremendously affect the CFR [23]. The lack of availability of widespread testing leads to an ascertainment bias toward severe cases [23].

Underestimation of death accounts can lead to erroneously low CFR. This could be due to: (1) in crude estimates, some patients

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encountered as non-dead are still hosted in intensive care units [2], (2) deaths caused by COVID-19 may be misattributed to other death classifications and codes [11], and (3)deaths confirmed counts are subject to time lags [4]. This means that reported cases with COVID-19 will die at a later date [5].

CONCLUSIONS

During the Covid-19 pandemic, the CFR is related to AR and MR values and measures.

Concepts regarding the severity of the disease should be directed to the ability to have high AR rather than to high CFR since CFR can change according to AR.

A possible important cause of variances CFR across the world seems to be due to be previously underestimated factor that is AR.

RECOMMENDATIONS

Increased AR is a very highly significant associated possible predictor for increased MR and CFR. Measures focused on the reduction of AR according to this study will certainly reduce MR and CFR.

Ethical approval was not required for this study, as we used publically available data, and patients were not involved.

(Appendix)

REFERENCES

1. Fountoulakis KN, Fountoulakis NK, Koupidis SA, Prezerakos PE. Factors determining different death rates because of the COVID-19 outbreak among countries. J Public Health (Oxf). 2020 Nov 23;42(4):681-687. doi: 10.1093/pubmed/fdaa119. PMID: 32728758; PMCID: PMC7454744.
2. Sorci G, Faivre B, Morand S. Explaining among-country variation in COVID-19 case fatality rate. Sci Rep. 2020 Nov 3;10(1):18909. doi: 10.1038/s41598-020-75848-2. PMID: 33144595; PMCID: PMC7609641.
3. World Health Organization (2020). Report of the WHO-China Joint Mission on Coronavirus Disease 2019 (COVID-19). https://bit.ly/32SFg3W
4. Nurses TICo. Immediate and serious threat: ICN calls on WHO member states to collect and share data on health worker COVID-19 infection rates and deaths 2020. https://bit.ly/2R2UReA
5. Lipsitch M, Donnelly CA, Fraser C, Blake IM, Cori A, Dorigatti I, Ferguson NM, Garske T, Mills HL, Riley S, Van Kerkhove MD, Hernán MA. Potential Biases in Estimating Absolute and Relative Case-Fatality Risks during Outbreaks. PLoS Negl Trop Dis. 2015 Jul 16;9(7):e0003846. doi: 10.1371/journal.pntd.0003846. PMID: 26181387; PMCID: PMC4504518.
6. Cao Y, Hiyoshi A, Montgomery S. COVID-19 case-fatality rate and demographic and socioeconomic influencers: worldwide spatial regression analysis based on country-level data. BMJ Open. 2020 Nov 3;10(11):e043560. doi: 10.1136/bmjopen-2020-043560. PMID: 33148769; PMCID: PMC7640588.
7. Raham, Tareef Fadhil. Epidemiological Philosophy of Pandemics. February 20, 2021. doi: http://doi.org/10.2139/ssrn.3789738
8. Al-Naqeeb AAA, Raham TF. Case Fatality Rate Components Based Scenarios for Covid-19 Lockdown. March 16, 2021. doi: http://doi.org/10.2139/ssrn.3806123
9. Rajgor DD, Lee MH, Archuleta S, Bagdasarian N, Quek SC. The many estimates of the COVID-19 case fatality rate. Lancet Infect Dis. 2020 Jul;20(7):776-777. doi: 10.1016/S1473-3099(20)30244-9. Epub 2020 Mar 27. PMID: 32224313; PMCID: PMC7270047.
10. Hale T, Webster S, Petherick A, et al. Oxford covid-19 government response tracker. Blavatnik School of Government. March 25, 2020.
11. National Center for Health Statistics. Provisional COVID-19 Death Counts by Week Ending Date and State. March 1, 2021. https://bit.ly/2Qq1nMU
12. Lowe A, Chang DD, Creek G. Multiple Fatalities in a Family Cluster of COVID-19 With Acute Respiratory Distress Syndrome. Ochsner J. 2020 Summer;20(2):134-138. doi: 10.31486/toj.20.0056. PMID: 32612465; PMCID: PMC7310175.
13. Vivian Thangaraj JW, Murhekar M, Mehta Y, Kataria S, Brijwal M, Gupta N, Choudhary A, Malhotra B, Vyas M, Sharma H, Yadav N, Bhatnagar T, Gupta N, Dar L, Gangakhedkar RR, Bhargava B. A cluster of SARS-CoV-2 infection among Italian tourists visiting India, March 2020. Indian J Med Res. 2020 May;151(5):438-443. doi: 10.4103/ijmr.IJMR_1722_20. PMID: 32474558; PMCID: PMC7530458.
14. Iritani O, Okuno T, Hama D, Kane A, Kodera K, Morigaki K, Terai T, Maeno N, Morimoto S. Clusters of COVID-19 in long-term care hospitals and facilities in Japan from 16 January to 9 May 2020. Geriatr Gerontol Int. 2020 Jul;20(7):715-719. doi: 10.1111/ggi.13973. PMID: 32634849; PMCID: PMC7361521.
15. Chidambaram P. State reporting of cases and deaths due to COVID-19 in long-term care facilities. https://bit.ly/3xpwV5U
16. Bensadoun, E. "Nearly half of Canada's COVID-19 deaths linked to long-term care facilities: Tam. 2020. https://bit.ly/3noN6f7
17. Vahabi N, Salehi M, Duarte JD, Mollalo A, Michailidis G. County-level longitudinal clustering of COVID-19 mortality to incidence ratio in the United States. *Sci Rep.* 2021;11:3088. doi: 10.1038/s41598-021-82384-0
18. Office for National Statistics. Analysis of geographic concentrations of COVID-19 mortality over time, England and Wales: deaths occurring between 22 February and 28 August 2020. https://bit.ly/2RUeAO7
19. Van Kerkhove MD, Asikainen T, Becker NG, Bjorge S, Desenclos JC, dos Santos T, Fraser C, Leung GM, Lipsitch M, Longini IM Jr, McBryde ES, Roth CE, Shay DK, Smith DJ, Wallinga J, White PJ, Ferguson NM, Riley S; WHO Informal Network for Mathematical Modelling for Pandemic Influenza H1N1 2009 (Working Group on Data Needs). Studies needed to address public health challenges of the 2009 H1N1 influenza pandemic: insights from modeling. PLoS Med. 2010 Jun 1;7(6):e1000275. doi: 10.1371/journal.pmed.1000275. PMID: 20532237; PMCID: PMC2879409.
20. Qualls N, Levitt A, Kanade N, et al. Community Mitigation Guidelines to Prevent Pandemic Influenza — United States, 2017. MMWR Recomm Rep. 2017;66(No. RR-1):1-34. https://bit.ly/3tV8WJV
21. Krämer A, Akmatov M, Kretzschmar M. Principles of Infectious Disease Epidemiology. *Modern Infectious Disease Epidemiology*. 2009;85-99. doi:10.1007/978-0-387-93835-6_5
22. Noushad M, Al-Saqqaf IS. COVID-19 case fatality rates can be highly misleading in resource-poor and fragile nations: the case of Yemen. Clin Microbiol Infect. 2021 Apr;27(4):509-510. doi: 10.1016/j.cmi.2021.01.002. Epub 2021 Jan 8. PMID: 33429029; PMCID: PMC7836539.
23. Newall AT, Leong RNF, Nazareno A, Muscatello DJ, Wood JG, Kim WJ. Delay-adjusted age- and sex-specific case fatality rates for COVID-19 in South Korea: Evolution in the estimated risk of mortality throughout the epidemic. Int J Infect Dis. 2020 Dec;101:306-311. doi: 10.1016/j.ijid.2020.09.1478. Epub 2020 Oct 2. PMID: 33011281; PMCID: PMC7529598.
24. Favero N. Adjusting confirmed COVID-19 case counts for testing volume. medRxiv. doi: https://doi.org/10.1101/2020.06.26.20141135