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Coronavirus Pandemic

Demystifying the varying case fatality rates (CFR) of COVID-19 in India: Lessons learned and future directions

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Abstract

Introduction: At the end of the second week of June 2020, the SARS-CoV-2 responsible for COVID-19 infected above 7.5 million people and killed over 400,000 worldwide. Estimation of case fatality rate (CFR) and determining the associated factors are critical for developing targeted interventions.

Methodology: The state-level adjusted case fatality rate (aCFR) was estimated by dividing the cumulative number of deaths on a given day by the cumulative number confirmed cases 8 days before, which is the average time-lag between diagnosis and death. We conducted fractional regression analysis to determine the predictors of aCFR.

Results: As of 13 June 2020, India reported 225 COVID-19 cases per million population (95% CI:224-226); 6.48 deaths per million population (95% CI:6.34-6.61) and an aCFR of 3.88% (95% CI:3.81-3.97) with wide variation between states. High proportion of urban population and population above 60 years were significantly associated with increased aCFR (p=0.08, p=0.05), whereas, high literacy rate and high proportion of women were associated with reduced aCFR (p<0.001, p=0.03). The higher number of cases per million population (p=0.001), prevalence of diabetes and hypertension (p=0.012), cardiovascular diseases (p=0.05), and any cancer (p<0.001) were significantly associated with increased aCFR. The performance of state health systems and proportion of public health expenditure were not associated with aCFR.

Conclusions: Socio-demographic factors and burden of non-communicable diseases (NCDs) were found to be the predictors of aCFR. Focused strategies that would ensure early identification, testing and effective targeting of non-literate, elderly, urban population and people with comorbidities are critical to control the pandemic and fatalities.

Key words: COVID-19; case fatality rate; CFR; predictors of CFR; fractional regression.

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Introduction

At the end of the second week of June 2020, the coronavirus named SARS-CoV-2 responsible for COVID-19 infected more than 7.5 million people, killed over 400,000 and around 4 million have recovered worldwide [1]. As the number of cases and deaths increase exponentially, the focus of many countries has shifted to clinical management of severely ill cases who have an increased risk of dying due to the disease. During an outbreak of a novel or emerging infectious agent, one of the most important epidemiological quantities to be determined is the case fatality rate (CFR) which is often used to express the extent of disease severity. It is essential for setting public health priorities and develop targeted interventions to reduce the severity of risk [2].

Studies indicate that the patients in the older age groups, patients with hypertension, diabetes, cardiovascular or cerebrovascular diseases, chronic digestive disorders, tuberculosis, chronic hepatic or renal insufficiency, peripheral vascular disease, and malignancy were disproportionately affected and died of the disease [3-5]. The other factors are occupational, socioeconomic and demographic characteristics, population density, the proportion of urban population, and migrant workers [6,7]. The different phases of the epidemic, the level of access to health services including testing, management of the epidemic, health-seeking behavior of the population, and efficiency of health systems are potential confounders that could affect the case fatality due to COVID-19 [8-10]. Screening and diagnostic testing strategies and data reporting systems adopted in countries could also play a major role in the estimation of CFR due to both, very high and low rate of identification of mild and asymptomatic cases, who have less risk of dying [11].

Globally, the estimated case fatality rates of COVID-19 appear to change as the epidemic progresses and the current case fatality rates indicate a wide variation between and within countries. As of 13 June 2020, the unadjusted global case fatality rate was estimated at 5.6%, ranging from 0.06% in Singapore to 19.3% in France, among the countries that reported more than 1,000 cases [1]. This could change significantly when the pandemic ends. India, with 1.37 billion population, has been reporting a huge variation in CFR across its 28 states and 8 union territories. However, the computation of CFR, which is the ratio of the number of deaths to the number of confirmed cases over a defined period of time may not represent the true case fatality rate during an ongoing epidemic. Because, the estimation ignores the patients who are recently diagnosed, hospitalized or isolated, whose outcome is still unknown and it is assumed that none will die eventually. Secondly, the calculation does not account the time difference between disease onset or diagnosis and death, which generally leads to an underestimation of CFR [12-14].

As accurate estimation and understanding the factors associated with case fatality are critical for developing interventions, allocation of resources and planning clinical management strategies, this paper aims to estimate the time-delay adjusted CFR (aCFR) and determine the associated factors of aCFR in India.

Methodology

We estimated the time-delay adjusted case fatality rate (aCFR) by dividing the number of deaths on a given day (13 June 2020) by the cumulative number of patients with confirmed COVID-19 infection 8 days before (5 June 2020) which is the average time-lag between diagnosis and death. Studies from different regions, indicated an average time-lag, ranging between 8 and 18 days [13-19]. We considered 8 days' time-lag to conservatively estimate the aCFR, considering the possible delays in seeking health care, diagnosis and reporting, which are widely reported across the country [20,21].

As states/union territories were the units of analysis, we considered the socioeconomic and demographic situation; health system performance and morbidities of the states and union territories of India, as potential predictors of case fatality. The variables included the median age of the population, the proportion of urban population, population density, proportion of population above 60 years, literacy rate, sex ratio (females/1000 males), per capita net state domestic product 2017-18 (SDP), COVID-19 tests per million population, confirmed cases per million population, the prevalence of diabetes, hypertension, cardiovascular diseases (CVD) and any cancer among those who were screened in non-communicable diseases (NCD) clinics in the respective states. Besides, we considered the proportion of state medical and public health expenditure (2018-19), and health system performance of the states, assessed by the Ministry of Health and Family Welfare, Government of India. The health system performance indicators are composite indicators of several technical aspects and the scores ranged from 0 to 100%. Overall health system performance is the summation of three domains that are, inputs/processes, health outcome, and governance and information. Inputs and processes indicate health infrastructure, financial and human resources, antenatal care (ANC) coverage, surveillance, etc. The health outcome indicates, natality, mortality, immunization, TB, and HIV services etc. Governance and information indicate governance, health monitoring and data integrity [22].

Data sources and statistical analysis

The COVID-19 data on confirmed cases and reported deaths were obtained from the Ministry of Health and Welfare (MoHFW), Government of India[23]; testing data from www.covid19india.org, a crowdsourced database, and the other covariates from multiple sources such as Census of India-2011[24]; National Health Profile-2019 [25]; Healthy States Progressive India: A report on the ranks of states and union territories [22]; and the report on State Finances: A study of budgets of 2019-20 by Reserve Banks of India [26]. We considered the state-wise projected population as of May 2020 [27] and included the states and union territories that reported more than 100 confirmed cases as on 13th June 2020 for analysis.

We performed the analysis using STATA version 15.0 (StataCorp LLC, College Station, Texas USA). We carried out basic descriptive analysis, and bivariate analysis to determine the correlation between independent variables. As the effects are most likely non-linear and the fractional nature of the dependent variable, we conducted fractional regression analysis to determine the predicting factors of aCFR in the states. In our analysis, the dependent variable (aCFR) was operationalized as a fraction bounded between zero and one. In regression analysis, we did not include the independent variables that indicated high correlation amongst them. The independent variables included were the proportion of urban population, proportion of population above 60 years, literacy rate, sex ratio (females/1000 males), per capita state domestic product(SDP), overall health system performance, proportion of public health expenditure, COVID-19 tests per million population, COVID-19 confirmed cases per million population, the prevalence of diabetes and hypertension combined, CVD and Cancer. The regression coefficients were converted to marginal effects so that they can be interpreted as the average effect of the explanatory variable on aCFR. We considered P-value <0.05 statistically significant.

Results

COVID-19 confirmed cases, deaths per million population, and adjusted CFR

Table 1 indicates the state-wise confirmed cases, deaths per million population, crude CFR and adjusted CFR. As of 13 June 2020, the country reported 225 confirmed cases per million population (95% CI: 224-226) and 6.48 deaths per million population (95% CI: 6.34-6.61) and an adjusted CFR of 3.88% (95% CI: 3.81-3.97) with wide variation between states/union territories. Delhi reported the highest confirmed cases per million population (1,968) followed by Maharashtra (821), Tamil Nadu (523), Gujarat (353) and Jammu & Kashmir (348). States such as Jharkhand, Arunachal Pradesh, Chhattisgarh, and Bihar reported less than 50 cases per million population. In terms of deaths, Delhi reported the highest deaths per million (64.9) followed by Maharashtra (30.2), Gujarat (22.2), Madhya Pradesh (5.2), and Tamil Nadu (4.7), whereas the northeastern states, Kerala, Bihar, Odisha, Jharkhand, Chhattisgarh and Goa reported less than one death per million population. The aCFR was found to be the highest in Gujarat (7.4%) followed by West Bengal (6.2%), Telangana (5.3%), Madhya Pradesh (4.9%), Maharashtra (4.6%) and Delhi (4.6%) whereas, the northeastern states, Jharkhand, Bihar, Chhattisgarh, Odisha, and Goa reported less than 1%.

Table 1. Number of cases, deaths per million population, and adjusted CFR (aCFR) by states.

Region	Cases per million	95% CI	Deaths per million	95% CI	Crude CFR %	95% CI	aCFR %	95% CI
Andhra Pradesh	105	103 - 108	1.48	1.16 - 1.81	1.41	1.10 - 1.71	1.88	1.47 - 2.29
Arunachal Pradesh	43	32 - 53	0.00		-	-	0.00	
Assam	98	95 - 101	0.22	0.07 - 0.38	0.23	0.07 - 0.39	0.36	0.11 - 0.60
Bihar	49	48 - 50	0.29	0.19 - 0.38	0.59	0.40 - 0.78	0.78	0.53 - 1.04
Chandigarh	288	257 - 319	4.32	0.53 - 8.10	1.50	0.19 - 2.80	1.62	0.21 - 3.02
Chhattisgarh	49	46 - 51	0.20	0.04 - 0.37	0.42	0.08 - 0.76	0.70	0.14 - 1.25
Delhi	1,968	1,948 - 1,988	64.88	61.23 - 68.53	3.30	3.11 - 3.48	4.61	4.36 - 4.86
Goa	292	265 - 318	0.00		-	-	0.00	
Gujarat	353	348 - 357	22.15	21.00 - 23.31	6.28	5.96 - 6.60	7.40	7.03 - 7.77
Haryana	225	219 - 230	2.48	1.90 - 3.06	1.11	0.85 - 1.36	1.95	1.49 - 2.40
Himachal Pradesh	65	59 - 71	0.81	0.16 - 1.45	1.23	0.25 - 2.22	1.53	0.31 - 2.74
Jammu & Kashmir	348	338 - 358	3.90	2.85 - 4.94	1.12	0.82 - 1.42	1.59	1.17 - 2.02
Jharkhand	42	40 - 44	0.21	0.06 - 0.35	0.49	0.15 - 0.84	0.87	0.27 - 1.47
Karnataka	96	94 - 99	1.17	0.91 - 1.43	1.21	0.95 - 1.48	1.63	1.28 - 1.99
Kerala	65	62 - 68	0.53	0.29 - 0.77	0.82	0.45 - 1.18	1.12	0.62 - 1.62
Madhya Pradesh	122	120 - 125	5.15	4.67 - 5.64	4.21	3.83 - 4.60	4.89	4.45 - 5.34
Maharashtra	821	816 - 826	30.18	29.21 - 31.15	3.68	3.56 - 3.79	4.63	4.49 - 4.78
Manipur	125	112 - 137	0.00	-	-	-	0.00	-
Mizoram	79	64 - 95	0.00	-	-	-	0.00	-
Nagaland	69	58 - 80	0.00	-	-	-	0.00	-
Odisha	75	73 - 78	0.22	0.08 - 0.35	0.29	0.11 - 0.46	0.38	0.15 - 0.62
Puducherry	111	94 - 128	1.41	0 - 3.38	1.27	0 - 3.03	1.92	0 - 4.56
Punjab	99	96 - 103	2.09	1.57 - 2.61	2.11	1.59 - 2.63	2.56	1.94 - 3.18
Rajasthan	149	146 - 152	3.36	2.96 - 3.76	2.25	1.99 - 2.52	2.70	2.38 - 3.01
Tamil Nadu	523	518 - 528	4.71	4.23 - 5.20	0.90	0.81 - 0.99	1.28	1.15 - 1.41
Telangana	114	111 - 117	4.42	3.76 - 5.08	3.88	3.32 - 4.45	5.29	4.52 - 6.05
Tripura	230	216 - 245	0.24	0 - 0.71	0.10	0 - 0.31	0.14	0 - 0.43
Uttarakhand	153	146 - 160	1.87	1.07 - 2.66	1.22	0.70 - 1.74	1.73	1.00 - 2.46
Uttar Pradesh	53	52 - 54	1.53	1.38 - 1.69	2.89	2.60 - 3.19	3.75	3.37 - 4.13
West Bengal	103	101 - 105	4.53	4.11 - 4.95	4.40	4.01 - 4.80	6.18	5.62 - 6.73
India	**225**	**224 - 226**	**6.48**	**6.34 - 6.61**	**2.88**	**2.82 - 2.93**	**3.88**	**3.81 - 3.97**

As depicted in Figure 1, Gujarat (GU), Maharashtra (MH) and Delhi (DL) reported higher number of COVID-19 cases per million population and aCFR, than the national average. West Bengal (WB), Telangana (TE) and Madhya Pradesh (MP) reported higher aCFR, though their confirmed cases per million population are less than the national average. Tamil Nadu (TN), Chandigarh (CHD), Jammu & Kashmir (JK) and Goa (GA) reported relatively less aCFR than the national average, though the cases per million population are above the national average.

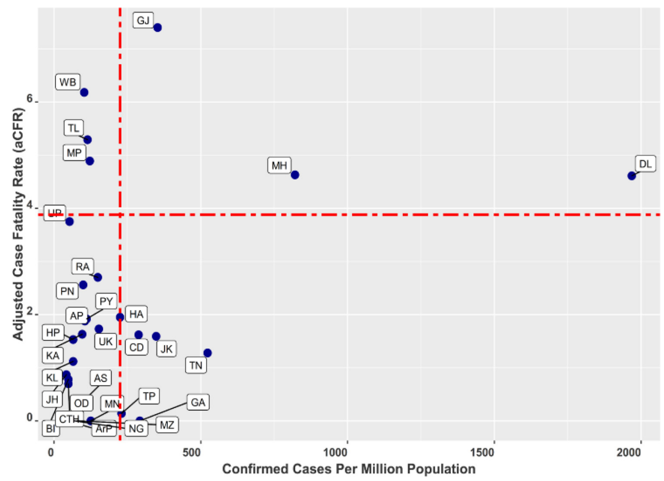
Predictors of Case Fatality Rate of COVID-19

The descriptive analysis of the explanatory variables is presented in Table 2. The fractional regression results that indicate the predicting factors and their association with aCFR are shown in Table 3.

Socioeconomic and demographic factors

The states with high proportion of urban population and population above 60 years were significantly associated with increased aCFR (p = 0.08, p = 0.005),

Figure 1. COVID-19 Confirmed Cases vs Adjusted CFR.



AP, Andhra Pradesh; ArP, Arunachal Pradesh, AS, Assam; BI, Bihar; CD, Chandigarh; CT, Chhattisgarh; DE, Delhi; GA, Goa; GU, Gujarat; HA, Haryana; HP, Himachal Pradesh; JK, Jammu and Kashmir; JK, Jharkhand; KA, Karnataka; KE, Kerala; MP, Madhya Pradesh; MH, Maharashtra; MN, Manipur; MZ, Mizoram; NG, Nagaland; OD, Odisha; PU, Puducherry; PU, Punjab; RA, Rajasthan; TN, Tamil Nadu; TE, Telangana; TP, Tripura; UK, Uttarakhand; UP, Uttar Pradesh; WB, West Bengal.

Table 2. Summary statistics of explanatory variables.

Variables	Mean/ Median	SD/IQR	Minimum	Maximum
Urban population %	41.3	22.4	10.3	99.7
Population > 60 years %	8.3	1.8	4.6	12.6
Literacy Rate	76.5	8.7	61.8	94
Gender ratio (Females/1000 Males)	952	53	818	1,084
Per capita state domestic product (2017-19)	113,708	68,391	28,101	337,605
State health system performance %	53.3	11.8	28.6	74.9
Medical &Public health expenditure % (2018-19)	5.5	1.5	3.6	11.9
COVID-19 tests per million	5,185	3,169 - 7,778	806	24,774
COVID cases per million	108	69,230	42	1,968
CVD %	0.53	0.25 - 0.83	0.057	5.93
Hypertension & Diabetes %	3.07	1.5 - 5.7	0.39	11.65
Any Cancer %	0.20	0.07 - 1.80	0.010	1.80

SD: Standard Deviation; IQR: Inter Quartile Range.

Table 3. Predicting factors of aCFR.

Explanatory Variables	Marginal effects	Marginal effect in %	95% CI	P value
Urban population %	0.0116	1.2	-0.0015 - 0.0248	0.082
Population > 60 years %	0.0824	8.2	0.0246 - 0.1403	0.005
Literacy Rate %	-0.1101	-11.0	-0.1600 - -0.0603	<0.001
Gender ratio (Females/1000 Males)	-0.1698	-17.0	-0.3264 - -0.0132	0.034
Per capita state domestic product	-0.0052	-0.5	-0.0215 - 0.0111	0.533
State health system performance %	-0.0023	-0.2	-0.028 - 0.0234	0.862
Public health expenditure %	-0.0004	-0.04	-0.0296 - 0.0288	0.978
COVID-19 tests per million	-0.0094	-0.9	-0.0149 - -0.0039	0.001
COVID-19 cases per million	0.0094	0.9	0.0038 - 0.0151	0.001
CVD %	0.0041	0.4	0.0009 - 0.0073	0.012
Hypertension & Diabetes %	0.0061	0.6	0 - 0.0122	0.050
Any Cancer %	0.0105	1.0	0.0073 - 0.0137	<0.001

whereas, high literacy rate and high proportion of women in the states were significantly associated with reduced aCFR ($p < 0.001$, $p = 0.03$). Though per capita income indicated a positive association, it was not statistically significant ($p = 0.53$). The marginal effect indicates that an increase of one per cent in urban population and population above 60 years, results in 1.2% and 8.2% increase in aCFR respectively. On the other hand, an increase of one per cent in literacy rate and proportion of women population, resulting in 11% and 17% decrease in aCFR respectively.

Health system performance

Although the overall performance of the state health systems and the proportion of public health expenditure of the states indicated a negative association with case fatality, they were not statistically significant. However, there is a reduction of 9% in aCFR, when there is an increase of 10% in COVID-19 tests per million population ($p = 0.001$).

The burden of COVID-19 and other morbidities

All the factors that were included in the analysis, such as COVID-19 cases per million population and prevalence of diabetes & hypertension, CVD and any cancer were significantly associated with increased aCFR. As per our findings, the aCFR increases by 9% if COVID-19 cases per million population increase by 10% ($p = 0.001$). Similarly, as the prevalence of CVD, Hypertension with diabetes and any cancer increase by 10%, the aCFR increases by 4% ($p = 0.01$), 6% (p-0.05) and 10% ($p < 0.001$) respectively.

Discussion

The study estimated the adjusted case fatality rate using the average duration from diagnosis to death, which could avoid the interference of hospitalized cases and the time-delay of death. The estimated aCFR in India was 3.88% (95% CI: 3.81-3.97), which is much higher than the crude CFR (2.88%) and the states and union territories have indicated similar trends. According to the literature, countries have reported a wide range of CFR at different stages of the epidemic, however, the CFR of COVID-19 seems to be low compared to other coronaviruses that caused major outbreaks of deadly pneumonia such as SARS, and MERS [2]. Within India, there is a huge variation in aCFR between states that ranges from zero to 7.4 per cent, which could be due to the variations in the socioeconomic and demographic situation; health system and COVID-19 programmatic performance; and the burden of morbidities that could potentially affect the fatality due to COVID-19.

It is well documented that the sociodemographic and socioeconomic factors are important predictors of the burden of infectious disease epidemics, the severity and mortality [28–30] and our study brings evidence to emphasize the fact in India. The positive association between the proportion of urban population and aCFR of COVID-19 is in concurrence with the existing literature. Pathogens in urban environments can spread more rapidly and be a greater burden to health care services [31]. The risk factors in the urban areas are poor housing with inadequate ventilation; inadequate water, sanitation and waste management; a high proportion of slum population; the density of the inhabitants; and close contact between people that lead to the rapid spread of emerging infectious diseases like COVID-19 and its higher fatality [32]. Similarly, it is well documented that the elderly were disproportionately affected and died due to COVID-19 across the world. Our study results also revealed old age as a significant predictor of increased mortality, which could be due to the declined immune system ability and presence of morbidities [10,33-35].

According to our study findings, overall population development in terms of literacy and gender equity were found to be significant predictors of aCFR due to COVID-19. This is in concurrence with the literature that infectious disease threats and deaths, disproportionately affect the urban poor and population of lower socioeconomic gradients, leading to the substantially unequal burden of COVID-19 outcomes [36]. It has been demonstrated that poverty, inequality, and poor social determinants of health, create conditions for the transmission of infectious diseases, and can further contribute to unequal burdens of morbidity and mortality [37]. In this connection, our findings emphasize the need for a sustained population health approach with effective primary health care that addresses the socio-economic and cultural determinants of health, rather than focusing on the individual and illness-based approach to prevent, manage and control the current pandemic and any potential epidemic of the future [38].

It is a common understanding that the performance of a health system in terms of adequate resources, efficient systems, processes and services would produce a better outcome and reduce the mortality due to an epidemic including COVID-19. According to our analysis, the overall health system performance and proportion of public health expenditure of the states were not found to be significant predictors of reduced case fatality. Prevention, control and management, including the reduction of fatality in COVID-19, require an efficient health system, however, the outcome depends on effective multisectoral and intersectoral coordination and response [39,40]. It is essential to ensure early detection, diagnosis, isolation and treatment of confirmed cases, in addition to contact tracing, risk communication, promotion of social distancing, maintenance of law and order etc. It requires a well-coordinated public health response with decentralised geopolitical responsibility and authority, efficient governance especially by local government, coordinated public services, engagement of different sectors coupled with a resilient and adaptive health care system and active community involvement, which could produce better outcomes.

Our analysis indicated a significant association between volume of COVID-19 tests per million population and reduced case fatality, which could be due to the difference in testing strategies and its effectiveness across states, early identification and management and identification of more asymptomatic cases [10]. In concurrence with a wide range of studies, the higher incidence of COVID-19 cases, the prevalence of morbidities such as CVD, diabetes & hypertension and cancers were significantly associated with an increased aCFR [10,41,42]. This stresses the need for prevention and control strategies that aimed at addressing the vulnerable population with risk behaviour and morbidities to reduce the severity and case fatality of COVID-19.

Our study has some limitations. The selection of time-lag between diagnosis and death could affect the estimation of aCFR. The time-lag could vary between and within countries at different stages of the epidemic. Besides, though the COVID-19 data are from official government sources, there may be under-reporting in some states due to slightly different reporting criteria, reporting methods, programme approach of the state governments and its effectiveness. However, this study provides valuable insights for further analysis in India as the epidemic progresses and data gets updated.

Conclusion

The evidence generated by our study helps to understand the predictors of case fatality due to COVID-19 in India, that are socio-demographic factors, and the burden of non-communicable diseases (NCDs). Focused strategies that would ensure early identification, testing and effective targeting of non-literate, elderly, male, urban population and people with comorbidities are critical to reduce the spread and case fatality. While the findings of the study emphasize the need for an effective population health approach that addresses the determinants of population health, an efficient public health response with intersectoral and multisectoral coordination is an urgent need for effective prevention, management and control of COVID-19 pandemic and fatalities in India.

References

1. World Health Organization (2020) Coronavirus disease 2019 (COVID-19) : Situation Report, 145. World Health Organization, Geneva. Available:https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200613-covid-19-sitrep-145.pdf?sfvrsn=bb7c1dc9_4. Accessed 13 June 2020.
2. Khafaie MA, Rahim F (2020) Cross-Country Comparison of Case Fatality Rates of COVID-19/SARS-COV-2. Osong Public Health Res Perspect 11: 74–80.
3. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, Liu L, Shan H, Lei CL, Hui DSC, Du B, Li LJ, Zeng G, Yuen KY, Chen RC, Tang CL, Wang T, Chen PY, Xiang J, Li SY, Wang JL, Liang ZJ, Peng YX, Wei L, Liu Y, Hu YH, Peng P, Wang JM, Liu JY, Chen Z, Li G, Zheng ZJ, Qiu SQ, Luo J, Ye CJ, Zhu SY, Zhong NS (2020) Clinical Characteristics of Coronavirus Disease 2019 in China. N Engl J Med 382: 1708–1720.
4. Guzik TJ, Mohiddin SA, Dimarco A, Patel V, Savvatis K, Marelli-Berg FM, Madhur MS, Tomaszewski M, Maffia P, D'Acquisto F, Nicklin SA, Marian AJ, Nosalski R, Murray EC, Guzik B, Berry C, Touyz RM, Kreutz R, Wang DW, Bhella D, Sagliocco O, Crea F, Thomson EC, McInnes IB (2020) COVID-19 and the cardiovascular system: implications for risk assessment, diagnosis, and treatment options. Cardiovasc Res 116: 1666-1667.
5. Priyadarsini SL, Suresh M (2020) Factors influencing the epidemiological characteristics of pandemic COVID 19: A TISM approach. Int J Healthc Manag 13: 89–98.
6. Bhopal R (2020) Covid-19: Undocumented migrants are probably at greatest risk. BMJ 369: m1673.
7. Chirico F, Magnavita N (2020) COVID-19 infection in Italy: An occupational injury. South Afr Med J 110: 12944.
8. Anderson RM, Heesterbeek H, Klinkenberg D, Hollingsworth TD (2020) How will country-based mitigation measures influence the course of the COVID-19 epidemic? The Lancet 395: 931–934.
9. Khan JR, Awan N, Islam MM, Muurlink O (2020) Healthcare Capacity, Health Expenditure, and Civil Society as Predictors of COVID-19 Case Fatalities: A Global Analysis. Front Public Health 8: 347.
10. Onder G, Rezza G, Brusaferro S (2020) Case-Fatality Rate and Characteristics of Patients Dying in Relation to COVID-19 in Italy. JAMA 323:1775–1776 .
11. Vincent JL, Taccone FS (2020) Understanding pathways to death in patients with COVID-19. Lancet Respir Med 8: 430–432.
12. Kucharski AJ, Edmunds WJ (2014) Case fatality rate for Ebola virus disease in west Africa. Lancet 384: 1260.
13. Battegay M, Kuehl R, Tschudin-Sutter S, Hirsch HH, Widmer AF, Neher RA (2020) 2019-novel Coronavirus (2019-nCoV):

estimating the case fatality rate - a word of caution. Swiss Med Wkly 150: w20203.
14. Chirico F, Nucera G, Magnavita N (2020) Estimating case fatality ratio during COVID-19 epidemics: Pitfalls and alternatives. J Infect Dev Ctries 14: 438-439. doi: 10.3855/jidc.12787.
15. Baud D, Qi X, Nielsen-Saines K, Musso D, Pomar L, Favre G (2020) Real estimates of mortality following COVID-19 infection. Lancet Infect Dis 20:773.
16. Mi Y, Huang T, Zhang J, Qin Q, Gong Y, Liu S, Xue H, Ning C, Cao L, Cao Y (2020) Estimating instant case fatality rate of COVID-19 in China. Int J Infect Dis 97: 1-6.
17. Nick W, Amanda K, Lucy Telfar B, Michael GB (2020) Case-Fatality Risk Estimates for COVID-19 Calculated by Using a Lag Time for Fatality. Emerg Infect Dis J 26: 1339.
18. Park S-M (2020) COVID-19 patients die 11 days after diagnosis on average. In: Dong- ILBO. https://www.donga.com/en/article/all/20200409/2033350/1/COVID-19-patients-die-11-days-after-diagnosis-on-average. Accessed 18 Jun 2020
19. Wang L, Li J, Guo S, Xie N, Yao L, Cao Y, Day SW, Howard SC, Graff JC, Gu T, Ji J, Gu W, Sun D (2020) Real-time estimation and prediction of mortality caused by COVID-19 with patient information based algorithm. Sci Total Environ 727: 138394.
20. Jain B, Debroy S (2020) Delay in seeking care leading cause for Covid deaths in Maharashtra. The Times of India. Available: https://timesofindia.indiatimes.com/city/mumbai/delay-in-seeking-care-leading-cause-for-covid-deaths-in-maharashtra/articleshow/76722603.cms. Accessed 1 July 2020.
21. Thakur R, Chakraborty R (2020) Delay in test results has Centre, states worried. Hindustan Times. Available: https://www.hindustantimes.com/india-news/delay-in-test-results-has-centre-states-worried/story-VJU6Doa3RSyxmWsWSf073J.html. Accessed 26 April, 2020.
22. Government of India (2019) Healthy States, Progressive India - Report on the Ranks of States and Union Territories: Health Index 2019. NITI Aayog, Ministry of Health and Family Welfare, New Delhi. Available: http://social.niti.gov.in/uploads/sample/health_index_report.pdf. Accessed 2 June 2020.
23. Government of India (2020) COVID-19 Statewise Status as on 13th June 2020. Available: https://www.mohfw.gov.in/. Accessed 13 Jun 2020.
24. Government of India (2019) Population Projections for India and States 2011–2036. National Commission on Population, Ministry of Health and Family Welfare, New Delhi. Available: https://nhm.gov.in/New_Updates_2018/Report_Population_Projection_2019.pdf. Accessed 2 June 2020.
25. Government of India (2019) National Health Profile - 2019. Central Bureau of Health Intelligence, Directorate General of Health Services, Ministry of Health & Family Welfare, New Delhi. Available: https://www.cbhidghs.gov.in/WriteReadData/l892s/8603321691572511495.pdf. Accessed 3 June 2020.
26. Reserve Bank of India (2019) State Finances: A study of Budgets of 2019-20. Reserve Bank of India, New Delhi. Available: https://rbidocs.rbi.org.in/rdocs/Publications/PDFs/STATEFINANCE201920E15C4A9A916D4F4B8BF01608933FF0BB.PDF. Accessed 3 June 2020.
27. Government of India (2020) State/UT wise Aadhaar Saturation 31st May, 2020. Available: https://uidai.gov.in/images/state-wise-aadhaar-saturation.pdf. Accessed 3 June 2020.
28. Burton DC, Flannery B, Bennett NM, Farley MM, Gershman K, Harrison LH, Lynfield R, Petit S, Reingold AL, Schaffner W, Thomas A, Plikaytis BD, Rose CE Jr, Whitney CG, Schuchat A (2010) Socioeconomic and racial/ethnic disparities in the incidence of bacteremic pneumonia among US adults. Am J Public Health 100: 1904-1911.
29. Bhutta ZA, Sommerfeld J, Lassi ZS, Salam RA, Das JK (2014) Global burden, distribution, and interventions for infectious diseases of poverty. Infect Poverty 3: 21.
30. Rubino S, Kelvin N, Bermejo-Martin J, Kelvin D (2020) As COVID-19 cases, deaths and fatality rates surge in Italy, underlying causes require investigation. J Infect Dev Ctries 14: 265-267. doi: 10.3855/jidc.12734.
31. Reyes R, Ahn R, Thurber K, Burke TF (2013) Urbanization and Infectious Diseases: General Principles, Historical Perspectives, and Contemporary Challenges. In: Fong IW (ed) Challenges in Infectious Diseases. Springer New York, New York, NY, 123-146 pp.
32. Neiderud C-J (2015) How urbanization affects the epidemiology of emerging infectious diseases. Infect Ecol Epidemiol 5:27060–27060.
33. Nikpouraghdam M, Farahani AJ, Alishiri G, Heydari S, Ebrahimnia M, Samadinia H, Sepandi M, Jafari NJ, Izadi M, Qazvini A, Dorostkar R, Tat M, Shahriary A, Farnoosh G, Zijoud SRH, Taghdir M, Alimohamadi Y, Abbaszadeh S, Ghaleh HEG, Bagheri M (2020) Epidemiological characteristics of coronavirus disease 2019 (COVID-19) patients in IRAN: A single center study. J Clin Virol Off Publ Pan Am Soc Clin Virol 127: 104378–104378.
34. Porcheddu R, Serra C, Kelvin D, Kelvin N, Rubino S (2020) Similarity in Case Fatality Rates (CFR) of COVID-19/SARS-COV-2 in Italy and China. J Infect Dev Ctries 14: 125-128. doi: 10.3855/jidc.12600.
35. Wu C, Chen X, Cai Y, Xia J, Zhou X, Xu S, Huang H, Zhang L, Zhou X, Du C, Zhang Y, Song J, Wang S, Chao Y, Yang Z, Xu J, Zhou X, Chen D, Xiong W, Xu L, Zhou F, Jiang J, Bai C, Zheng J, Song Y (2020) Risk Factors Associated With Acute Respiratory Distress Syndrome and Death in Patients With Coronavirus Disease 2019 Pneumonia in Wuhan, China. JAMA Intern Med 180: 934-943.
36. Chen JT, Krieger N (2020) Revealing the unequal burden of COVID-19 by income, race/ethnicity, and household crowding: US county vs. ZIP code analyses. J Public Health Manag Pract (2020). doi: 10.1097/PHH.0000000000001263.
37. World Health Organization (2008) Our Cities, Our Health, Our Future: Acting on Social Determinants for Health Equity in Urban Settings. World Health Organization, Japan. Available:https://www.who.int/social_determinants/resources/knus_final_report_052008.pdf?ua=1. Accessed 3 July 2020.
38. Commission on a Global Health Risk Framework for the Future; National Academy of Medicine, Secretariat. The Neglected Dimension of Global Security: A Framework to Counter Infectious Disease Crises. Washington (DC): National Academies Press (US) (2016). 3, Strengthening Public Health as the Foundation of the Health System and First Line of Defense. Available: https://www.ncbi.nlm.nih.gov/books/NBK368392/. Accessed 2 June 2020.

39. Koplan JP, Butler-Jones D, Tsang T, Yu W (2013) Public Health Lessons from Severe Acute Respiratory Syndrome a Decade Later. Emerg Infect Dis J 19: 861.
40. Chen Z, Cao C, Yang G (2020) Coordinated multi-sectoral efforts needed to address the COVID-19 pandemic: lessons from China and the United States. Glob Health Res Policy 5: 22.
41. Guan W-J, Liang W-H, Zhao Y, Liang H-R, Chen Z-S, Li Y-M, Liu X-Q, Chen R-C, Tang C-L, Wang T, Ou C-Q, Li L, Chen P-Y, Sang L, Wang W, Li J-F, Li C-C, Ou L-M, Cheng B, Xiong S, Ni Z-Y, Xiang J, Hu Y, Liu L, Shan H, Lei C-L, Peng Y-X, Wei L, Liu Y, Hu Y-H, Peng P, Wang J-M, Liu J-Y, Chen Z, Li G, Zheng Z-J, Qiu S-Q, Luo J, Ye C-J, Zhu S-Y, Cheng L-L, Ye F, Li S-Y, Zheng J-P, Zhang N-F, Zhong N-S, He J-X, China Medical Treatment Expert Group for C (2020) Comorbidity and its impact on 1590 patients with COVID-19 in China: a nationwide analysis. Eur Respir J 55: 2000547.
42. Li X, Xu S, Yu M, Wang K, Tao Y, Zhou Y, Shi J, Zhou M, Wu B, Yang Z, Zhang C, Yue J, Zhang Z, Renz H, Liu X, Xie J, Xie M, Zhao J (2020) Risk factors for severity and mortality in adult COVID-19 inpatients in Wuhan. J Allergy Clin Immunol 146: 110-118.

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