Original Article

Higher coronavirus disease-19 mortality linked to comorbidities: A comparison between low-middle income and high-income countries

Har Ashish Jindal, Soumya Swaroop Sahoo[1], Limalemla Jamir[2], Ashwini Kedar, Sugandhi Sharma[3], Bhumika Bhatt[4]

Abstract:

BACKGROUND: Global burden of disease (GBD) provides the estimates of mortality and morbidity, while case fatality rate (CFR) helps in understanding the severity of the disease. People infected with severe acute respiratory syndrome coronavirus 2 (SARS CoV-2) with underlying medical conditions have shown higher levels of unfavorable outcomes including mortality. We assessed the association of SARS-CoV-2 CFR with disability-adjusted life years (DALY) of various comorbidities in the low-middle income countries (LMIC) and high-income countries (HIC) to study the relationship of coronavirus disease-19 (COVID-19) mortality with GBDs and to understand the linkage between COVID-19 mortality and comorbidities.

MATERIALS AND METHODS: This was an ecological study with secondary data analysis comparing the DALY of various morbidities from GBD with CFR of COVID-19. Gross domestic product was the basis of stratifying 177 countries into low-middle income (LMIC) and high-income groups (HIC). The mortality was analyzed using Pearson correlation and linear regression.

RESULTS: The median global CFR of SARS-CoV-2 was 2.15. The median CFR among LMIC ($n = 60$) and HIC ($n = 117$) was 2.01 (0.00–28.20) and 2.29 (0.00–17.26), respectively. The regression analysis found that, in both LMIC and HIC, maternal disorders were associated with higher SARS-CoV-2 CFR, while tuberculosis, mental health disorders, and were associated with lower CFR. Further, in LMIC, musculoskeletal disorders and nutritional deficiencies were associated with higher CFR, while respiratory disorders were associated with lower CFR.

CONCLUSIONS: SARS-CoV-2 infection appears to be a systemic disease. Individuals with comorbidities, such as maternal disorders, neurological diseases, musculoskeletal disorders, and nutritional deficiencies, have poorer outcomes with COVID-19, leading to higher mortality.

Keywords:

Communicable disease, corona virus disease-19, global disease burden, morbidity, mortality, noncommunicable disease, severe acute respiratory syndrome coronavirus 2

Senior Consulatant, Ministry of Health and Family Welfare, New Delhi, India, [1]Department of Community and Family Medicine, All India Institute of Medical Sciences, Bathinda, Punjab, India, [2]Department of Community and Family Medicine, All India Institute of Medical Sciences, Guwahati, Assam, India, [3]Department of Community Medicine, Post Graduate Institute of Medical Education and Research, Chandigarh, India, [4]Department of Community Medicine, KD Medical College, Mathura, Uttar Pradesh, India

Address for correspondence:
Dr. Soumya Swaroop Sahoo, Department of Community and Family Medicine, All India Institute of Medical Sciences, Bathinda, Punjab, India.
E-mail: swaroop. drsoumya@gmail.com

Introduction

Novel coronavirus infection has now emerged as an unprecedented threat to mankind with more than 17 million confirmed cases and 0.68 million deaths.[1] Coronavirus disease-19 (COVID-19) is caused by a novel strain of coronavirus, named the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Initially, presumed to be a disease of the respiratory system, it is now speculated that it has a systemic impact involving all the major organ systems. To start with, the disease was limited to a few countries, but within months, COVID-19 has spread all over the world at a tremendous

How to cite this article: Jindal HA, Sahoo SS, Jamir L, Kedar A, Sharma S, Bhatt B. Higher coronavirus disease-19 mortality linked to comorbidities: A comparison between low-middle income and high-income countries. J Edu Health Promot 2021;10:377.

pace. The disease has overtly spread to both developed and developing nations. Although high-income countries (HICs) have successfully vanquished many infectious diseases, the novel coronavirus has proved challenging to quell.

Novel coronavirus mortality has been linked to the patients' comorbidities majorly noncommunicable diseases (NCDs).[2] The world has transitioned gradually from a predominant communicable disease pattern to a largely NCD-dominated disease burden, with the changing disease landscape in the developing countries too. Globally, it has been found that NCDs contribute to 48% of premature deaths and nearly 40 million NCD mortality in 2015.[3] The COVID-19 mortality among patients has shown an increasing trend among those with age more than 60 years, and people with preexisting conditions (such as heart diseases, diabetes, kidney diseases, and respiratory conditions).[2,4-9] It has also been found that severity of COVID-19 was higher among patients with preexisting NCDs such as hypertension (23.75%), diabetes mellitus (16.2%), coronary artery disease (5.8%), chronic obstructive pulmonary disease (3.5%), and cerebrovascular disease (2.3%).[8] Studies also suggest the evidence of severe disease in patients of COVID-19 admitted with preexisting neurological disease and may have a significantly higher in-hospital mortality, incident delirium, higher disability than patients without COVID-19.[10-12] Some studies have reported poor prognosis in maternal conditions such as pregnancy and can lead to complications and death.[13,14]

Surprisingly, there has been some connection between COVID-19 mortality and other communicable diseases such as tuberculosis (TB), malaria, and maternal disorders. However, rigorous infection control practices and personal protection are fundamental to prevent the risk of in-hospital transmission, especially when dealing with a highly vulnerable population.[15,16]

However, with the rapidly evolving dynamics of the pandemic across the world, the comorbidities continue to influence the mortality due to COVID-19. The dynamics of the disease may be affected by the disease patterns already existing in the countries. Moreover, there are limited data in a comprehensive form to assess the linkage between the preexisting diseases. Therefore, we assessed the link between the burden of major diseases (both communicable and noncommunicable) NCDs and CDs with COVID-19 case fatality rate (CFR). Our study explored the relation of NCDs and CDs with COVID-19 outcomes among different countries to get a better perspective of the disease. This would provide evidence to the health system to deal efficiently affected patients with coexistent morbidities, which in turn

can reduce the severity and burden of COVID in the community.

Materials and Methods

Study design and setting
This ecological study is a secondary data analysis of data from 177 countries selected based on the availability of the data on novel coronavirus mortality and the global burden of disease (GBD).

Study participants and sampling
All 177 countries were stratified into four groups based on gross domestic product as – low income, ($1,025 or less), low middle ($1,026 to $3,995), high ($3,996 to $12,375) and very high-income groups ($12,376 or more). The data were collected for a period of December 01, 2019–July 31, 2020.[17]

Data collection tool and techniques
The COVID-19 variables were collected in terms of the total number of cases and the total number of deaths for the countries.[1] CFR for every country was calculated separately.

CFR of COVID-19 = Number of deaths from COVID-19/ number of total cases of COVID-19 × 100.

CFR depicts the severity of the disease. The CFR was used to assess the link between COVID-19 severity and the burden of NCDs and communicable diseases.

The burden of the NCD and CD was measured in terms of disability-adjusted life years (DALY). DALY was defined as the years of healthy life lost to premature death and disability. It is a measure of the overall disease burden.

DALY = year lived with disability + years of life lost.

For our study, the DALY for NCD and CD was obtained from the GBD.[18,19]

The cardiovascular diseases included were rheumatic heart disease, hypertension, ischemic heart disease, cardiomyopathy, and other circulatory system disorders. Respiratory diseases included chronic obstructive disease, asthma, and other respiratory disease. Digestive diseases included peptic ulcer disease, cirrhosis, inflammatory bowel disease, and other digestive disorders including genitourinary disease. Musculoskeletal disease included rheumatoid arthritis, osteoarthritis, gout, and neck and back problems. Neurological diseases included Alzheimer's disease, parkinsonism epilepsy, migraine, headaches, and other neurological diseases. Diabetes and other endocrine disorders included diabetes and chronic

kidney disorders. Cancer included tumors of all major organs. Other NCDs included accidents, and injuries. In CD, maternal and neonatal disorders included common disorders such as congenital anomalies, birth asphyxia, preterm babies, and respiratory system included upper and lower respiratory infections. Diarrheal disease included the intestinal nematodes infection. Malaria and neglected tropical diseases included diseases caused by parasites such as lymphatic filaria, malaria, dengue, and chikungunya. Human immunodeficiency virus (HIV) and TB were considered a separate entity.[20]

Data were extracted and tested for normality. Data analysis was done using the Statistical Package for the Social Sciences (SPSS) version 20.0 (Armonk, NY: IBM Corp). DALY and CFR being nonnormally distributed were expressed in median. Kruskal–Wallis test was used to assess the significance of the CFRs. However, for analysis, the data were converted for normal distribution using a logarithmic scale. Pearson correlation was used to analyze the relationship between the COVID-19 CFR and the GBD (DALY) of various countries. The factors were further analyzed with linear regression with the backward elimination method, and the beta coefficient was interpreted.

Ethical consideration

As the study involved secondary data analysis from publicly available free datasets, ethical permission was not required.

Results

The median global CFR of SARS-CoV-2 was 2.15 as per the data available in our study period. The CFR of 177 countries ranged of COVID-19 ranged from 0.00 to 28.20. The median CFR in low-income countries ($n = 29$) and low-middle income countries (LMIC) ($n = 36$) was 1.98 (0.72–4.21) and 2.09 (1.35–3.14), respectively. The SARS-CoV-2-2 CFR among the HIC ($n = 52$) and the very HIC ($n = 60$) was comparatively higher 1.72 (0.89–3.40) and 3.74 (2.83–5.04), respectively [Figure 1]. For further analysis, the low and LMIC were emerged as "LMIC" and high and very HIC were merged to form "HIC."

LMICs contribute to the majority of the global burden of maternal disorders (86.7), neonatal disorders (79.2), nutritional deficiencies (83.2), malaria and neglected tropical diseases (82.8), HIV / AIDS (70.3), and TB (85.3). NCDs are nearly equally contributed by low middle-income countries (47.2) and high and very HICs (52.8). Further, LMICs contribute to high burden of cardiovascular diseases (43.9), cancer (32.2), respiratory disorders (53.1), diabetes and endocrine disorders (49.5), liver disorders (56.5), mental and substance abuse (44.5), neurological disorders (41.9), musculoskeletal
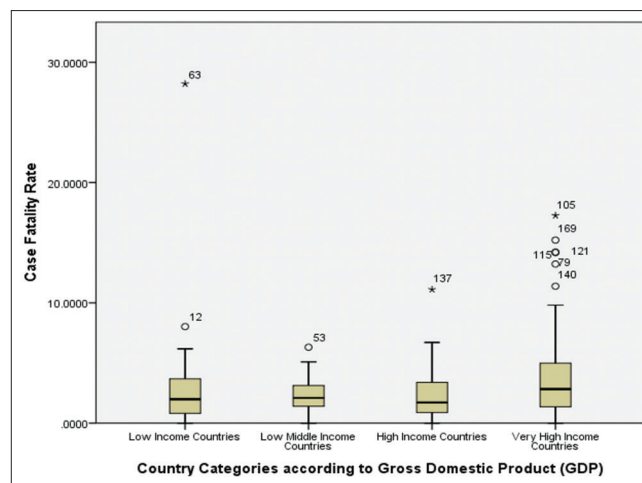

Figure 1: Severe acute respiratory syndrome coronavirus 2 case fatality rate with country categories according to gross domestic product

disorders (38.9), digestive disorders (53.0), and other NCDs (58.5) [Figure 2].

A positive correlation was found with the NCD in high-income group neurological disorders, musculoskeletal disorder, digestive disorders, cardiovascular disorders, cancer, respiratory disorders, and liver disorders [Table 1].

The regression analysis found that, in both LMICs and HICs, burden of maternal disorders was associated with higher SARS-CoV-2 CFR, while TB, mental health disorders, and were associated with lower SARSsu-CoV-2 CFR [Table 2]. In LMICs, musculoskeletal disorders and nutritional deficiencies; while in HICs, burden of cancer, neurological disorders, and other NCDs were associated with higher CFR. In low-income countries, respiratory disorders were associated with lower CFR while malaria and neglected tropical diseases and neonatal disorders were associated with lower CFR [Table 3].

Discussion

COVID-19 initially originated as pneumonia-like disease, but recent evidence shows that it affects almost every system of the body. Similar to SARS-CoV, SARS-CoV-2 enters through angiotensin-converting enzyme 2 receptors that have been found in many different organs of the body. Our study found a positive correlation between COVID-19 mortality with majority of the NCDs in the bivariate correlation analysis. Many other studies have also reported higher severity of the disease with NCDs.[8,10-14,21,22]

Studies have shown diabetes as a worsening factor for SARS-CoV-2 infection, as it can augment the risk of acute complications through direct negative effects on β-cell function. This effect may lead to diabetic

Table 1: Correlation between noncommunicable disease (disability adjusted life years) and case fatality rate (correlation coefficient)

Noncommunicable disease (DALY)	Low middle-income countries - CFR (*n*=65)	High income countries - CFR (*n*=112)
Cardiovascular disorders		
Rho	0.076	0.256
P	0.563	0.01*
Cancer		
Rho	0.011	0.316
P	0.934	0.01*
Respiratory disorders (DALY)		
Rho	0.024	0.245
P	0.858	0.01*
Diabetes and endocrine disorders (DALY)		
Rho	0.065	0.220
P	0.620	0.01
Liver disorders (DALY)		
Rho	−0.015	0.265
P	0.908	0.01*
Mental and substance abuse (DALY)		
Rho	0.041	0.257
P	0.756	0.04
Neurological disorders (DALY)		
Rho	0.044	0.26
P	0.738	0.01*
Musculoskeletal disorders (DALY)		
Rho	0.074	0.243
P	0.573	0.01*
Digestive disorders (DALY)		
Rho	0.013	0.257
P	0.964	0.016*
Other NCD (DALY)		
Rho	0.047	0.203
P	0.724	0.04*

*$P<0.05$ considered as statistically significant. DALY=Disability adjusted life years, CFR=Case fatality rate, NCD=Noncommunicable disease, Rho=Correlation coefficient
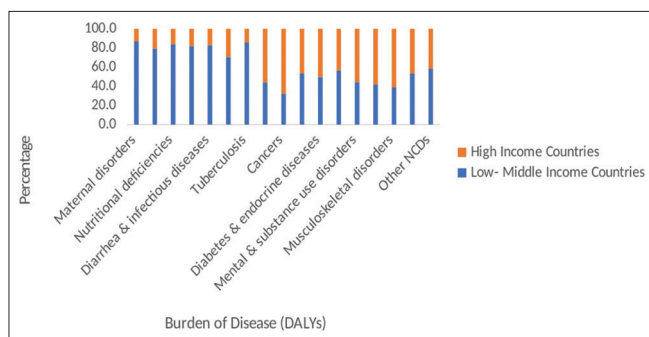

Figure 2: Contribution of country categories according to the global burden of disease

ketoacidosis, hyperglycemia, and an increase in hospital admission.[23,24] Our study found an association of COVID-19 and diabetes in bivariate analysis in HICs with higher severity of the disease. Furthermore, we found an association with severity of SARS-CoV-2 with nutritional deficiencies, there have been studies that reported the role of Vitamin D in the prevention of progress and severity of the SARS-CoV-2.[25]

Our study also found an association of neurological disorders with an increased CFR of SARS-CoV-2. Previously, Kim *et al*. reported similar findings that patients requiring treatment in the intensive care unit were more likely to be older, male sex, and have an underlying comorbidity.[26] In another study conducted by Du *et al*., the univariate analysis showed that preexisting cerebrovascular diseases were predictive of mortality (odds ratio [OR] = 11.09, 95% confidence interval = 4–30).[27] In addition, there have been studies that found the coexistence of Parkinson's disease in COVID-19 with a poor prognosis.[28,29]

Severe disease in preexisting neurological disease, such as dementia may be due to limited access to accurate information about preventive measures during the pandemic period of social distancing and home isolation.[30] Neurological disease leads to neuromuscular weakness or musculoskeletal weakness or invasion of the medullary cardiorespiratory center that may lead to respiratory insufficiency in COVID-19 patients, leading

Table 2: Correlation between communicable disease (disability adjusted life years) and case fatality rate (correlation coefficient)

Communicable disease (DALY)	Low middle-income countries - CFR (*n*=65)	High income countries - CFR (*n*=112)
Maternal disorders		
Rho	0.006	0.07
P	0.601	0.435
Neonatal disorders		
Rho	0.010	0.112
P	0.939	0.254
Nutritional deficiencies		
Rho	0.014	0.108
P	0.916	0.274
Malaria and neglected tropical diseases		
Rho	0.066	−0.020
P	0.617	0.836
Diarrheal and infectious diseases		
Rho	−0.060	0.155
P	0.646	0115
HIV/AIDS		
Rho	−0.179	0.833
P	0.171	0.399
Tuberculosis		
Rho	−0.207	0.048
P	0.113	0.630

DALY=Disability adjusted life years, CFR=Case fatality rate, Rho=Correlation coefficient, HIV=Human immunodeficiency virus

Table 3: Regression analysis between burden of the disease (disability adjusted life years) and case fatality rate

Burden of disease (DALY)	Standardized β coefficient	*t*	*P*	95%CI (lower limit-upper limit)	Model equation for linear regression
Low -middle income countries					
Musculoskeletal disorders	3.94	3.109	0.03*	−0.817-3.789	R^2=0.36
Maternal disorders	0.748	2.173	0.01*	0.031-0.781	
Nutritional deficiencies	0.874	2.054	0.04*	0.012-1.012	
Mental and substance abuse	−3.27	−2.724	0.01*	−3.509--0.533	
Respiratory disorders	−1.131	−2.018	0.04*	−1.313--0.04	
Tuberculosis	−1.039	−4.118	0.01*	−0.765--0.264	
Very high-income countries					
Cancers	0.962	1.726	0.08	−0.069-0.994	R^2=0.426
Mental and substance use disorders	−4.831	−4.864	0.01*	−3.328--1.399	
Neurological disorders	2.946	2.206	0.03*	0.143-2.710	
Maternal disorders	1.347	3.810	0.00*	0.280-0.890	
Neonatal disorders	−1.516	−2.340	0.02*	−1.325--0.109	
Malaria and neglected tropical diseases	−0.387	−2.125	0.03*	−0.253--0.009	
Tuberculosis	−0.489	−2.078	0.04*	−0.376--0.009	
Other NCDs	2.167	1.942	0.05	−0.024-2.153	

*P<0.05 statistically significant. DALY=Disability adjusted life years, NCD=Noncommunicable disease, CI=Confidence interval

to adverse outcomes.[31] The SARS-CoV-2 receptor is expressed in the nervous system. Commonly reported symptoms included hyposmia, headaches, weakness, and altered consciousness. Encephalitis, demyelination, neuropathy, and stroke have been associated with COVID-19. Therefore, it can be speculated that SARS-CoV-2 has a detrimental effect on the nervous system, leading to poor outcomes is in people with preexisting neurological diseases. Further studies are needed to clarify the prevalence of the neurological complications of SARS-CoV-2 infection, investigate their

biological backgrounds, and test treatment options. In COVID-19, increased D-dimer levels caution the risk of microthrombosis.[31] Physicians should be cautious not to overlook other neurological diagnoses that can mimic COVID-19 during the pandemic.[32,33]

In COVID-19 cases, some studies suggest that viral shedding may be prolonged in patients treated with corticosteroids, and their routine use is currently avoided.[34] In addition, immunoglobulins are used to treat neuroinflammatory diseases that increase the

risk of thromomembolism.[35] However, in our study, association of preexisting musculoskeletal disorders with higher case fatality, similar reasoning can be sought. Further, our study demonstrated lower mortality with malaria and neglected tropical disease which may be because of the usage of chloroquine and its derivatives that have some antiviral properties for reducing the severity of the disease.[36-41]

Our study shows an increase in the severity of COVID-19 with preexisting maternal disorders. It may be due to the hypercoagulable state during pregnancy. Previous studies indicate that pregnant women were more likely to be hospitalized and have adverse events than normal women but mortality remained the same. Our study corroborates with recommendations that pregnant women and their families take preventive measures to reduce their risk of contracting COVID-19.[42]

Our study found lower severity of SARS-CoV-2 with preexisting neonatal disorders. There are very few studies that report fatality in newborns and few cases have been observed in children and adolescents who seem to have a more favorable clinical course than other age groups, and even fewer in newborn babies. Studies found that most newborns who have tested positive for COVID-19 had mild or no symptoms and have recovered fully. Only a small number of other complications, such as preterm (early) birth, have been reported in babies born to mothers who tested positive for COVID-19. Although vertical transmission from the mother to her fetus or neonate has yet to be proven, case reports of sick neonates exist. Early identification and isolation, adequate management, prevention, and vaccine development are the keys to controlling disease spread. Further studies on the different faces of COVID-19 are required to fight this viral pandemic.[43,44]

In LMICs, TB and respiratory diseases are the major public health problems and in our study, they were found to be associated with lower mortality. However, it has been found that the majority of the people suffering from such diseases are young with fewer comorbidities, although studies show higher mortality is likely to occur in elderly patients with comorbidities and TB. However, mortality benefit in TB may be due to better respiratory hygiene and social distancing among the patients and general public. Studies have also reported that COVID-19 cases on active TB are clinically manageable with adequate care. With infection control practices and social distancing, the risk of in-hospital transmission can be prevented.[45]

Mental health and substance abuse were associated with lower severity of the diseases. There are very limited data published in how preexisting mental health has been associated with mortality in COVID-19 infections. The behavioral disorders that improve personal hygiene and personal protective measure in mental ailments may help patients to protect themselves from SARS-CoV-2. Studies have reported a social change toward improved personal hygiene and personal protective measure.[46] However, other NCDs such as intentional harm and suicides may be associated with higher case fatality due to paranoid behaviors. COVID-19 appears to be a systemic disease that affects on all the major health systems of the body. Hence, health practitioners in COVID-19 crisis need reliable information and evidence. Majority of this is derived from new experiences, such as lessons learned from the initial spread in China and continuation of use, improve personal hygiene and personal protective measure.[47]

Limitation and recommendation

Our study has demonstrated a series of associations with preexisting diseases in LMIC and HIC. Our study is novel to depict a mortality pattern of COVID-19 according to pre-existing disease patterns prevalent in LMICs and HIC. Although we have tried to discuss every factor irrespective of their country group, the CFR does depend on the response and surge capacity of the health care system. Furthermore, this being an ecological study, the results need to be interpreted with caution, with potential for systematic differences between areas in recording disease frequency and measurement of exposure. This study was an attempt to discuss every factor irrespective of their country group, the CFR depends on many factors such as health-seeking behavior, health system, and surveillance that have not been considered in the present study. A better reporting system provides us with accurate parameters and a better understanding of the novel coronavirus in HIC.[47] However, the common factors influencing the CFR in low-income countries also add upon the epidemiological knowledge of the COVID 19 pandemic. Our study warrants further research into the comorbidities aspects of COVID-19 mortality to be better prepared and save lives of the individuals with preexisting diseases within the limited surge capacity of the health system.

Conclusions

COVID-19 has spread all over the world with varying mortality in different countries. There are links of SARS-CoV-2 mortality and severity with preexisting NCDs and CDs. SARS-CoV-2 appears to be a systemic disease than just a respiratory illness. Preexisting maternal disorders, neurological diseases, musculoskeletal disorders, and nutritional deficiencies may have poorer outcomes with COVID-19. Our study warrants further studies into the comorbidity's aspects of COVID-19 mortality to be better prepared and save lives of the

individuals with preexisting diseases with adequate and timely interventions.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. World Health Organization. WHO Coronavirus Disease (COVID-19) Dashboard; 2020. Available from: https://covid19.who.int/. [Last accessed on 2020 Aug 02].
2. World Health Organization. Information Note COVID-19 and NCDs; 2020. Available from: https://www.who.int/publications/m/item/covid-19-and-ncds. [Last accessed on 2020 Jul 12].
3. World Health Organization. Global Health Observatory (GHO) Data Noncommunicable Diseases (NCD); 2020. Available from: https://www.who.int/gho/ncd/en/. [Last accessed on 2020 Jul 31].
4. Wang B, Li R, Lu Z, Huang Y. Does comorbidity increase the risk of patients with COVID-19: Evidence from meta-analysis. Aging (Albany NY) 2020;12:6049-57.
5. Singh AK, Gupta R, Misra A. Comorbidities in COVID-19: Outcomes in hypertensive cohort and controversies with renin angiotensin system blockers. Diabetes Metab Syndr 2020;14:283-7.
6. Yang J, Zheng Y, Gou X, Pu K, Chen Z, Guo Q, *et al*. Prevalence of comorbidities and its effects in patients infected with SARS-CoV-2: A systematic review and meta-analysis. Int J Infect Dis 2020;94:91-5.
7. 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;395:497-506.
8. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, *et al*. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med 2020;382:1708-20.
9. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, *et al*. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. JAMA 2020;323:1061-9.
10. Yang X, Yu Y, Xu J, Shu H, Xia J, Liu H, *et al*. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: A single-centered, retrospective, observational study. Lancet Respir Med 2020;8:475-81.
11. Benussi A, Pilotto A, Premi E, Libri I, Giunta M, Agosti C, *et al*. Clinical characteristics and outcomes of inpatients with neurological disease and COVID-19 in Brescia, Lombardy, Italy. Neurology 2020;95:e910-20.
12. Mao L, Jin H, Wang M, Hu Y, Chen S, He Q, *et al*. Neurologic manifestations of hospitalized patients with coronavirus disease 2019 in Wuhan, China. JAMA Neurol 2020;77:1-9.
13. Hantoushzadeh S, Shamshirsaz AA, Aleyasin A, Seferovic MD, Aski SK, Arian SE, *et al*. Maternal death due to COVID-19. Am J Obstet Gynecol 2020;223:109.e1-6.
14. Metz TD, Collier C, Hollier LM. Maternal mortality from coronavirus disease 2019 (COVID-19) in the United States. Obstet Gynecol 2020;136:313-6.
15. Tadolini M, Codecasa LR, García-García JM, Blanc FX, Borisov S, Alffenaar JW, *et al*. . Active tuberculosis, sequelae and COVID-19 co-infection: First cohort of 49 cases. Eur Respir J 2020;56:2001398.
16. Motta I, Centis R, D'Ambrosio L, García-García JM, Goletti D, Gualano G, *et al*. Tuberculosis, COVID-19 and migrants: Preliminary analysis of deaths occurring in 69 patients from two cohorts. Pulmonology 2020;26:233-40.
17. World Bank. Data World Bank Country and Lending Groups. Classifications; 2020. Available from: https://datahelpdesk.worldbank.org/knowledgebase/articles/906519-world-bank-country-and-lending-groups. [Last accessed on 2020 Sep 08].
18. Global Burden of Disease Collaborative Network. Global Burden of Disease Study 2017 (GBD 2017) Results. Seattle, United States: Institute for Health Metrics and Evaluation (IHME); 2018.
19. Roser M, Ritchie H. OurWorldInData.org. "Burden of Disease"; 2018. Available from: https://ourworldindata.org/burden-of-disease. [Last accessed on 2020 Aug 02].
20. World Health Organization. Department of Information, Evidence and Research. WHO Methods and Data Sources for Global Burden of Disease Estimates 2000-2016 – Global Health Estimates Technical Paper WHO/HIS/IER/GHE/2018.4; June 2018. Available form: https://www.who.int/healthinfo/global_burden_disease/GlobalDALY_method_2000_2016.pdf?ua=1. [Last accessed on 2020 Aug 02].
21. Liang WH, Guan WJ, Li CC, Li YM, Liang HR, Zhao Y, *et al*. Clinical characteristics and outcomes of hospitalised patients with COVID-19 treated in Hubei (epicentre) and outside Hubei (non-epicentre): A nationwide analysis of China. Eur Respir J 2020;55:2000562.
22. Sahu KK, Jindal V, Siddiqui AD, Cerny J. Facing COVID-19 in the hematopoietic cell transplant setting: A new challenge for transplantation physicians. Blood Cells Mol Dis 2020;83:102439.
23. Roncon L, Zuin M, Rigatelli G, Zuliani G. Diabetic patients with COVID-19 infection are at higher risk of ICU admission and poor short-term outcome. J Clin Virol 2020;127:104354.
24. Ali N. Role of vitamin D in preventing of COVID-19 infection, progression and severity. J Infect Public Health 2020;13:1373-80.
25. Herman C, Mayer K, Sarwal A. Scoping review of prevalence of neurologic comorbidities in patients hospitalized for COVID-19. Neurology 2020;95:77-84.
26. Du RH, Liang LR, Yang CQ, Wang W, Cao TZ, Li M, *et al*. Predictors of mortality for patients with COVID-19 pneumonia caused by SARS-CoV-2: A prospective cohort study. Eur Respir J 2020;55:2000524.
27. Deng SQ, Peng HJ. Characteristics of and public health responses to the coronavirus disease 2019 outbreak in China. J Clin Med 2020;9:575.
28. Moni MA, Liò P. Network-based analysis of comorbidities risk during an infection: SARS and HIV case studies. BMC Bioinformatics 2014;15:333.
29. Wang H, Li T, Barbarino P, Gauthier S, Brodaty H, Molinuevo JL, *et al*. Dementia care during COVID-19. Lancet 2020;395:1190-1.
30. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, *et al*. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: A retrospective cohort study. Lancet 2020;395:1054-62.
31. Bikdeli B, Talasaz AH, Rashidi F, Sharif-Kashani B, Farrokhpour M, Bakhshandeh H, *et al*. Intermediate versus standard-dose prophylactic anticoagulation and statin therapy versus placebo in critically-ill patients with COVID-19: Rationale and design of the INSPIRATION/INSPIRATION-S studies. Thromb Res 2020;196:382-94.
32. Ghannam M, Alshaer Q, Al-Chalabi M, Zakarna L, Robertson J, Manousakis G. Neurological involvement of coronavirus disease 2019: A systematic review. J Neurol 2020;267:3135-3153.
33. Montalvan V, Lee J, Bueso T, De Toledo J, Rivas K. Neurological manifestations of COVID-19 and other coronavirus infections: A systematic review. Clin Neurol Neurosurg 2020;194:105921.
34. Russell CD, Millar JE, Baillie JK. Clinical evidence does not support corticosteroid treatment for 2019-nCoV lung injury. Lancet 2020;395:473-5.
35. Stiehm ER. Adverse effects of human immunoglobulin therapy.

Transfus Med Rev 2013;27:171-8.

36. d'Arminio Monforte A, Tavelli A, Bai F, Marchetti G, Cozzi-Lepri A. Effectiveness of Hydroxychloroquine in COVID-19 disease: A done and dusted situation? Int J Infect Dis 2020;99:75-6.

37. Arshad S, Kilgore P, Chaudhry ZS, Jacobsen G, Wang DD, Huitsing K, *et al*. Henry ford COVID-19 task force. Treatment with hydroxychloroquine, azithromycin, and combination in patients hospitalized with COVID-19. Int J Infect Dis 2020;97:396-403.

38. Liu J, Cao R, Xu M, Wang X, Zhang H, Hu H, *et al*. Hydroxychloroquine, a less toxic derivative of chloroquine, is effective in inhibiting SARS-CoV-2 infection *in vitro*. Cell Discov 2020;6:16.

39. Gautret F, Lagier JC, Parola P, Hoang VT, Meddeb L, Mailhe M, *et al*. Hydroxychloroquine and azithromycin as a treatment of COVID-19: Results of an open-label non-randomised clinical trial. Int J Antimicrob Agents 2020;56:105949.

40. Devaux CA, Rolain JM, Colson P, Raoult D. New insights on the antiviral effects of chloroquine against coronavirus: What to expect for COVID-19? Int J Antimicrob Agents 2020;55:105938.

41. Tang W, Cao Z, Han M, Wang Z, Chen J, Sun W, *et al*. Hydroxychloroquine in patients with mainly mild to moderate coronavirus disease 2019: Open label, randomised controlled trial. BMJ 2020;369:m1849.

42. Ellington S, Strid P, Tong VT, Woodworth K, Galang RR, Zambrano LD, *et al*. Characteristics of women of reproductive age with laboratory-confirmed SARS-CoV-2 infection by pregnancy status – United States, January 22-June 7, 2020. MMWR Morb Mortal Wkly Rep 2020;69:769-75.

43. Jeng MJ. Coronavirus disease 2019 in children: Current status. J Chin Med Assoc 2020;83:527-33.

44. COVID-19: Maternal and Child Health during COVID-19; 2020. Available from: https://www.aha.org/system/files/media/file/2020/05/COVID-19-Maternal-Guidelines_rev6.pdf. [Last accessed on 2020 Aug 02].

45. Stochino C, Villa S, Zucchi P, Parravicini P, Gori A, Raviglione MC. Clinical characteristics of COVID-19 and active tuberculosis co-infection in an Italian reference hospital. Eur Respir J 2020;56:2001708.

46. Saji JA, Babu BP, Sebastian SR. Social influence of COVID-19: An observational study on the social impact of post-COVID-19 lockdown on everyday life in Kerala from a community perspective. J Educ Health Promot 2020;9:360.

47. Panahi S, Ashrafi-Rizi H, Panahi M. Exposure to coronavirus (COVID-19) using narrative and simulated experience approaches: A commentary. J Educ Health Promot 2020;9:135.