


Trend of COVID-19 Hospital Cases Fatality Rate in Iran: A Multicenter Study of 5318 Hospitalized COVID-19 Patients from March 2020 to March 2021

Mehdi Azizmohammad Looha¹, Seyed Amir Ahmad Safavi-Naini¹, Nazanin Taraghikhah¹, Mohammad Tayefeh Norooz², Nasser Malekpour Alamdari², Zahra Azizan³, Nadia Zameni³, Mohamad Amin Pourhoseingholi^{1*} 

1. Basic and Molecular Epidemiology of Gastrointestinal Disorders Research Center, Research Institute for Gastroenterology and Liver Diseases, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

2. Department of Surgery, Modarres Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

3. School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

ABSTRACT

Background and Aim: Case fatality ratio (CFR) is an indicator of disease severity that can help policymakers make decisions. This study aims to evaluate the trend of CFR of hospitalized COVID-19 patients since the outset of the pandemic in Iran and identify variables that affect CFR.

Methods: 5318 confirmed COVID-19 inpatients were enrolled in this multicentric observational study. Patients admitted from March 20, 2020, to March 18, 2021, in three general hospitals were collected. The medical team gathered patients' demographics, past medical history, and outcomes by reviewing patients' medical records. The time trend of CFR was investigated by joinpoint regression analysis to calculate weekly percent change (WPC) and confidence interval (CI).

Results: Significant upward trend was observed in CFR of hospitalized COVID-19 patients during study weeks (WPC= 1.2, 95% CI: 0.7, 1.7; P < 0.001). The increase was more evident in men than in women (WPC: 1.4 vs. 1.1). The rise of CFR was observed in patients with cancer (WPC: 4.5), dialysis (WPC: 2.1), diabetes (WPC: 1.0), and old age (WPC: 1.0).

Conclusion: There was a significant rise in the trend of in-hospital CFR from March 2020 to March 2021 in Iran. This rise was also evident with the same rate in patients with old-age and DM. However, the rate of this rise was higher in male and cancerous patients. Worldwide variation was reported by few studies investigating the trend of hospital CFR, and further studies are warranted.

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*CORRESPONDING AUTHOR

Mohamad Amin Pourhoseingholi

Email: Pourhoseingholi@sbmu.ac.ir

 0000-0002-0121-8031

INTRODUCTION

Coronavirus Disease 2019 (COVID-19), which has been recognized as a pandemic in March 2020, has become the foremost global health concern (1). Iran has emerged as one of the epicenters of COVID-19 with 124,256 deaths as of October 18, 2021 (2). The most at-risk population for the severe outcome should be the priority of interventions by policymakers to prevent further fatality of COVID-19.

The case fatality rate (CFR) is an indicator of disease severity, defined as the percent of deaths from a specified disease among all diagnosed cases during a period of time. The mean CFR of COVID-19 is 2% - 3% globally, with a significant variation between countries (3). Although a low number of diagnostic tests, low health expenditure, old population, and high rate of smokers will increase the CFR; these features do not explain the disparity in CFR among



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countries (4). However, there are limited data regarding the trend of CFR over time in Iran (5). Successful implementation of guidelines needs accurate information on mortality and its related factors. Therefore, this study aimed to evaluate the trend of CFR of COVID-19 since the outset of the pandemic in Iran and identify variables that affect CFR.

METHODS

Data of COVID-19 patients admitted to three educational hospitals in Tehran from March 20, 2020, until March 18, 2021, was gathered. Cases were confirmed by reaction (RT-PCR) of oropharyngeal or nasopharyngeal swab samples on the admission date. Patients' demographics, symptoms, admission vital signs, comorbidities, patient allocation (Intensive / ward), and outcome (death) were gathered using the hospital information system and patient's medical record. In this study, CFR was calculated for each week. Five weeks from the beginning and end of the study were excluded. This was done because the quality of data collection might not have been adequate during this period. In the next step, the joinpoint regression analysis was used, which fitted a series of straight lines on a log scale to the trends in the weekly CFR. A joinpoint represents a change in the trend in CFR and the extent of these changes was estimated with the Weekly Percent Change (WPC). In the absence of a joining point, the WPC was fixed. All analyzes were performed using SPSS (version 26) and the joinpoint Regression Program, Version

4.9.0.0 (Statistical Research and Applications Branch, National Cancer Institute) (6).

The Institutional Review Board (IRB) at the Shahid Beheshti University of Medical Science approved the study (IR.SBMU.RIGLD.REC.1399.004). Data were anonymized before analysis, and patients' confidentiality and data security were concerned.

RESULTS

A total of 5318 patients with COVID-19 were included to the study. As shown in **Table 1** and **Figure 1**, a significant upward trend was observed in CFR of hospitalized COVID-19 patients during study weeks (WPC= 1.2, 95% CI: 0.7, 1.7; $P < 0.001$). The COVID-19 CFR increased more rapidly in men than in women (WPC: 1.4 vs. 1.1). The CFR in COVID-19 patients older than 75 years also was increased significantly each week (WPC: 1, 95% CI: 0.1, 1.8; $P = 0.012$). Overall, the CFR of COVID-19 patients with at least one comorbidity was significantly increasing over the study period (WPC: 0.7, 95% CI: 0.1, 1.3; $P = 0.016$). The highest increasing trend in CFR was seen in cancer patients with COVID-19 (WPC: 4.5, 95% CI: 1.1, 8.0; $P = 0.011$). In addition, the weekly CFR was upward in hospitalized COVID-19 patients with DM (WPC: 1.0, 95% CI: 0.1, 2.0; $P = 0.026$).

Table 1. The WPC of CFR among patients with COVID-19 during study period

Variable	Level	Period (week)	WPC (95% CI)	P-value
Total	----	6-50	1.2 (0.7, 1.7)	< 0.001
Sex	Female	6-50	1.1 (0.4, 1.7)	0.002
	Male	6-50	1.4 (0.6, 2.2)	0.001
Comorbidity	Yes	6-50	0.7 (0.1, 1.3)	0.016
	No	6-50	1.3 (-0.5, 3.2)	0.153
Age > 75	Yes	6-50	1.0 (0.1, 1.8)	0.012
HTN	Yes	6-50	0.6 (-0.1, 1.2)	0.094
IHD	Yes	6-50	0.5 (-0.4, 1.5)	0.294
DM	Yes	6-50	1.0 (0.1, 2.0)	0.026
Cancer	Yes	6-50	4.5 (1.1, 8.0)	0.011
CVA	Yes	6-50	1.57 (-1.6, 4.8)	0.325
Intubation	Yes	6-50	0.3 (-0.4, 1.1)	0.417
Dialysis	Yes	6-50	2.1 (0.1, 4.1)	0.040

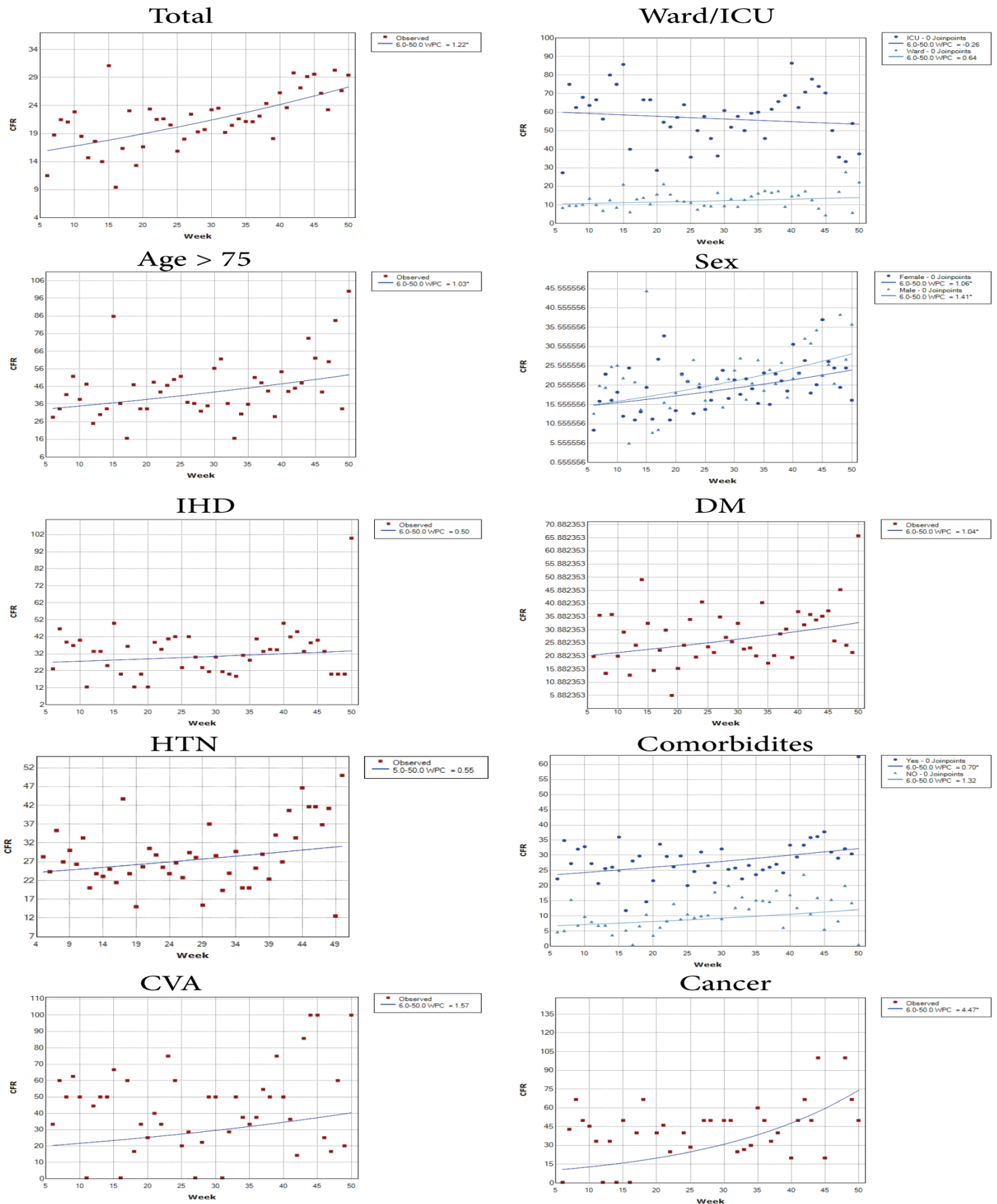


Figure 1. The CFR of hospitalization patients with COVID-19 by different risk factors (The first and last five weeks were removed)

DISCUSSION

To our knowledge, few studies have been investigated the trend of hospital CFR. This study explored the trend of CFR in 5318 COVID-19 inpatients from March 2020 to March 2021, in three educational hospitals in Tehran. We observed a rise in CFR over time, especially in patients with cancer, DM, and old age. The continued rise of hospital CFR in Iran was rare, although each country showed a distinct pattern. During the first year of the pandemic hospital CFR in South Africa (7) had a rising trend, in France (8) made a rise and fall pattern, in the USA (9, 10) decreased and then remained constant, and in Brazil (11) hospital CFR decreased over time. The percent of ICU patients, healthcare personnel (HCP) burnout, and patient late referral may to some extent explain the situation. Further studies are needed worldwide for an explanation of this variation.

In most of the countries worldwide CFR peaked during the first months of the COVID-19 pandemic and then decreased gradually (12). However, in-hospital CFR is different since the population of study gets limited to admitted patients, with more severe diseases. In weeks 40-50 (winter 2021), we observed the highest in-hospital CFR while there was no outbreak in the COVID-19 cases in Iran (2). However, Iran's third outbreak of COVID-19, in autumn 2020 (2), put the well-being of HCP in a fragile state, and this burnout may have some impact on the care of patients (13). Moreover, the delta variant (B.1.617.2), a variant detected in India in late 2020, spread rapidly in the world. The fatality of delta variants remained obscure and controversial, but some studies suggest higher fatality (14). On 19 February, Iran reported two delta cases in Qom, a city in the center of Iran (15). All in one, the new COVID-19 variant and HCP burnout may explain the rise of hospital CFR in winter 2021.

Cases with Old-age, DM, and female gender showed a rise with almost the same rate of total cases. However, male gender (WPC= 1.44) and cancerous patients (WPC= 4.47) had higher rates of CFR rise. A study reported a significantly higher CFR in patients with cancer (WPC= 37%) in the USA (16). To our knowledge, no study investigated the trend of CFR in this group. The delay in referral of patients with comorbidity and higher severity of the underlying disease may give some clarification, although this assumption was made on our limited results and further studies are needed.

There is a marginal improvement of CFR in patients admitted to ICU over time. In alignment, substantial

improvement was evident in ICU admitted cases in the UK, even after adjusting the demographics and comorbidities of patients (17). Improvement of treatment protocols and experience of intensivists may clarify the condition.

There are several limitations to this study. First, this study was conducted in three educational hospitals, and there is a probability that our population does not represent the population of hospitalized patients. The hospital policy may influence the number of beds allocated for COVID-19 patients. Moreover, the educational hospitals are referral centers and more complicated cases are admitted.

CONCLUSION

There was a significant rise in the trend of in-hospital CFR from March 2020 to March 2021 in Iran. This rise was also evident with the same rate in patients with old-age and DM. However, the rate of this rise was higher in male and cancerous patients. Worldwide variation was reported by few studies investigating the trend of hospital CFR, and further studies are warranted.

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CONFLICT OF INTEREST

No potential conflict of interest was declared by authors.

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AUTHORS' CONTRIBUTION

MAL: Methodology, Formal Analysis, Writing the Original Draft

SAASN: Methodology, Writing the Original Draft, Administration

NT: Writing the Original Draft, Investigation

MTN: Investigation, Validation

NMA: Investigation, Validation

ZA: Investigation, Data gathering

NZ: Investigation, Data gathering

MAP: Methodology, Validation, Supervision, Administration

REFERENCES

1. World Health Organization. WHO Timeline COVID-19 [Internet]. Who. 2020 [cited 2021 Oct 18]. p. 2020. Available from: https://www.who.int/news-room/detail/27-04-2020-who-timeline---covid-19?gclid=EAIaIQobChMI4MaewOeo6gIVyyMrCh2JRgUIEAAYASAAEgLo3_D_BwE
2. Iran COVID: 5,796,659 Cases and 124,256 Deaths - Worldometer [Internet]. 2021 [cited 2021 Oct 18]. Available from: <https://www.worldometers.info/coronavirus/country/iran/>

3. 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* [Internet]. 2020;10(11). Available from: <https://bmjopen.bmj.com/content/10/11/e043560>
4. Sorci G, Faivre B, Morand S. Explaining among-country variation in COVID-19 case fatality rate. *Sci Rep* [Internet]. 2020;10(1):18909. Available from: <https://doi.org/10.1038/s41598-020-75848-2>
5. Ahammed T, Anjum A, Rahman MM, Haider N, Kock R, Uddin MJ. Estimation of novel coronavirus (COVID -19) reproduction number and case fatality rate: A systematic review and meta-analysis . *Heal Sci Reports* [Internet]. 2021 May 3;4(2):e274–e274. Available from: <https://pubmed.ncbi.nlm.nih.gov/33977156>
6. Kim HJ, Fay MP, Feuer EJ, Midthune DN. Permutation tests for joinpoint regression with applications to cancer rates. *Stat Med*. 2000 Feb;19(3):335–51.
7. Jassat W, Mudara C, Ozougwu L, Tempia S, Blumberg L, Davies M-A, et al. Increased mortality among individuals hospitalised with COVID-19 during the second wave in South Africa. *medRxiv* [Internet]. 2021 Jan 1;2021.03.09.21253184. Available from: <http://medrxiv.org/content/early/2021/03/10/2021.03.09.21253184.abstract>
8. Souris M, Gonzalez J-P. COVID-19: Spatial analysis of hospital case-fatality rate in France. *PLoS One* [Internet]. 2020 Dec 15;15(12):e0243606. Available from: <https://doi.org/10.1371/journal.pone.0243606>
9. Garg S, Patel K, Pham H, Whitaker M, O'Halloran A, Milucky J, et al. Clinical Trends Among U.S. Adults Hospitalized With COVID-19, March to December 2020. *Ann Intern Med* [Internet]. 2021 Aug 10;174(10):1409–19. Available from: <https://doi.org/10.7326/M21-1991>
10. Horwitz LI, Jones SA, Cerfolio RJ, Francois F, Greco J, Rudy B, et al. Trends in COVID-19 Risk-Adjusted Mortality Rates. *J Hosp Med*. 2021 Feb;16(2):90–2.
11. Zimmermann IR, Sanchez MN, Frio GS, Alves LC, Pereira CC de A, Lima RT de S, et al. Trends in COVID-19 case-fatality rates in Brazilian public hospitals: A longitudinal cohort of 398,063 hospital admissions from 1st March to 3rd October 2020. *PLoS One* [Internet]. 2021 Jul 16;16(7):e0254633. Available from: <https://doi.org/10.1371/journal.pone.0254633>
12. Hasan MN, Haider N, Stigler FL, Khan RA, McCoy D, Zumla A, et al. The Global Case-Fatality Rate of COVID-19 Has Been Declining Since May 2020. *Am J Trop Med Hyg* [Internet]. 2021 Apr 21;104(6):2176–84. Available from: <https://pubmed.ncbi.nlm.nih.gov/33882025>
13. Shoja E, Aghamohammadi V, Bazayr H, Moghaddam HR, Nasiri K, Dashti M, et al. Covid-19 effects on the workload of Iranian healthcare workers. *BMC Public Health* [Internet]. 2020;20(1):1636. Available from: <https://doi.org/10.1186/s12889-020-09743-w>
14. Khedar RS, Mittal K, Ambaliya HC, Mathur A, Gupta JB, Sharma KK, et al. Greater Covid-19 Severity and Mortality in Hospitalized Patients in Second (Delta Variant) Wave Compared to the First: Single Centre Prospective Study in India. *medRxiv* [Internet]. 2021 Jan 1;2021.09.03.21263091. Available from: <http://medrxiv.org/content/early/2021/09/07/2021.09.03.21263091.abstract>
15. Iran Reports Its First 2 Cases of the New Coronavirus - The New York Times [Internet]. The New York Times. 2020 [cited 2021 Nov 6]. Available from: <https://archive.ph/CuAQZ>
16. Mehta V, Goel S, Kabarriti R, Cole D, Goldfinger M, Acuna-Villaorduna A, et al. Case Fatality Rate of Cancer Patients with COVID-19 in a New York Hospital System. *Cancer Discov* [Internet]. 2020 Jul 1;10(7):935 LP – 941. Available from: <http://cancerdiscovery.aacrjournals.org/content/10/7/935.abstract>
17. Dennis JM, McGovern AP, Vollmer SJ, Mateen BA. Improving Survival of Critical Care Patients with Coronavirus Disease 2019 in England: A National Cohort Study, March to June 2020*. *Crit Care Med*. 2021 Feb;49(2):209–14.