Survival Rates and Prognostic Factors of COVID-19 Patients: A Registry-Based Retrospective Cohort Study

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Research article

Keywords: Survival, Epidemiology, Mortality, COVID-19, Iran.

Posted Date: January 14th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-143701/v1>

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Abstract

Background: Coronavirus disease 2019 (COVID-19) is a contagious disease caused by a newly identified coronavirus. Our knowledge about survival rate and prognostic factors of the disease is not established well. This study proposed to estimate the survival function of COVID-19 in western Iran.

Methods: This retrospective cohort study was performed in Hamadan province, western Iran. The study included patients that referred to the provincial hospitals during 7 months period from February 20 to September 20, 2020. The follow up of each subject was calculated from the date of onset of respiratory symptoms to the date of death. Demographic and clinical data were extracted from patients' medical records. Kaplan-Meier method, log-rank test, and Cox regression were used for the analysis of the data.

Results: The overall 1, 5, 10, 20, 30 and 49-day survival rate were 99.57%, 95.61%, 91.15%, 87.34%, 86.91%, and 86.74% respectively. A significant association was observed between survival time with age, gender, history of traveling to contaminated areas, co-morbidity, malignancies, and chronic diseases, and hospital units.

Conclusion: Educational programs and access to healthcare could be implemented as modifiable factors to reduce the mortality rate and burden of this disease in COVID-19 patients.

Background

Coronavirus disease 2019 (COVID-19) is an emerging and major public health problem caused by a newly discovered coronavirus. By October 2020, the disease had infected more than 35 million people and killed approximately 1,200,000 people (1). Most people infected with the COVID-19 virus will experience mild to moderate respiratory illness and attain recovery without any specific treatment (2). Older people and those with underlying medical problems such as cardiovascular disease, diabetes, chronic respiratory disease, and cancer are more likely to develop serious illness and death (3–5). Based on the findings of the previous studies, this disease is associated with complications such as encephalopathy, thromboembolism, acute myocarditis, rhabdomyolysis, renal failure, heart failure, shock, and multi-organ failure. (5–8).

Despite the clinical and epidemiological aspects of the disease have been widely studied, many other aspects of the disease including the patient's survival rate and factors affecting the survival are not well known. Informing about survival rate and effect of risk factors on the survival of the patients is so crucial for policy-makers and health service providers which trade-off the existing treatments, assessing drug safety, identify the factors that increase patient survival, apportioning the cost of future medical care, estimating years of life lost, evaluating product reliability, measuring the viability of medical therapies and devices. (9). Accordingly, this study aimed to specify the survival rate and prognostic factors in patients with COVID-19 in Hamadan province in the west of Iran.

This retrospective cohort study was performed from February 20 to September 20, 2020, in Hamadan province, the west of Iran.

3,922 patients with positive RT-PCR tests were included in the study. In this study, all men and women with a confirmed diagnosis of COVID-19 hospitalized in the provincial hospitals were examined. All patients who had undergone Anti-COVID-19 treatment were follow-up after discharge to September 2020. The follow-up of each individual (in person-day) was calculated from the date of onset of respiratory symptoms to date of death. The patients that not experience death due to coronavirus or died from other reasons and cases who lost to follow-up during the study period were considered censored observations.

The data collection tool was a checklist include demographic and clinical characteristics such as age group (< 40 , $40-59$, ≥ 60), gender (man, woman), residence (rural, urban), having an underlying disease (yes, no), type of co-morbidity (coronary heart disease (CHD), pulmonary diseases, diabetes, hypertension, neurological disease, neoplasms, liver and kidney diseases, Simultaneous infection with several diseases, and other), hospitalization sector (coronary care unit (CCU), intensive care unit (ICU), general, infectious unit, emergency unit, respiratory isolation section, neonatal care unit, internal care unit), history of traveling to contaminated areas (yes, no). The outcome variable was time from the onset of symptoms (including Fever or chills, Cough, Shortness of breath or difficulty breathing, Fatigue, Muscle or body aches, Headache, New loss of taste or smell, Sore throat, Congestion, or runny nose, nausea or vomiting, Diarrhea) to the occurrence of death.

Statistical analysis

The qualitative data were presented using frequency and percent, and quantitative data were described as the mean and standard deviation. We used the Kaplan-Meier method to measure the survival rate of the patients. Differences in the Survival rate were explored by the Log-Rank test. Finally, a cox-proportional hazard model or extended-cox model was used to evaluate the association between survival rates with independent predictors of survival. The Schoenfeld residuals method was used to choose the best model (proportional hazard cox model or extended cox model). The Schoenfeld residuals model evaluates the proportional hazard (PH) assumption. If the PH assumption holds for all particular covariates we used the proportional hazard cox model. But if the PH assumption does not hold even for one variable, we used the extended cox model. All statistical analyses were performed at a significance level of 0.05 using Stata software, version 14 (StataCorp, TX, USA).

Ethical Consideration

The Ethics Committee of the Hamadan University of Medical Sciences approved the study (IR.UMSHA.REC.1399.633).

Results

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Descriptive analysis

In this retrospective cohort study, 3922 patients with a confirmed diagnosis of COVID-19 with a mean age of 56.05 ± 19.03 years were studied. More than half of the patients were female (51.38%), 46.24% were over 60 years old and 73.92% of them lived in urban areas. Accompanying diseases such as CHD, diabetes, hypertension, and pulmonary disease were observed in 33.81% of the patients. Majority corona positive patients were admitted to the ICU of the hospital (50.23%). The average mortality rate was 15.3 per 10000 people (95% CI: 13.89 to 16.49). There is a dose-response relationship between increasing age and mortality rate from COVID-19. Also, the mortality rate of male patients, residents in rural areas, and patients with underlying diseases were higher than females, residents in urban areas, and healthy people. The highest mortality rate was observed in patients with malignancy and the lowest rates were seen in people with hypertension. More information about patients with Covid-19 is presented in Table 1. Figure 1 illustrates the Kaplan–Meier survival diagram. As shown, 1, 5, 10, 20, 30, and 49- day survival probabilities of the patients were 99.57%, 95.61%, 91.15%, 87.34%, 86.91%, and 86.74% respectively. The patients who survived more than 49 days after their onset of symptoms had a survival function of the straight line with no reduction in survival probability (Fig. 1).

Table 1
Clinical and demographical characteristics in patients with COVID-19 infection

Variable	Number (%)	Mortality rate due to COVID-19 per 10000 person		Estimated survival time (Days)		
		Rate	95% CI	Mean	Median	P-value
Age group (year)	912 (23.26)	2.95	2.02; 4.30	100.33	89	0.001
< 40		6.62	5.28; 8.30	94.72	87	
40 to 59	1196 (30.50)	30.30	27.52; 33.36	75.77	71	
≥ 60	1813 (46.24)					
Sex	2015 (51.38)	11.97	10.48; 13.69	89.08	82	0.001
Female		18.61	16.63; 20.83	85.42	79	
Male	1907 (48.62)					
Place of residence	1023 (26.08)	16.14	13.71; 19.01	87.20	79	0.326
Rural		14.78	13.35; 16.35	87.34	80	
Urban	2899 (73.92)					
History of traveling to contaminated areas	3863 (98.50)	15.49	14.21; 16.88	86.28	79	0.028
No		2.20	0.55; 8.80	154.22	181	
Yes	59 (1.50)					
Underlying disease	2596 (66.19)	8.26	7.19; 9.48	94.21	86.5	0.001
No		32.33	28.96; 36.10	73.76	70	
Yes	1326 (33.81)					

Variable	Number (%)	Mortality rate due to COVID-19 per 10000 person		Estimated survival time (Days)		
		Rate	95% CI	Mean	Median	P-value
Type of disease	548 (41.05)	37.19	31.29; 44.19	63.30	65.5	0.001
CHD	131 (9.81)	33.07	23.51; 46.52	76.17	72	
Pulmonary diseases	286 (21.42)	21.15	15.94 ; 28.06	79.64	75	
Diabetes	48 (3.60)	13.29	6.92; 25.55	141.06	175	
Hypertension	43 (3.22)	27.66	14.88; 51.41	84.07	71	
Neurological disease	38 (2.85)	110.007	71.01; 170.61	47.81	15	
Neoplasms	47 (3.52)	40.96	24.26; 69.16	72.72	71	
Liver & kidney diseases	118 (8.84)	55.01	40.93; 73.92	67.79	53	
Simultaneous infection	76 (5.69)	16.49	9.36; 29.04	95.75	93.5	
Other						

Variable	Number (%)	Mortality rate due to COVID-19 per 10000 person		Estimated survival time (Days)		
		Rate	95% CI	Mean	Median	P-value
Hospital units	61 (1.56)	54.36	35.07; 84.26	60.31	54	0.001
CCU	1970 (50.23)	19.09	16.97; 21.47	73.96	71	
ICU	444 (11.32)	16.11	12.21; 21.25	69.91	77	
General	107 (2.73)	4.65	2.32; 9.29	160.89	177	
Infectious	65 (1.66)	28.53	17.48; 46.57	86.28	88	
Emergency	786 (20.04)	12.06	9.91; 14.67	105.51	97.5	
Respiratory isolation unit	39 (0.99)	3.29	0.46; 23.38	77.85	70	
Neonatal care unit	375 (9.56)	9.81	7.22; 13.2	111.44	100	
Internal care unit	75 (1.91)	3.52	1.32; 9.37	151.64	169	
other						

Based on our results in Table 1 there was a significant difference in the proportion of COVID-19 positive subjects who progressed to death in terms of age group, gender, having underlying disease, coexisting disease, hospital units (p-value for all these variable = 0.001), and history of traveling to contaminated areas (p = 0.028). However, the proportion of progression from COVID-19 infection to death from it was not statistically significant between rural and urban areas (p = 0.236).

Analytical Analysis

The results of the univariate and multivariable analysis, using the cox proportional hazard model are shown in Table 2. The second column in Table 2 shows the p-value for the Schoenfeld residual. Schoenfeld residuals examined the proportional hazards (PH) assumption. The p-values are quite high for all variables, suggesting that all variables satisfy the PH assumption so we used the proportional hazard cox model, not the extended cox model. Based on the univariate and multivariable analyses, the male gender, age over 60 years, and co-infection with multiple diseases are associated with a statistically significant increased risk of death among COVID-19 patients. Figure 2 illustrates the Kaplan-Meier

patients' survival based on the results in Table 2.

Table 2

The result of univariate and multivariate Cox proportional hazards survival analysis in COVID-19 patients

Variable	P- value for schoenfeld residuals	Crude HR	95% CI	p-value	Adjusted HR	95% CI	p-value
Age group (year)	0.192	1.00	-	-	1.00	-	-
< 40		2.15	1.38; 3.33	0.001	0.87	0.45; 1.69	0.683
40 to 59		8.58	5.81; 12.67	0.001	2.56	1.41; 4.62	0.002
≥ 60							
Sex	0.497	1.00	-	-	1.00	-	-
Female		1.53	1.28; 1.82	0.001	1.74	1.38; 2.18	0.001
Male							
Place of residence	0.799	1.00	-	-	1.00	-	-
Rural		0.91	0.75; 1.11	0.328	0.90	0.70; 1.15	0.390
Urban							
History of traveling to contaminated areas	0.781	1.00	-	-	1.00	-	-
No		0.24	0.06; 0.96	0.044	0.51	0.12; 2.06	0.344
Yes							
Underlying disease	0.428	1.00	-	-	1.00	-	-
No		3.36	2.81; 4.01	0.001	0.64	0.20; 2.04	0.456
Yes							

Variable	P- value for schoenfeld residuals	Crude HR	95% CI	p- value	Adjusted HR	95% CI	p- value
Type of disease	0.309	1.00	-	-	1.00	-	-
Hypertension		1.28	0.65; 2.51	0.474	1.44	0.69; 2.98	0.326
CHD		1.34	0.64; 2.81	0.430	1.61	0.73; 3.52	0.235
Pulmonary diseases		0.86	0.42; 1.76	0.610	1.98	0.54; 2.44	0.155
Diabetes		1.26	0.51; 3.11	0.002	4.53	0.77; 5.06	0.001
Neurological disease		3.48	1.58; 7.65	0.029	2.74	1.97; 10.41	0.008
Neoplasms		1.60	0.69; 3.69	0.627	1.28	0.90; 5.26	0.588
Liver & kidney diseases		2.23	1.08; 4.56			1.29; 5.79	
Simultaneous infection		0.81	0.34; 1.91			0.52; 3.17	
Other							
Hospital units	0.865	1.00	-	-	1.00	-	-
Neonatal care unit		15.09	2.03; 112.49	0.008	2.76	0.34; 22.60	0.344
CCU		5.79	0.81; 41.22	0.080	1.59	0.21; 12.46	0.661
ICU		4.55	0.62; 32.92	0.134	1.55	0.19; 12.40	0.676
General		2.91	0.36; 23.29	0.313	1.99	0.22; 17.48	0.539
Infectious		11.32	1.50; 85.39	0.019	4.91	0.57; 42.06	0.147
Emergency		5.16	0.72; 36.97	0.103	1.78	0.22; 14.09	0.587
Respiratory isolation unit		4.39	0.60; 31.97	0.143	2.46	0.30; 19.87	0.398
Internal care unit		2.07	0.23; 18.52	0.515	0.90	0.08; 10.49	0.930
other							

Discussion

The aim of this study was to specify the effect of prognostic factors on the survival of COVID-19 patients using a proportional hazard cox model. Based on our results, the overall 1, 5, 10, 20, 30 and 49-day survival rate were 99.57%, 95.61%, 91.15%, 87.34%, 86.91%, and 86.74% respectively. In addition, we found a significant association between survival time and age, gender, history of traveling to contaminated areas, having underlying disease, malignancies, and chronic diseases, and hospitalization sector.

The present study indicated that elderly patients with COVI-19 had the highest mortality rate and lowest survival rate. This finding is concordance with the previous studies which demonstrated a higher mortality rate between the elderly populations (10, 11). Principally, elderly people have a weak immune response to infectious agents, and therefore, are more susceptible to severe infection (12). On the other hand, the prevalence of bacterial infection and underlying diseases such as diabetes, hypertension, cardiovascular disease, and cerebrovascular disease is higher in the elder population than in young and middle-aged patients, which puts them at higher risk of COVID-19 infection and its adverse consequences including death. Additionally, in Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS) diseases, aging has been introduced as an important independent risk factor for mortality (13).

Our findings showed that the median and mean survival time is significantly lower in men than in women. Epidemiological studies show sex-specific differences in the incidence and mortality rates in humans after COVID-19 infection, with males experiencing a higher mortality rate compared with females (14). Previous Investigations showed that men manifest more serious forms of the disease during the COVID-19 epidemic compared to women (14–16). This decreased vulnerability of women to viral infections may be attributed to the sex hormones and the X chromosome, which perform an essential role in innate and adaptive immunity (17). On another aspect, a higher incidence rate of COVID – 19 in men might be due to higher social interactions in workplaces. National office for statistics reported that men included 81 percent of the workforce in Iran during 2018-19; while more than 50 percent of them are employed in service occupations. Therefore, there is a higher possibility for men to obtain COVID – 19 infection due to higher social interactions in work environments (18).

Our findings revealed that the mortality rate of COVID-19 in residents of rural areas is higher than urban areas but their survival function is not significantly different. The high mortality rate in rural areas may happen because of factors correlated with poor access to healthcare or inadequate surveillance and monitoring in rural regions (19).

According to the present study, the mortality rate of COVID-19 in patients with underlying disease is four times higher than the healthy people. On the other hand, survival time in people with the underlying diseases is significantly shorter than people who do not have these diseases. Previous literatures showed that underlying diseases such as diabetes, hypertension, and coronary heart disease increased the risk of consequences such as hospitalization in invasive care units

and death (3, 20). This occurs because of several mechanisms including direct damage by the virus, systematic inflammatory responses, and weakening the immune system. Consistent with our study in research conducted by Emami and et al patients with malignancies are more in danger for mortality from COVID-19 than those without any tumor (3). Anticancer treatments such as chemotherapy and surgery put this group into an immunosuppressive state and subsequently at higher risk of MERS-CoV-2 infection (21).

There were some limitations in our study. First, estimation of survival rate requires reliable sources of data obtained from the prospective design while we conducted a retrospective cohort study. Second, information about potential confounding factors was not available, such as access to health care insurance and the severity of the disease. Third, this study was performed in a specific geographic area of Iran. On the other hand, there might be some unknown genetic or environmental factors influencing the results; therefore, the findings might not be completely generalizable to other populations. Despite these limitations, the study author was able to use the estimated 20 and 49-day survival rates, measuring the time from symptom onset to outcome.

Conclusions

Overall survival rate of the patients is relatively low and several factors such as age, gender, history of traveling to contaminated areas, having underlying disease, malignancies, and chronic diseases, and hospital units influence survival. Infection prevention and control strategy plan include entry/exit screening, restriction of movement, closure education centers, wearing mask, imposing quarantine and active surveillance is recommended.

Abbreviations

COVID-19: Coronavirus disease 2019, CHD: coronary heart disease, CCU: coronary care unit, ICU: intensive care unit, PH: proportional hazard, SARS: Severe Acute Respiratory Syndrome, MERS: Middle East Respiratory Syndrome.

Declarations

Ethics approval and consent to participate

The Ethics Committee of the Hamadan University of Medical Sciences approved the study (IR.UMSHA.REC.1399.633).

Consent for publication

Not applicable.

Availability of data and material

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The datasets used and/or analyzed during the current study can be made available by the corresponding author on a reasonable request.

Competing interests

The authors have declared no conflicts of interest.

Funding

The study was funded by the Hamadan University of Medical Sciences (No. 990223978). Funder has no role in the design of the study and collection, analysis, and interpretation of data and in writing the manuscript.

Authors' contributions:

FSH: Conceptualization, Methodology, Data curation, Formal analysis, Writing-Original draft, and final manuscript. YM: Conceptualization, Methodology, Supervision of the paper writing. MK: Methodology, Supervision of the paper writing. MM: Data preparation. All authors have read and approved the final manuscript

Acknowledgment

This study (ID: IR.UMSHA.REC.1399.347) was funded by the Vice-Chancellor of Research and Technology of Hamadan University of Medical Sciences. The funders had no role in study design, data collection, and analysis, decision to publish, or preparation of the manuscript.

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Figures

Figure 1

Kaplan–Meier estimate of the surviving function in patients with COVID-19 infection

Figure 2

Kaplan–Meier estimate of the surviving function for all independent variables