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ORIGINAL ARTICLE

Risk Factors Affecting the Death of Hospitalized Patients with COVID-19 in the South of Iran

Ehsan Goroei Sardu [1], Fatemeh Rezabeigi Davarani [2], Bahareh Kermani [3], Reza Faryabi [4], Shiva Kargar [5], Shamim Tashakori [1], Salman Daneshi [4]*

[1] Clinical Research Development Unit of Imam Khomeini Hospital, Jiroft University of Medical Sciences, Jiroft, Iran
[2] Student Research Committee, Kerman University of Medical Sciences, Kerman, Iran
[3] Department of Medicine, Jiroft University of Medical Sciences, Jiroft, Iran
[4] Department of Public Health, Jiroft University of Medical Sciences, Jiroft, Iran
[5] Department of Epidemiology and Biostatistics, School of Health, Zahedan University of Medical Sciences, Zahedan, Iran

A B S T R A C T

Background: Identifying effective factors in death caused by the infection of COVID-19 is one of the most worrisome issues in the globe. This study aims to investigate the frequency of risk factors leading to death in patients with COVID-19.

Methods: This was a retrospective descriptive study done on 150 confirmed cases of COVID-19 in Imam Khomeini Hospital in Jiroft in 2019. Patients were included in the study by census method. The required information was extracted and recorded in the researcher's checklist; which included demographic and social characteristics of patients (age, gender, smoking, and opium consumption), underlying disease,test results (leukopenia, leukocytosis, neutropenia, decrease in albumin, increase in creatinine, ALT, AST, LDH and CRP), and the RT-PCR test.,. The researchers analyzed data using independent sample *t*-test, and chi-square by SPSS-V22.

Results: The mean age of the patients was 72.19 ± 15.97. Most of those who died with COVID-19 were men. There was a statistically significant relationship between the use of drugs and the death of patients with COVID-19(P-value<0.05). The average body mass index (BMI) of the confirmed patients was 31.14 ± 7.08 kg/m2 in the overweight group (P-value<0.001). Moreover, there was a significant relationship between the risk factors CRP, ALB, AST, ALT, Cr, lym, Neut, WBC and inevitable death in patients with COVID-19(P-Value<0.001). Regarding underlying diseases, diabetes, lung, and kidney diseases have been observed in most terminal patients (P-value<0.001).

Conclusion: Old age, male gender, high BMI, blood pressure, increased factors of CRP, AST, ALT, Cr, lym, Neut, WBC, and decreased ALB are among the risk factors leading to death in COVID-19 patients.

Keywords: Risk Factor, Death, COVID-19, Hospitalization, Infection

Introduction

In December 2019, in Wuhan, China, doctors reported the occurrence of pneumonia with unknown origin in some patients, which scientists later identified as SARS-Cov-2(1). With the outbreak of COVID-19, many countries faced various health, economic, and challenges (2). Due to the high prevalence of this disease worldwide, on March 11, 2020, this disease was declared a pandemic by the World Health Organization (3). In Iran, the first case of infection was reported in Qom on February 29, 2019, and after a short time, it spread to other parts of the country (4). This virus has a higher transmission power than Sars and MERS, and its incubation period lasts between 2-14 days. This feature increases the spread of virus and makes it harder to prevent and control the wave of the disease (5). According to global statistics, the death rate of this disease was

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Corresponding Author: Salman Daneshi
Email: salmandaneshi008@gmail.com
Tel: +98 3443310916
Department of Public Health, Jiroft University of Medical Sciences, Jiroft, Iran

reported to be 3.4% (6), which was less than SARS (with a death rate of about 10%) and MERS (with a death rate of about 35%) (6). Symptoms and signs of infection with COVID-19 include feeling of boredom, fatigue, and body pain, fever, dry cough and shortness of breath, loss of sense of taste and smell. In more severe cases, the infection can lead to pneumonia, serious respiratory problems ,and eventually, death (7, 8).

The incidence and severity of disease and mortality are higher in some populations and the risk of disease is different (9).

According to the Center for Disease Control and Prevention (CDC), people with cardiovascular diseases are most susceptible to this virus, followed by people with diabetes, chronic respiratory diseases, high blood pressure, and cancer. Moreover, according to statistics, the risk of this virus increases with aging (10). The results of investigations have shown that COVID-19 virus was more dangerous for men (with a death rate of 2.8%) than women (with a death rate of 1.7%)(11). Examining laboratory parameters will be useful in determining acute or less severe cases of COVID-19, identifying patients at higher risk of mortality, and increasing awareness for proper performance in clinical condition (12). Recognizing risk factors as variables whose presence increases the probability of contracting a disease or death seems necessary to prevent health problems (illness, controlling the disease, and death). As a result, this study is done to i the frequency of risk factors influencing death in patients with COVID-19 admitted to Imam Khomeini Hospital, Jiroft in 2019.

Materials and Methods

This was a cross-sectional (descriptive-analytical) study performed through census method on 150 people who died due to COVID-19 in Imam Khomeini Hospital in Jiroft from April to the end of March 2019 . Data collection tool included a researcher-made checklist. The:following data which have already been recorded, were extracted and recorded in the checklist made by the researcher;demographic and social characteristics of people (including age, gender, smoking, and opium consumption), underlying diseases (history of diseases: heart disease, diabetes, high blood pressure, obesity (BMI higher than 30), asthma, chronic obstructive pulmonary disease, chronic kidney disease, chronic blood disease), test results (c-reactive protein, creatinine, aspartate transaminase, alanine aminotransferase), lymphocyte (lymphocyte), neutrophil (neutrophil), albumin (albumin), white blood cells count (white blood cells) and RT-PCR test.

In this study, definite cases refer to people whose RT-PCR tests are positive, and suspicious cases include patients whose PCR results were negative, but the laboratory results and symptoms of COVID-19 indicate.

The inclusion criteria for the study included all death cases of COVID-19 from April to the end of March 2019. Cases with incomplete files were excluded from the study.

Data were analyzed using SPSS-V22. Mean and standard deviation were used to describe quantitative variables, and frequency and percentage were used for qualitative data. To determine normality, the kolmogorov-smirnov test was conducted, which indicated that data were normal. Data were analyzed through independent sample t-test, and chi-square by SPSS software version 22 .The P-value for all the tests was considered less than 0.05.

Ethics approval

This study was approved by the Ethics Committee of Jiroft University of Medical Sciences with number IR.JMU.REC.1401.012. All the methods were performed in accordance with relevant guidelines and regulations.

Results

This study was conducted on 150 cases who died of COVID-19 in Imam Khomeini Hospital in Jiroft. 64 people (42.6 %) were women and 86 people (57.4 %) were men .There was a significant relationship between male gender and death from

COVID-19 (P-value<0.03). The average age of the patients was 72.19 ± 15.97 Out of 150 deaths, 9 people (6%) were in the age group of 20 to 35, 18 (12%), 35 to 50, 60 (40%), 50 to 80, and 63 people (42 percent) were above 80 . Statistically, there was a significant relationship between the age groups of deceased patients. (P-value<0.001) (Table 1).

The average BMI of terminal patients leading to death was 31.14 ± 7.08 kg/m2, 90 (60%) of whom were obese. Statistically, There was a significant relationship between these groups of body mass index of deceased patients (P-Value<0.001). 17

(11.3 %) of the deceased patients were smoking and 22 (14.7 %) of them were smoking opium. (P-Value<0.05). According to Table 2, there was a statistically significant relationship between laboratory indicators and death in patients with COVID-19(P-value<0.001). 48% of those who died of COVID-19 had high blood pressure, 43.3%, lung and kidney disease, and 35.3% suffered from diabetes. A significant statistical relationship was seen between death from COVID-19 and heart disease, lung disease, kidney disease, diabetes, prostate cancer, thyroid diseases, and Rheumatism (P-value<0.001) (Table 3).

Table 1. Frequency of risk factors leading to death in patients with COVID-19 based on demographic and social characteristics

Variables	Frequency	Percent	P-value
Sex			
Male	86	57.4	0.03
Female	64	42.6	
Age			
20-35	9	6	
35-50	18	12	< 0.001
50-80	60	40	
> 80	63	42	
BMI			
> 18.5	10	6.6	
18.5 – 24.9	27	18	< 0.001
25 – 29.9	23	15.4	
>30	90	60	
Smoking			
Yes	17	11.3	0.01
No	133	88.7	
Opium			
Yes	22	14.7	0.04
No	128	85.3	

Table 2. Frequency of risk factors leading to death in patients with COVID-19 regarding laboratory indicators

Variables	Mean	Standard deviation	Maximum	Minimum	P-value
WBC	10/49	9/31	55	2	
Neutrophils	80/73	11/48	95	10	
Lymphocytes	13/12	10/56	85	2	
Cr	1/83	1/07	5	1	< 0.001
ALT	84/17	164/7	1560	3	
AST	87/21	142/5	1550	10	
ALB	2/77	1/03	5	1	
CRP	75/81	54	392	1	

Table 3. Frequency of risk factors leading to death in patients with COVID-19 regarding underlying diseases

Variables	Yes		No		P-value
	Frequency	Percent	Frequency	Percent	
Heart disease	13	% 8/7	137	% 91/3	< 0.001
Lung disease	65	% 43/6	85	% 56/4	< 0.001
kidney disease	65	% 43/3	85	% 56/4	< 0.001
Blood pressure	72	% 48	78	% 52	0.629
Diabetes	53	35/3	97	% 64/7	< 0.001
Prostate cancer	11	% 7/3	139	% 92/7	< 0.001
Thyroid diseases	2	% 1/3	148	% 98/7	< 0.001
Rheumatism	3	% 2	147	% 98	< 0.001

Discussion

Most of those who died from COVID-19 were over 80 years old. Based on systematic reviews and meta-analysis studies by Dessie and Zewotir, the risk of death from COVID-19 increased with age, one of the main risk factors (13) addressed in the study conducted by Grasselli et al. in (14). According to a study performed by Caramelo et al. (15)in China, aging was associated with a higher risk of mortality due to COVID-19, which was consistent with the results of this study. Considering that older people are more likely to suffer from chronic diseases than younger ones, higher death rate caused by COVID-19 in older people is inevitable.

Most of the deceased infected with COVID-19 were men in this study. Gender was known as one of the risk factors of death from COVID-19, indicated by most studies. For example, in the study by WU et al.(16) in the United States, the highest mortality rate was reported in elderly men with underlying disease . According to the results of Caramelo et al.'s(15) research in China and WU et al.'s(16) project, death from COVID-19 was reported to be more in men than in women. Gholmani et al.(2) revealed one of the risk factors related to the mortality of patients with COVID-19. According to the results of a systematic review and meta-analysis, a significant relationship was observed between mortality rate of COVID-19 and gender, with males being more at risk(13). Probably, the reason for the increase of death rate in men compared to women is more consumption of tobacco and the subsequent increase of underlying diseases in men.

There was a significant relationship between the consumption of opium and cigarettes and the death of patients with COVID-19. COVID-19 Patients with a history of smoking were twice at risk of death compared to other patients (17). The results of a systematic review and meta-analysis showed that smoking was significantly associated with the risk of mortality in patients with COVID-19 (13). Karanasos et al.'s(18) research showed that smoking affected the severity of illness and mortality of hospitalized COVID-19 patients, especially with regard to younger patients . There can be interventions for smoking and opium for better controlling of COVID-19 pandemic and reducing the death rate.

Most of the dead cases were obese; in a systematic review, researchers found that obesity was one of the main factors associated with the necessity of hospitalization and death from COVID-19, and in most studies, it was revealed out that people with a high BMIwere at a higher risk of death(9). In a structured review conducted by Wolf, high BMI was considered a risk factor in COVID-19 patients (19). Obesity is one of the risk factors which can be corrected by providing proper training for diet modification and increasing physical activity.

According to the results of the present study, high blood pressure, diabetes, lung and kidney diseases have been observed in most of terminal patients. According to the report by CDC, the risk of contracting COVID-19 and becoming a serious case was higher in patients with chronic diseases such as hypertension, lung disease, kidney

problems, diabetes, and heart disease compared with healthy people.

According to Caramelo's study in China, cardiovascular and chronic respiratory problems were the most dangerous underlying diseases related to COVID-19(15). In the study done by Zali et al.(20) in Tehran, mortality rate was higher in diabetes , heart (38.46%), and lung patients (35.79%) . Risk factors related to mortality in patients with COVID-19 in the intensive care unit in Italy also introduced discussed diseases such as diabetes, heart disease, kidney disease, lung disease and hypercholesterolemia(14). Jalali et al.(21) analyzed the data from 28981 patients with COVID-19 from 1034 hospitals in Iran and related heart disease, asthma, chronic obstructive pulmonary disorder, chronic kidney disease, cancer and chronic liver problem with death in patients with COVID-19.

The results of this study presented that the average risk factors of CRP, AST, ALT, Cr and WBC in the studied cases were more than normal. According to the study by Chen et al. (22) among 99 infected patients in Wuhan, an increase in the serum level of ALT and AST was reported in 53 people (53.4%), and a decrease in lymphocytes and an increase in AST were risk factors in patients with COVID-19. Moreover, there was a significant relationship between these blood factors and death. In a group of 1099 patients with COVID-19 in China, 59.4% of people had an AST of over 40 U/L, and 58.1% had an ALT of over 40 U/L; most of these cases were reported in deceased patients with increased creatinine, bilirubin and LDH ; 63% of them had lymphocytes levels below normal (23). In a diferent study on 32 patients, the average level of ALT and AST was significantly higher in severe patients than in the control group(24) In addition, Cai et al.'s(25) project, among 298 chinese patients with COVID-19, suggested that the percentage of liver damage among the deceasedpatientswas significantly higher than that of the living ones ., Zhu et al(26) concluded that WBC count was within the normal range at the time of admission to hospital, but those with higher

WBC faced a much higher chance of death; their results also showed that there was a significant relationship between WBC count and death. The average CRP of the study was 75.81 ± 54; increase in CRP indicated the systemic release of cytokines and th increase in CRP > 41 indicated the worsening of the disease(23). Liu et al.(27) conducted a research with the aim of describing clinical manifestations and characteristics of CT scan and laboratory results of COVID-19 disease regarding 15 pregnant women. the most common abnormal finding was a decrease in blood lymphocytes (12.15 patients) and an increase in CRP (10.15). AST and ALT levels in this study were more than 40, which were regarded abnormal. Based on the results of Li et al.'s(25) study, from 417 patients with COVID-19, 76 % showed liver test abnormalities and 21.5 % showed liver damage.

According to the current research, a decrease in the level of lymphocytes was found in patients. In a study conducted on 799 patients in China, a significant decrease in the total number of lymphocytes indicated that COVID-19 affects immune cells which inhibits the function of the cellular immune system(16). A cohort study on 201 patients showed that the disease may have a major effect on lymphocytes, as the virus spreads and invades respiratory mucosa, resulting in a series of immune responses; this causes a cytokine storm inside the body; which changes immune components such as peripheral blood leukocytes and lymphocytes(28) . This study had some limitations, including incompleteness of the files of the deceased patients, and because the study group was no longer alive, for access ; the incomplete cases were, therefore, excluded from the study.

Conclusion

According to the results of this study, aging, being male, high BMI, underlying diseases such as heart disease, increase in laboratory indicators of CRP, AST, ALT, Cr, and WBC, and decrease in lym are risk factors leading to death in patients suffering from COVID-19 admitted to Imam Khomeini Hospital in Jiroft in 2019.

For more clarity, it is necessary to expand the scope of the study from a single center to the investigation of several referral centers; thus, by examining the number of patients, the dimensions of the subject can be better analyzed and interpreted. It seems that it is necessary to investigate and evaluate mortality rate during the pandemic and the subsequent peaks.

Acknowledgments

Conflict of interests

The authors declared no conflict of interests.

Authors' contributions

Daneshi S, Goroei Sardu E, and Rezabeigi Davarani F designed research; Tashakori S and Faryabi A conducted research; Daneshi S analyzed data; and Kermani B, Kargar S, Faryabi A and Tashakori S wrote the paper. Daneshi S had primary responsibility for final content. All authors read and approved the final manuscript.

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