

Symptoms and underlying diseases associated with the hospitalization period of 3,480 Covid-19 patients in Hormozgan, Iran

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Objectives

COVID-19 has a relationship with patients' demographic characteristics as well as their underlying diseases. This research has been conducted to evaluate factors' effect on Covid-19 patient's hospitalization rate and period in Hormozgan, Iran.

Methods

The inclusion criteria of this retrospective study included all patients diagnosed as COVID-19 patients after PCR who were referred to Covid-19 hospitals from February 2020 to June 2020 in Hormozgan province (3480 patients). The checklist was designed according to COVID-19 guidelines and approved by the World Health Organization and Iran Ministry of Health and Medical Education. These data were analyzed using descriptive (average-standard deviation-percentage) and analytical (including Chi-square, t-test, and regression tests) statistics with SPSS Ver.23 software.

Results

In this study, 1852 male patients (53.20%) with a median age of 43.11 ± 21.72 and 1628 female patients (46.80%) with a median age of 44.86 ± 22.40 . The median age of men was significantly lower than the women's median age ($P = 0.02$). The hospital stay length of male and female patients was reported 2.64 ± 4.14 and 2.76 ± 4.297 ; the death rate of patients in our study was 6.6%.

Conclusions

The results of this study showed that the hospital stay length of HIV-positive patients and patients with cardiovascular and pulmonary diseases is much longer than other people, which imposes many human and financial costs on the country's health care system. These results can improve health care system planning and improve medical services presented to covid-19 patients.

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INTRODUCTION

In late December 2019, a strange case of pneumonia was reported in Wuhan with similar clinical symptoms to viral pneumonia.¹ The WHO introduced the virus as COVID-19. This virus is from the beta-corona genera with different potential hosts.²⁻⁴ Coronaviruses are single-stranded, enveloped RNA viruses with 120-180 nm diameter. Before the COVID-19, there were only six coronaviruses that could infect humans. Among coronaviruses, four strains, including OC43, 229E, HKU1, and NL63, have less pathogenicity and cause mild respiratory illness. Strains that are SARS-CoV and MERS-CoV have caused two fatal epidemics. The homology and pathogenesis mechanism of COVID-19 is very similar to the SARS-CoV pathogenesis mechanism.^{5,6} Based on recent studies, there is a correlation between COVID-19 and demographic characteristics. The highest mortality rate is related to elderly men at the age of 65 years or older⁷ with underlying diseases such as diabetes, high blood pressure, chronic respiratory disease, cancer, high interleukin-6 level, or a history of previous surgery. The cellular immune system function- an important immune system feature against viral infections- decreases in the elderly.^{2,8-11} The most common clinical symptoms of COVID-19 infection are fever (87.9%), cough (67.7%), fatigue (38.1%), vomiting (5%) and diarrhea (3.7%).¹² Also, confusion, forgetfulness, olfactory dysfunction, neuropathic pain, seizure, and stroke are among the neurological symptoms of this virus that result in hypoxia and inflammation of the brain. Brain inflammation can be indirectly caused by a cytokine storm (autoimmune encephalitis) or directly caused by a broken blood-brain barrier by a virus (viral encephalitis).^{13,14} Besides, Acute Respiratory Distress Syndrome (ARDS) occurs around 90 days after infection. The virus also damages other tissues, including the heart, kidneys, liver, eyes, and nervous systems.¹² A healthy lifestyle, including exercise, good nutrition, a balanced weight, and non-smoking, contributes to a balanced immune system and Covid-19 prevention. Based on recent findings, the most prominent reason for the morbidity and mortality rate caused by Covid-19 in the US is overweight.^{15,16} Also, personal hygiene, using the face mask, adequate rest, and proper ventilation are effective ways to prevent infection.² Disease occurrence depends on the interaction between the virus and the immune system. Virus-related factors also include the type of virus, mutation, and the number of viruses. Genetics (e.g., HLA gene), age, gender, nutritional status, homeostasis between the immune, nervous and endocrine systems, and physical condition affect a person's immune system. These factors contribute to an individual's infection, the duration and severity, and the recurrence of the disease. Since the exact mechanism of transmission of the disease is not fully understood, and vaccines do not make permanent protection, the most important task now is to interrupt the chain of transmission.¹⁶ People with

chronic disease with Covid have 19 more severe symptoms and are more likely to be admitted to the intensive care unit than people without chronic illness.¹⁷

Therefore, special attention is paid to patients with underlying diseases. This study aimed to identify the underlying diseases and investigate the relationship between these diseases and the length of hospitalization in patients with Covid-19 in 1399 in Bandar Abbas.

MATERIALS AND METHODS

This study was conducted from January 21, 2020, to May 30, 2020, in Hormozgan province (Hormozgan province is one of the 31 provinces of Iran, which is in the south of the country and the capital of the province is the city of Bandar Abbas), Iran (the Islamic Republic of Iran is a country in West Asia and Tehran is also its capital) to analyze the Hospital length of stay) LOS of COVID-19 patients. The research participants of this study were all patients referred to hospitals in Hormozgan province with a diagnosis of COVID-19 based on a PCR test.

Inclusion criteria were patients diagnosed with COVID-19 after a Real-time PCR test. Exclusion criteria were patients who did not consent to participate in this study or had incomplete or distorted information. Based on these inclusion and exclusion criteria, 3480 patients were included in the study.

Patients' data has been collected through the interview by MCMC (Medical care monitoring center) personnel in the hospitals after completing the consent form and observing ethical principles. The checklist used to collect information has been designed according to Iran national COVID-19 guidelines and approved by the Iran Ministry of Health and Medical Education and the World Health Organization. The studied variables were gender, age, patients' resident place, history of smoking and drug use, pregnancy, referral type to the hospital (by or without an ambulance), history of contact with COVID-19 patients, early symptoms (including cough, muscular pain, level of consciousness, respiratory, olfactory and taste dysfunction, seizure, headache, dizziness, paresis and limb palsy, chest pain, inflammation, and skin lesions, stomach ache, nausea, vomiting, diarrhea, and anorexia), intubation, Po2 level, history of cancer, chronic liver diseases, diabetes, chronic blood diseases, HIV/AIDS, acquired or congenital immunodeficiency, cardiovascular diseases, chronic kidney diseases and dialysis status, asthma and other chronic lung diseases and chronic neurological disorders. Multinomial logistic regression was used with hospitalization less than one day as the reference group; the baseline model included Cancer, Liver disease, Diabetes, High blood pressure, HIV positive, Immune system defects,

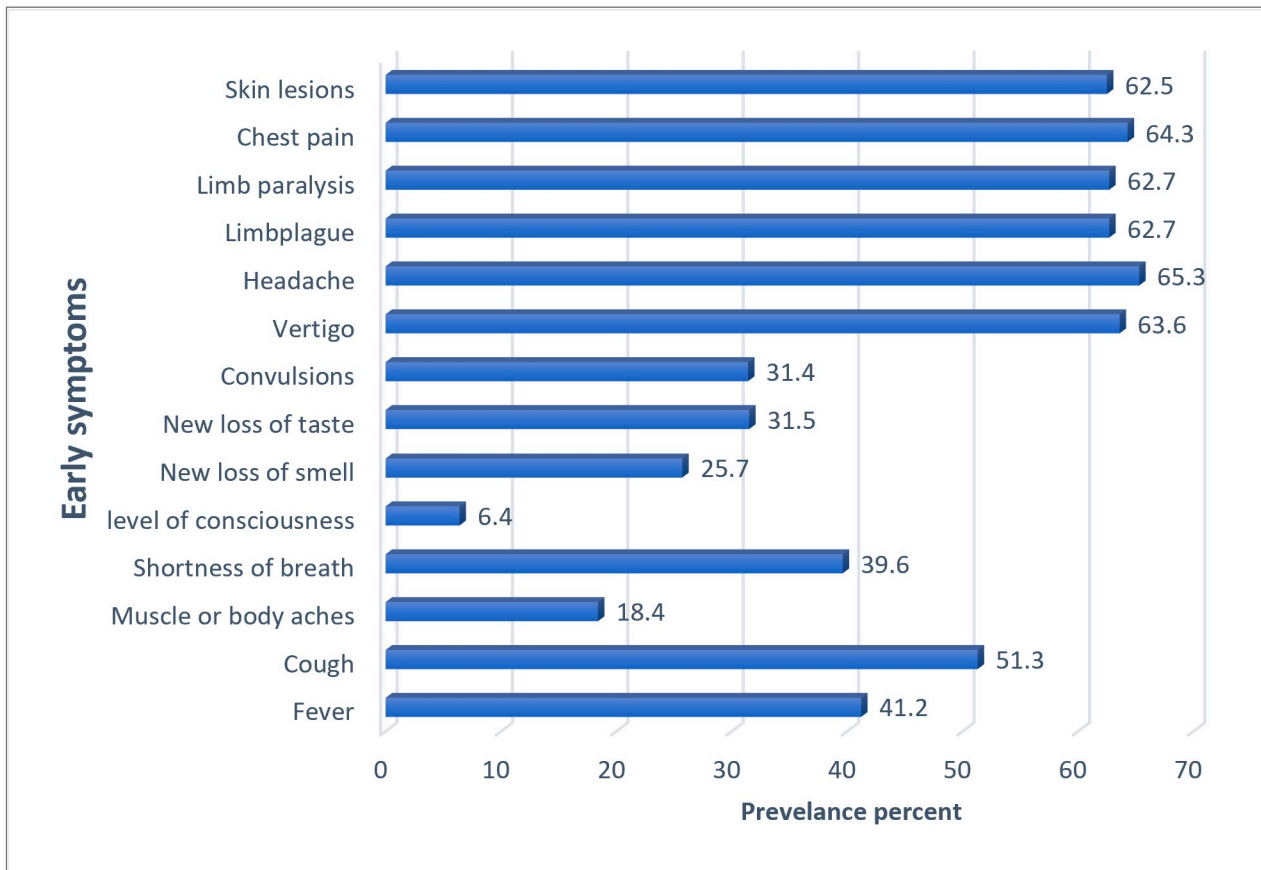


Figure 1 Early symptoms of patients referred to Hormozgan province hospitals

Cardiovascular disease, Pregnancy, kidney disease, Asthma, Lung Disease, Nervous disease.

These data were entered into SPSS V.23 software and analyzed using descriptive (average - standard deviation - percentage) and analytical (including Chi-square, t-test, and regression tests) tests.

RESULTS

In this study, 3480 patients referred to hospitals in Hormozgan province with COVID-19 diagnosis have been evaluated. This number includes 1852 male patients (53.20%) with a median age of 43.11 ± 21.72 and 1628 female patients (46.80%) with a median age

of 44.86 ± 22.40 . The median age of men was lower than women significantly ($p=0.02$). The hospital LOS of male and female patients has been reported 2.64 ± 4.14 and 2.76 ± 4.297 , respectively, without a statistically significant relationship between the hospital LOS between different genders

According to Figure 1, the most prevalent early symptoms in patients were headache (65.3%), chest pain (64.3%), and dizziness (63.6%).

After examining the patients' gastrointestinal symptoms, it was found that the most common symptoms were vomiting (55.7%) and diarrhea (55.6%). Gastrointestinal symptoms are shown in Figure 2.

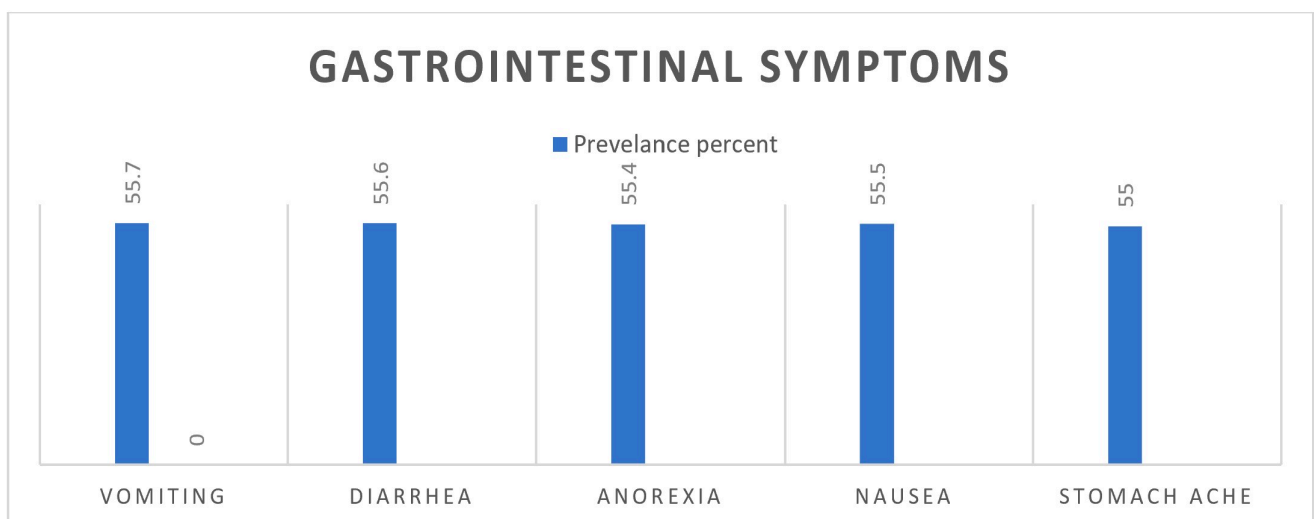


Figure 2 Gastrointestinal symptoms of patients referred to Hormozgan province

Table 1 shows the distribution of the variables between men and women. The mean age in men is lower than women and is statistically significant ($p=0.020$). Liver disease, diabetes, hypertension, cardiovascular disease, and asthma are different between men and women and are statistically significant. ($p<0.05$ for all). The hospital LOS, cancer, HIV positive, immune deficiency, kidney, lung, and nervous system diseases showed no significant difference between men and women. Statistically, they were not significant ($p>0.05$ for all).

Table 2 Regression model with time response variable based on hospitalization time grouping (according to the schedule less than one day - one day to the end of 7 days (week) - 8 days to the end of 30 days (one

month) - more than 30 days (More) more than a month) has been done with independent variables showed that, diabetic Covid-19 patients have a higher risk of prolonging hospitalization to one-seven days range (OR = 1.445, CI95% = 1.113-1.876, P = 0.006). In addition, Pregnancy increased hospital LOS in Covid-19 patients to one-seven days range (OR = 2.187, 95% CI = 1.245-3.842, P = 0.006). Covid-19 infected patients with cardiovascular disease had more risk of prolonging hospitalization to eight to 30 days range. (OR = 1.581, 95% CI = 1.073-2.331, P = 0.021). Also, our study showed that Covid-19 patients with kidney disease have more risk of prolonging hospitalization to eight to 30 days range. (OR = 2.889, 95% CI = 1.535-5.435, P = 0.001). Besides, cancer can increase the

Table 1 Percentage number of patients with their respective CURB-65 score

Variable	Category/Scale	Male 1852 (%53.20) Mean ± SD or N (%)	Female 1628 (%46.80) Mean ± SD or N (%)	p-value*
Age	Years	43.11±21.72	44.86±22.40	0.020
Duration of hospitalization	Day	2.64±4.14	2.76±4.297	0.356
Cancer	Yes	34(%1.80)	33(%2.00)	0.682
	No	1818(%98.20)	1595(%98.00)	
Liver disease	Yes	21(%1.10)	4(%0.20)	0.002
	No	1831(%98.90)	1624(%99.80)	
Diabetes	Yes	125(%6.70)	171(%10.50)	<0.001
	No	1727(%93.30)	1457(%89.50)	
High blood pressure	Yes	19(%1.00)	45(%2.80)	<0.001
	No	1833(%99.00)	1583(%97.20)	
HIV positive	Yes	1(%0.10)	1(%0.10)	0.927
	No	1851(%99.90)	1627(%99.99)	
Immune system defects	Yes	4(%0.20)	7(%0.40)	0.262
	No	1848(%99.80)	1621(%99.60)	
Cardiovascular disease	Yes	187(%10.10)	204(%12.50)	0.023
	No	1665(%89.90)	1424(%87.50)	
Kidney disease	Yes	50(%2.70)	40(%2.50)	0.653
	No	1802(%97.50)	1588(%97.50)	
Asthma	Yes	70(%3.80)	98(%6.00)	0.002
	No	1782(%96.20)	1530(%94.00)	
Lung disease	Yes	52(%2.80)	39(%2.40)	0.447
	No	1800(%97.20)	1589(%97.60)	
Nervous system disease	Yes	21(%1.10)	21(%1.30)	0.674
	No	1831(%98.90)	1607(98.70)	

*p-values have been calculated based on Chi-Square or independent samples t-test.

Table 2

Factors related to the length of hospitalization period of COVID-19 patients

Hospitalization period Variable	1-7			8-30			30+		
	OR*	95% CI	P-value	OR*	95% CI	P-value	OR*	95% CI	P-value
Cancer									
No	Ref		1.00	Ref	-	1.00	Ref	-	1.00
Yes	0.88	0.52 - 1.51	0.65	1.507	0.67 - 3.418	0.33	26.48	7.69 - 91.19	<0.001
Liver disease									
No	Ref		1.000	Ref	-	1.00	Ref	-	1.00
Yes	2.08	0.88 - 4.92	0.096	0.154	0.003 - 7.86	0.35	0.54	0.00 - 145.3	0.88
Diabetes									
No	Ref		1.00	Ref	-	1.00	Ref	-	1.00
Yes	1.45	1.11 - 1.88	0.006	1.223	0.77 - 1.96	0.40	0.25	0.013 - 4.79	0.38
High blood pressure									
No	Ref	-	1.00	Ref	-	1.00	Ref	-	1.00
Yes	0.80	0.47 - 1.37	0.41	1.602	0.72 - 3.55	0.25	0.28	0.00 - 189.7	0.70
HIV positive									
No	Ref	-	1.00	Ref	-	1.00	Ref	-	1.00
Yes	160	0.00 - 0.001	1.00	1141.584	0.00 - 0.001	1.00	3.14	3.13 - 3.13	<0.001
Immune system defects									
No	Ref	-	1.00	Ref	-	1.00	Ref	-	1.00
Yes	0.44	0.10 - 1.87	0.27	1.091	0.16 - 7.49	0.93	0.25	1.44 - 434.8	0.78
Pregnancy									
No	Ref	-	1.00	Ref	-	1.00	Ref	-	1.00
Yes	2.19	1.25 - 3.84	0.006	1.457	0.49 - 4.33	0.50	0.31	1.78 - 547.4	0.85
Cardiovascular disease									
No	Ref	-	1.00	Ref	-	1.00	Ref	-	1.00
Yes	1.17	0.93 - 1.48	0.18	1.581	1.07 - 2.33	0.021	5.54	1.83 - 16.75	0.002
kidney disease									
No	Ref	-	1.00	Ref	-	1.00	Ref	-	1.00
Yes	1.29	0.80 - 2.07	0.29	2.889	1.53 - 5.44	0.001	0.32	0.002-42.4	0.65
Asthma									
No	Ref	-	1.00	Ref	-	1.00	Ref	-	1.00
Yes	0.94	0.68 - 1.30	0.70	0.76	0.39 - 1.48	0.41	0.27	0.005 - 15.7	0.53
Lung disease									
No	Ref	-	1.00	Ref	-	1.00	Ref	-	1.00
Yes	1.044	0.67 - 1.62	0.85	0.55	0.19 - 1.56	0.26	8.82	2.12 - 36.67	0.003
Nervous disease									
No	Ref	-	1.00	Ref	-	1.00	Ref	-	1.00
Yes	1.141	0.61 - 2.15	0.69	0.97	0.28 - 3.32	0.96	0.25	3.07 - 198.7	0.81

* Multinomial logistic regression was used with Hospitalization less than one day as the reference group; the baseline model included Cancer, Liver disease, Diabetes, High blood pressure, HIV positive, Immune system defects, Cardiovascular disease, Pregnancy, kidney disease, Asthma, Lung Disease, Nervous disease

hospitalization period in Covid-19 patients to more than 30 days. (OR = 26.475, 95% CI = 7.687-91.185, p

<0.001). Concurrent HIV and Covid-19 infection increases risk of hospitalization to more than 30 days (OR = 3.136, 95% CI = 3.136-3.136, p <0.001). Compared to patients with less than one day of hospitalization and more than 30 days of hospitalization, people with cardiovascular disease have more risk of prolonging hospitalization. Concurrent lung disease and Covid-19 infection increases the risk of hospitalization to more than 30 days (OR=5.542, 95%CI=1.834-16.746, p=0.002).

DISCUSSION

The Covid-19 disease severity depends on the interaction between the virus and the immune system. Virus-related factors include mutations and the number of viruses exposed. An individual's immune system is also affected by genetics (e.g., HLA gene), age, gender, nutritional status, homeostasis in the immune system, nervous system, endocrine system, and physical condition. These factors contribute to an increased risk of an individual's infection, duration, severity, and recurrence of the disease. Due to the increasing need for covid-19 clinical areas¹⁸, this study was conducted in the Hormozgan province to analyze factors affecting the COVID-19 patients' hospital LOS.

The results of the study showed that the most common early symptoms of the disease include headache, dizziness, sore throat, and cough, which are consistent with other studies.

The most common symptoms of this disease, which have been reported in several articles, are fever higher than 38 degrees (78%), cough (76%), fatigue and muscle pain (44%), shortness of breath (55%), headache (8%), bleeding (5%), and diarrhea (3%).^{14, 19-21}

The results of the study showed that among the gastrointestinal symptoms of patients, vomiting and then diarrhea are the most common symptoms among patients. And these symptoms usually appear after the initial symptoms of the disease and are consistent with the results of other studies. In a study conducted by Erika et al., ten patients infected with COVID-19 presented gastrointestinal symptoms such as abdominal pain, nausea, and vomiting. The results indicated that nine of the patients had mild respiratory symptoms and fever before hospital admission.²² In recent studies, fever and respiratory distress prevalence in Covid-19 patients reported 80.2% and 23.4%, respectively.²³ SARS-CoV-2 can also cause gastrointestinal symptoms such as vomiting, diarrhea, or abdominal pain in the early stages of the disease. Intestinal dysfunction causes changes in intestinal microbes and an increase in inflammatory cytokines.²⁴

The present study shows that the relationship between the length of hospitalization of patients with Covid-19 is from high to low, respectively: lung disease, cancer, AIDS, kidney, heart, diabetes, and then pregnancy are at higher risk for long-term hospitalization. Prolonged hospitalization, in

addition to mental and physical problems, increases the cost to the patient and the community and the government and is an important problem. The results were consistent with other studies conducted in the world, but no study on this subject was found in Iran.

The study Semenzato, et al showed that with age, the risk of Hospitalization for COVID-19 increased more than fivefold. Almost all chronic diseases were associated with an increased risk of COVID-19-associated hospitalization and in-hospital mortality.²⁵

A study by Villapol, et al showed that the severity of COVID-19 is usually combined with a set of comorbidities such as hypertension, diabetes, obesity and / or old age that seriously aggravate the consequences of infection.²⁴ The study Petrilli, et al. Showed that age, heart problems and obesity were the main reasons for the prolongation of Hospitalization in Covid 19 patients.²⁶ This results also indicate importance of screening of covid-19 patients with underlying diseases to manage covid-19 pandemic and improve health status of society which is in line with Ardaneh et al. study.²⁷

CONCLUSION

The death rate of patients in our study was 6.6%. Although Hormozgan province was categorized in the red zone in COVID-19 spread during this study but had a clearance rate of 96.4%, all of which were in good general condition. This shows the acceptable and valuable performance of health services personnel in this province. This study also showed that the hospital LOS of HIV-positive patients and patients with cardiovascular and pulmonary diseases is much longer than other people, which imposes many human and financial costs on the country's health care system. Therefore, to maintain individual health and help improve the critical condition of the virus, it is better to develop and apply stricter protocols to prevent further outbreaks of the disease and check underlying diseases of people suspected to have Covid-19. These results can improve health care system planning and improve medical services presented to covid-19 patients.

ETHICAL CONSIDERATIONS

The authors declare that the investigations were carried out following the rules of the Declaration of Helsinki of 1975. The ethics committee approved the study protocol of Hormozgan University of Medical Sciences with IR.HUMS.REC.1400.029 code.

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SUMMARY BOX

What is already known about this subject:

- Based on recent studies, there is a correlation between COVID-19 and demographic characteristics. The highest mortality rate is related to elderly men at 65 years or older with underlying diseases such as diabetes, high blood pressure, chronic respiratory disease, cancer, high interleukin-6 level, or a history of previous surgery.
- The most common clinical symptoms of COVID-19 infection are Fever (87.9%), cough (67.7%), fatigue (38.1%). Vomiting (5%) and diarrhea (3.7%).
- Disease occurrence depends on the interaction between the virus and the immune system. Virus-related factors also include the type of virus, mutation, and the number of viruses. Genetics (e.g., HLA gene), age, gender, nutritional status, homeostasis between the immune, nervous and endocrine systems, and physical condition affect a person's immune system. These factors contribute to an individual's infection, the duration and severity, and the recurrence of the disease.

What are the new findings:

- The death rate of patients in our study was 6.6%.
- The results of this study also showed that the hospital LOS of HIV-positive patients and patients with cardiovascular and pulmonary diseases is much longer than other people, which imposes many human and financial costs on the country's health care system.
- The results of the study showed that gastrointestinal symptoms such as vomiting (55.7%), diarrhea (55.6%), nausea (55.5%), and abdominal pain (55%) are the most common gastrointestinal symptoms among patients

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