

## COVID-19

# Epidemiological characteristics and outcomes of COVID-19 in asymptomatic versus symptomatic patients

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## Keywords:

COVID-19 • Asymptomatic infection • Patients with clinical symptoms

## Summary

**Background.** *The clinical manifestations of COVID-19 are different, which can be attributed to asymptomatic carriers, acute respiratory disease and pneumonia with different severities. The aim of this study was to compare the epidemiological characteristics and outcomes of COVID-19 in patients with clinical symptoms versus asymptomatic patients.*

**Methods.** *In this retrospective cohort study, the epidemiological characteristics of two groups of patients, with clinical symptoms (n = 38,630) and without clinical symptoms who were definitive cases of COVID-19 (n = 2,327) were investigated in the southwestern of Iran. Chi-square test was used to evaluate the differences between qualitative variables in the two study groups.*

**Results.** *Of 40,957 patients with COVID-19, 2,327 (5.68%) were asymptomatic, of whom 1391 (59.77%) were males, 1841 patients (79.11%) had a history of contact with definite or suspected cases of COVID-19. Asymptomatic patients were older than symptomatic cases. Patients with clinical symptoms had higher mortality rate than asymptomatic patients (2.68% in symptomatic patients vs 0% in asymptomatic patients).*

**Conclusion.** *According to the results of our study, the detected viral load in asymptomatic individuals was similar to that of symptomatic patients, indicating that asymptomatic infections can potentially transmit the disease. Therefore, screening and detection of asymptomatic cases is an important and key measure in prevention and early control of COVID-19 worldwide.*

## Introduction

Coronaviruses are a large family of viruses that may cause respiratory infections ranging from colds to more severe conditions, such as MERS and SARS [1]. A type of the virus called coronavirus 2019 also known as COVID-19 has spread rapidly around the world, and has been declared as pandemic by the world health organization [2-5].

In late December 2019, a series of unexplained cases of pneumonia were reported in Wuhan, China, and the government and health researchers in China took swift measures to control the epidemic and began etiological research. On January 12, 2020, the World Health Organization (WHO) temporarily named the new virus the novel coronavirus 2019 (2019-nCoV). On January 30, 2020, the WHO declared the 2019-nCoV outbreak as a public health emergency of international concern. On February 11, 2020, the WHO officially named the disease caused by the 2019-nCoV as coronavirus disease 2019 (COVID-19) [6-9].

On February 23, 2020, 77,041 cases of COVID-19 infection were confirmed in China [10]. To date, COVID-19 has affected people in all countries/regions and has become a global threat to the general

population [11]. COVID-19 has also spread rapidly in Iran and threatened the mental and physical health of Iranian people [12]. Recent clinical observations have shown that patient's age, male gender, and certain and chronic medical conditions, such as diabetes, cardiovascular disease, and chronic obstructive pulmonary disease appeared to increase the risk of COVID-19 infection as well as the severity of the disease [2].

The clinical manifestations of COVID-19 are significantly different, which can be due to asymptomatic carriers, acute respiratory disease and pneumonia with various degrees of severity [13]. As the COVID-19 has become pandemic, more evidence has emerged that many COVID-19 infections are asymptomatic while can still transmit the virus to the others [14]. In addition, there is growing evidence that asymptomatic cases may accelerate the spread of SARS-COV-2 from person to person [13]. Asymptomatic patients with COVID-19 are those who carry the virus but display no symptoms, including fever, gastrointestinal or respiratory symptoms, and reported no magnificent radiograph abnormalities in laboratory chest radiographs [15].

Identification and isolation of asymptomatic carriers and patients with mild COVID-19 is very important in preventing the disease spread in the later stages.

Therefore, we carried out this study to determine the prevalence of asymptomatic cases of COVID-19 and symptoms of patients with mild COVID-19.

## Methods

### STUDY DESIGN AND DATA COLLECTION

This retrospective cohort study examined 40,957 patients with COVID-19 who were admitted to hospitals under the auspices of Abadan University of Medical Sciences in the southwest of Khuzestan province. The total population of this region regarding the annual growth, was estimated 627,970 using the databases of the health centers and the national census in 2020.

All COVID-19 patients who were hospitalized from February, 2020 to February, 2021 were recruited into this study. Confirmation of the definite COVID-19 infection was done by real-time polymerase chain reaction (RT-PCR) using nasal and throat swab samples or CT scan imaging. Duplicate items have been identified and excluded based on the national identity code. Subjects were divided into two groups: patients with clinical symptoms ( $n = 38,630$ ) and patients without clinical symptoms ( $n = 2,327$ ). Patients without clinical symptoms were identified and selected through the screening plan performed on office personnel, people who tended to settle in/out the country, people with a history of contact with positive cases, people who referred to health centers, the elderly, people who were referred for surgery and pregnant women. Then, demographic characteristics and other comorbidities were compared between the two groups of symptomatic patients and asymptomatic patients. The variables used in this study include: age, gender, occupation, final outcome (e.g. death and recovery), comorbid diseases, such as diabetes, cardiovascular disease, kidney disease, liver disease, immune deficiency and chronic lung disease and thyroid disease, history of contact with infected cases and ICU stay.

### STATISTICAL ANALYSIS

Quantitative variables were descriptively expressed as median and qualitative variables as percentage and frequency. Chi-square test and Fisher's exact test were also used to evaluate the differences between qualitative variables in the two study groups. A significance level of 0.05 was considered as statistically significant. Data analysis was performed using SPSS software 20.0 and Excel 2010.

## Results

During the study period, a total of 40957 new cases of COVID-19 occurred in the cities under the auspices of Abadan University of Medical Sciences. The median age of patients was 45.73 years (IQR 29-50), and 57.4% of subjects were males, of whom 2,327 (5.68%) were asymptomatic, and 1391 (59.77%) of the participants

were males, 1841 patients (79.11%) had a history of contact with definite or suspected cases of COVID-19. Also, 2.53% of all COVID-19 patients ( $n = 1,038$ ) died, none of whom were asymptomatic (Table I).

Asymptomatic patients were older than symptomatic cases. The median age of asymptomatic and symptomatic patients was 51.70 years (IQR: 29-52) and 45.37 years (IQR: 29-50), respectively. However, this difference was not statistically significant ( $p = 0.537$ ). In both groups of patients, symptomatic and asymptomatic, the disease was more prevalent in age group of 20-34 years (34.60% of patients with symptoms and 34.90% of patients without symptoms) and the lowest frequency in both groups was observed in patients aged  $< 5$  years (0.80% of symptomatic and 0.70% of asymptomatic patients). Besides, comorbidities, such as heart disease, diabetes, hypertension, chronic lung and kidney disease, liver disease, thyroid and immunodeficiency, and occupation, ICU stay and history of contact with definite or suspected cases of COVID-19 were not significantly different between the study groups (Tab. I). Patients with clinical symptoms had also higher mortality rate than asymptomatic patients (2.68% in symptomatic patients vs 0% in asymptomatic patients).

## Discussion

The present study, was a retrospective observational study that examined the epidemiological characteristics of asymptomatic patients with COVID-19 compared with symptomatic patients. Of 40957 cases of COVID-19 in the cities under the auspices of Abadan University of Medical Sciences, 2327 (5.68%) were asymptomatic, and 1391 subjects (59.77%) were asymptomatic males. Also, 2.53% of the patients (1038) died, none of whom were asymptomatic.

In addition, comorbidities, such as heart disease, diabetes, hypertension, chronic lung and kidney disease, liver disease, thyroid and immunodeficiency, and occupation, ICU stay and history of contact with definite or suspected cases of COVID-19 were not significantly different between the study groups. Patients with symptoms displayed higher mortality rate than asymptomatic patients (2.68% in symptomatic patients vs 0% in asymptomatic patients).

In our study, 5.68% of patients were asymptomatic. A wide range of proportion of asymptomatic patients has been reported in various studies. For example, Kimball and colleagues reported the prevalence of asymptomatic patients as 34.8% [16], Kim and colleagues investigated 72314 patients in China and reported this proportion as 1% [17], Lai and colleagues as 1.95% [11], Bai et al. as 12.9% [18], Tong and colleagues as 51.7% [19], Wei and colleagues as 4.12% [20]. Liu and colleagues as 15.8% [15], Qian and colleagues as 43% [21], Luo and colleagues as 65.9% [22], Mizumoto et al. as 87.9% [23], Zou and colleagues as 56.5% [24], and Gao reported this prevalence as 1.6% in China [14], 30.8% in Japan [25], and 10.7% in Korea [26]. Each person may display

Tab. I. Demographic and Clinical Characteristics of asymptomatic and symptomatic patients with COVID-19.

Variable Number (%)		Total (n = 40957)	Asymptomatic patients (n = 2327)	symptomatic patients (n = 38630)	P-value
		Number (%)	Number (%)		
Age, median (IQR)		45.73(29-50)	51.70 (29-52)	45.37 (29-50)	0.570
Gender	Male	23521 (57.42)	1391 (59.77)	22130 (57.28)	0.018
	Female	17436 (42.58)	936 (40.23)	16500 (42.78)	
Occupation	Worker	831 (2.02)	41 (1.76)	790 (2.04)	0.404
	Healthcare worker	2692 (6.57)	177 (7.60)	2515 (6.51)	
	Employee	7263 (17.73)	428 (18.39)	6835 (17.69)	
	Freelance job	6154 (15.02)	407 (17.49)	5747 (14.87)	
	Student	1736 (4.23)	91 (3.91)	1645 (4.25)	
	Elderly	1121 (2.73)	69 (2.96)	1052 (2.72)	
	housekeeper	7622 (18.60)	449 (19.29)	7173 (18.56)	
	Children	186 (0.45)	11 (0.47)	175 (0.45)	
	Retired	705 (1.72)	44 (1.89)	661 (1.71)	
	Unemployed	1229 (3.00)	67 (2.87)	1162 (3.00)	
	Farmer	217 (0.52)	11 (0.47)	206 (0.53)	
	unknown	11201 (27.34)	532 (22.86)	10669 (27.61)	
Comorbidities	Cardiovascular	1998 (4.87)	100 (4.29)	1898 (4.91)	0.365
	Diabetes mellitus	2842 (6.93)	141 (6.05)	2701 (6.99)	0.229
	Hypertension	1927 (4.70)	94 (4.03)	1833 (4.74)	0.254
	Immunodeficiency	389 (0.94)	23 (0.98)	366 (0.94)	0.686
	Chronic liver disease	101 (0.24)	8 (0.34)	93 (0.24)	0.533
	Thyroid disease	140 (0.34)	9 (0.38)	131 (0.33)	0.609
	Chronic kidney disease	588 (1.43)	34 (1.24)	554 (1.43)	0.720
	Chronic pulmonary disease	988 (2.41)	55 (2.36)	933 (2.42)	0.870
	History of ICU stay	148 (0.36)	7 (0.30)	141 (0.37)	0.611
	Exposure to disease	32858 (80.22)	1841 (79.11)	31017 (80.29)	0.186
	Mortality	1038 (2.53)	0 (0.00)	1038 (2.68)	<0.001

different clinical symptoms, and the results of previous studies have shown that asymptomatic infections are more common in young and middle-aged populations and those without comorbid diseases [14]. In this disease, the window period lasts about 7 days. Detection of viral nucleic acids by RT-PCR is the standard method for detecting coronavirus infection. Although, this screening method has high specificity, its low sensitivity may lead to a number of false negatives and the method is time consuming [27]. The presence of negative results led to the conclusion that the combined use of CT imaging of clinical signs plus laboratory tests can be the initial diagnosis of pneumonia caused by COVID-19. Antibody-based immunoassay techniques are complemented by molecular techniques as complementary tools. These techniques are fast and inexpensive, but have low sensitivity and are the best tools in epidemiological studies and diagnosis of asymptomatic patients. For molecular detection, the WHO recommends screening samples with E Envelope corona gene and then confirming with the RNA-dependent RNA polymerase (RdRP, RDR). In the United States, the two proteins, nucleocapsid N1 and N2 genes of coronavirus are tested. Immunoassay for detection of anti-N protein antibody, which is an immunodominant antigen, is used for early

detection of COVID-19 [28]. Sample size of studies, age groups of under study patients, individuals with different comorbid diseases, access to diagnostic tests and time of referrals to be associated with this difference.

In our study, asymptomatic patients were older than symptomatic patients. The median age of asymptomatic and symptomatic patients were 51.70, and 45.37 years, respectively. In asymptomatic patients, the highest frequency was observed in the age group of 20-34 years (34.60% of symptomatic patients *vs* 34.90% of asymptomatic patients), and the lowest frequency belonged to those younger than 5 years (0.80% of symptomatic patients *vs* 0.70% of asymptomatic patients). According to the results stated by Gau and colleagues, asymptomatic infection was more prevalent in people under 15 years of age [14]. Wang and colleagues also reported that the median age of asymptomatic patients was 49 years and was more prevalent at age group of 30-49 years [27]. It is assumed to be lower in children than in the general population, which can be due to the specific immune response and ACE2 levels in children [28], and the cellular immune system, which is the most important part of the immune system against viral infections, is weakened in the elderly [29]. The spread of the disease depends on

the interaction between the virus and the individual's immune system. Factors associated with the pathogen also include type of virus, mutation, and the number of viruses. A person's immune system is influenced by genetics, such as the HLA gene, age, gender, nutritional status, homeostasis between the immune, nervous and endocrine systems, and physical condition. All of these factors play a key role in the onset, duration and severity and recurrence of the disease [27, 30].

In our study, 1841 (79.11%) of the patients had a history of contact with definite or suspected cases of COVID-19. Hu and colleagues [31], reported that 33.3% of asymptomatic patients had a history of travel to high-risk areas [2]. The patient's age and physical status may be major determinants of COVID-19 severity, which can be related to the state of the patient's immune response to coronavirus [14]. Due to the lack of knowledge about asymptomatic infections and the limited ability to detect the disease in these patients, the frequency of asymptomatic patients in this study was estimated as 5.6% which may be underestimated. Also, lack of published similar studies has made it difficult to compare the results of our study with other studies.

## Conclusion

According to the results of this study, the viral load detected in asymptomatic individuals was similar to that of symptomatic patients, indicating that asymptomatic infections can potentially transmit COVID-19, and may occur more frequently at early stages of the disease [24], and is considered as a challenge in disease prevention and control. Therefore, screening and detection of asymptomatic cases is a key measure in prevention and early control of COVID-19 worldwide.

We recommend that the necessary measures should be taken to identify asymptomatic cases of COVID-19, such as seriously screening those in contact with the COVID-19 positive cases, people who intend to enter the area, screening elderly and high risk individuals, as well as staff of the health system and other departments.

## Abbreviations

WHO: World Health Organization; RT-PCR: Real-time Polymerase Chain Reaction

## Availability of data and material

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

## Ethical statement

Ethics approval and consent to participate: the analysis

data file did not contain the name of the participants. The study was reviewed and approved by Medical Ethics Committee of Abadan University of Medical Sciences (Code: IR.ABADANUMS.REC.1399.051).

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## Conflict of interest statement

The authors declare no conflict of interest.

## Authors' contributions

All authors contributed to the study conception and design. HA participated in the design of the study. MD, AV, and AJ performed data collection and wrote the manuscript. MGG and EP helped with statistical analysis and prepared the illustrations. EP edited the manuscript. All authors read and approved the final manuscript.

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