Babol university of Medical Sciences
Current Research in Medical Sciences
ISSN: 2538-6212
Student Research Committee
Current Research in Medical Sciences

Signs and symptoms across different age groups in COVID-19 patients

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Article Info

Article type:
Research Article

Received: 13 February 2022
Revised: 20 May 2022
Accepted: 15 June 2022

ABSTRACT

Background and Objective: In humans, viruses cause respiratory infections that are usually mild, including the common cold, or sometimes it can be fatal. The outbreak of coronavirus disease 2019 (COVID-19) occurred in Wuhan, China was more expansive than initially estimated, with cases now confirmed in several countries. Therefore, it is crucial to determine the clinical symptoms of COVID-19 in different age groups.

Methods: This cross-sectional study evaluated the presence of SARS-CoV-2 infection in 219 throat and nasal swab samples using Real-time PCR. All samples were collected from people with respiratory symptoms who went to the grand bazaar.

Findings: Of 219 patients examined, 19 (8.6%) positive cases out of 219 for SARS-CoV-2 were found by using Real-time PCR. Among these 19 positive cases of SARS-CoV-2, 6 (2.7%) were under 5, 3 (1.3%) were between 5-18, 4 (1.8%) were between 18-50 and 6 (2.7%) were over 50 years old respectively. Most common symptoms in positive group was cough (89%) and despite other age groups, in patients over 50 years old, myalgia and diarrhea was common.

Conclusion: It seems that SARS-CoV-2 symptoms can vary in different age groups but unlike other age groups, in elderly, uncommon symptoms like eyes redness, myalgia and diarrhea seems is seen following COVID-19 infection.

Keywords: Respiratory Infection, Diarrhea, Myalgia, COVID-19, SARS-CoV-2

Cite this article: Eyvazzadeh N, et al. Signs and symptoms across different age groups in COVID-19 patients .*Current Research in Medical Sciences*. 2022; 6(2): 50-57.

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Publisher: Babol University of Medical Sciences

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[Downloaded from crms.mubabol.ac.ir on 2026-10-17]

[DOI: 10.22088/crms.6.2.50]

Introduction

Acute respiratory infections (ARIs) are related to lots of morbidity and mortality among community members all over the world. Viruses are the major cause of ARIs among all pathogens. the most common viruses cause ARIs include influenza A and B virus (Flu-A and Flu-B), rhinovirus (RhV), parainfluenza virus (PIV) type 1-4, respiratory syncytial virus (RSV), adenovirus (AdV), human bocavirus (BoV), human metapneumovirus (hMPV) and coronavirus (CoV). Coronaviruses are a large family of viruses that range from the common cold virus to the causative agent of Severe Acute Respiratory Syndrome (SARS) (1). The family *coronaviridae* belongs to the order Nidovirales. In this family, there are four genera which are: α-CoV, β-CoV, δ-CoV and γ-CoV, respectively. To date, 7 CoVs can infect humans. Including 2 α-CoV, (229E and NL63) and 5 β-CoV, (OC43, HKU-1, SARS, MERS, and SARS-CoV-2) (2). Upper Respiratory Infection (URI) is an acute respiratory disease located in the upper respiratory tract and can be one of the following conditions: Nasopharyngitis (common cold), Sinusitis, Pharyngitis, Laryngitis, and Laryngotracheitis. It seems the infection causes of these conditions are be mainly viral from 6 main families; Rhinovirus (RV), Influenza A/B/C Virus (Flu-A/B/CV), Human Para Influenza Virus (HPIV), Respiratory Syncytial Virus (RSV), Coronavirus (CoV) and Adenovirus (AdV) (3-6).

Viral infections of the lower respiratory tract cause many illnesses in children and other age groups. (7). Lower respiratory tract infections mostly include Bronchitis, Pneumonia, and Bronchiolitis. LRIs caused by viruses are a major cause of morbidity and mortality in children and adults (8). Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) has spread rapidly throughout the world since the first cases of coronavirus disease 2019 (COVID-19) were observed in December 2019 in Wuhan, China. It has been suspected that asymptomatic people play a significant role in the ongoing pandemic, but their relative number and effect have been number and effect have been uncertain. The authors ought to review and synthesize the available evidence on asymptomatic SARS-CoV-2 infection. Asymptomatic individuals seem to account for approximately 40% to 45% of SARS-CoV-2 infections, and they can transmit the virus to other people for an extended period, perhaps longer than 14 days. Because of the high risk for silent spread by asymptomatic persons, testing programs must include those asymptomatic patients carefully (9).

Omicron has gathered such a high number of mutations in less time. Almost two years of Coronavirus pandemic leads to about 5.5 million deaths out of over 340 million worldwide. The ratio of peak Emergency Department (ED) visits cases (event-to-case ratios) (87 per 1,000 cases), hospital admissions (27 per 1,000 cases), and deaths (nine per 1,000 cases) were lower during the Omicron than those in the Delta periods and winter 2020-21 (10). Studies showed that the average testing rate per million people is less than 32,000 in Africa and 160,000 in Asia, while it is more than 800, 000 in High-Income Countries (HICs) (Europe and North America). As of 12 January 2022, there were over 314 million confirmed cases and over 5.5 million deaths by COVID-19 notified around the world since the start of the pandemic (11). Also, studies from 199 U.S hospitals showed that the hospitalized COVID-19 patients who were admitted to ICU and got invasive mechanical ventilation (IMV) reduced during the omicron wave compared to the last waves of the other strains, indicating that omicron has a lower morbidity rate compared to the last strains (12). This study aimed to investigate the prevalence of SARS-CoV-2 infection among people with respiratory symptoms who went to the Grand bazaar of Tehran.

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[DOI: 10.22088/crms.6.2.50]

Materials and Methods

Study Population

This was a cross-sectional study including 219 samples of people without symptoms (119 male and 100 female), who attended in Grand bazaar of Tehran in the period between Jan 2022 and Feb 2022. Written informed consent was obtained from all patients and ethical approval (401) were obtained from Besat hospital Committee.

Collection samples and transportation

A nasal and nasopharyngeal swab samples were collected from each people and transported in Viral Transport Medium (VTM) to Besat Hospital with appropriate conditions, then stored in 2-8°C for a day to perform Real-time PCR test.

Nucleic acid extraction and virus detection

Ribonucleic acid (RNA) extraction was performed by ROJE Viral Nucleic Acid kit (ROJE, Qods, Iran). For SARS-CoV-2 RNA detection in the swab samples, one step Real-time PCR was performed using Amplicon mastermix based on the manufacturer's instructions. Primers and probe for Envelope (E) and RNA-dependent RNA polymerase (RdRp) genes were selected for amplification of SARS-CoV-2 RNA. RNA was added to a 25 µL PCR mixture containing 12.5µL of amplicon mastermix, 1 µL (10pmol) of each primers, and 0.5 µL (10pmol) probe. The reaction consisted of 35 minutes at 38°C and 15 min at 90°C, followed by 40 cycles of amplification, including 15s at 94°C and 30s at 57°C for E gene detection and 30s at 58°C for RdRp gene detection.

Statistical analysis

Categorical variables were summarized as n (%). The $\chi 2$ test or Fisher's exact test was used where appropriate. A two-sided α of less than 0.05 was considered statistically significant. Statistical analysis was done using R version 4.1.3 (2022-03-10).

Results

219 people examined, 19 participants tested positive for SARS-CoV-2 infection consisting of 12 (63.1%) females and 7 (36.8%) males. **(**Table 1**).** Myalgia, hoarseness, diarrhea, and eye redness were diagnosed in 5 patients (26%), in 5 patients (26%), 4 patients (21%), and 3 patients (16%) respectively, all from those over 50 's group. These symptoms were not seen in other age classes. The most common COVID-19-related symptom was cough which was seen in 17 patients (89%) within all classes of age except 2 patients over 50 years old (33%). After that, rhinorrhea was frequent among 11 patients (58%) 4 of them were under 5 years old (67%), 3 were between 5 to 18 (100%), one was between 18 to 50 (25%) and 3 were over 50 years old (50%). One of the less common symptoms in these cases was fever (16%) which was seen in 2 patients under 5 (33%) and 1 patient between 18 to 50 years old (25%) (Tables 1,2).

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Table 1. The prevalence of SARS-CoV-2 in grand bazaar divided by age and gender

Age (*P-value=0.73*)	Total cohort (*N = 219*)	*Gender (P-value=0.65)*		*Positive for SARS-COV-2 (N=16)*
		Male	*Female*	
<5	45 (20.5%)	22 (10%)	23 (10.5%)	6 (2.7%)
5 - 18	49 (22.3%)	25 (11.4%)	24 (10.9%)	3 (1.3%)
18 - 50	53 (24.2%)	33 (15%)	20 (9.1%)	4 (1.8%)
>50	72 (32.8%)	3 (1.3%)	3 (1.3%)	6 (2.7%)

Table 2. The prevalence of SARS-CoV-2 in grand bazaar divided by symptoms

Variable	N	overall, N=19	<5, N=6	5-18, N=3	18-50,N=4	>50, N=6	p-value
Eye redness	19						0.11
Negative		16 (84%)	6 (100%)	3 (100%)	4 (100%)	3 (50%)	
Positive		3 (16%)	0(0%)	0 (0%)	0(0%)	3 (50%)	
Myalgia	19						0.003
Negative		14 (74%)	6 (100%)	3 (100%)	4 (100%)	1 (17%)	
Positive		5 (26%)	0 (0%)	0(0%)	0(0%)	5 (83%)	
Diarrhea	19						0.015
Negative		15 (79%)	6 (100%)	3 (100%)	4 (100%)	2 (33%)	
Positive		4 (21%)	0 (0%)	0 (0%)	0 (0%)	4 (67%)	
Hoarseness	19						0.003
Negative		14 (74%)	6 (100%)	3 (100%)	4(100%)	1(17%)	
Positive		5(26%)	0 (0%)	0(0%)	0(0%)	5 (83%)	
Rhinorrhea	19						0.3
Negative		8(42%)	2 (33%)	0(0%)	3 (75%)	3 (50%)	
Positive		11(58%)	4 (67%)	3 (100%)	1 (25%)	3 (50%)	
Fever	19						0.4
Negative		16 (84%)	4 (67%)	3 (100%)	3 (75%)	6 (100%)	
Positive		3 (16%)	2 (33%)	0 (0%)	1 (25%)	0 (0%)	
Cough	19						0.3
Negative		2 (11%)	0 (0%)	0(0%)	0 (0%)	2 (33%)	
Positive		17 (89%)	6 (100%)	3 (100%)	4 (100%)	4 (67%)	
SARS-CoV-2	19						
Positive		19 (100%)	6 (100%)	3 (100%)	4 (100%)	6 (100%)	

*chi-square or Fisher exact test was used

Discussion

Members of *coronaviridae* are large, enveloped, single-stranded RNA viruses. *coronavirinae* subfamily members are widespread among mammals, frequently causing moderate respiratory or enteric

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[DOI: 10.22088/crms.6.2.50]

infections. Until 2002, human coronaviruses (hCoVs) have been associated only with mild respiratory tract disease with estimates that they caused 15%–25% of all common colds. In 2002, when a human coronavirus was recognized as the cause of a new disease called SARS. The SARS outbreak was controlled. However, in 2014, another novel CoV from patients with extreme respiratory ailment hospitalized in Saudi Arabia was isolated. MERS was a name of new disease and the coronavirus responsible is called MERS-CoV and most infected patients lived in or had traveled to Middle East countries implying that coronaviruses can cause serious disease (13). As the biggest recognized RNA viruses, CoVs are further divided into four genera: α-coronavirus, β-coronavirus, γ-coronavirus and δ-coronavirus (14). Seven human coronaviruses (hCoVs) have been identified, such as the α-CoVs like hCoVs-NL63 and hCoVs-229E, β -CoVs like hCoVs-OC43, hCoVs-HKU-1, a severe acute respiratory syndrome caused by SARS-CoV, MERS-CoV and SARS-CoV-2 (15).

SARS-CoV host entry is by the way of the respiratory tract, airway, and alveolar epithelial cells and their first targets of viral entry are vascular endothelial cells (16-18). Angiotensin-converting enzyme 2 (ACE-2) is the place where SARS-CoV-2 binds and causes activation of replication and releasing of the virus in the lung cells leading to non-specific signs and symptoms such as fever, myalgia, headache, and respiratory symptoms (19). In the study of Kuhlmann C Et al. about clinical symptoms of COVID-19, most Initial symptoms were sore throat, fatigue, headaches, dry cough, chest pressure, sinus pressure, rhinitis and nausea. Night sweats were seen in one patient within the first three days after clinical manifestation. As the infection progressed, all patients who developed a dry cough had sinus pressure and had rhinitis (20). In the study by Letafati A Et al. about SARS-CoV-2 clinical symptoms in the group of children under 5, among SARS-CoV-2 positive patients, 50% were under 1 years old and 50% were between 1 and 5 years old. The most clinical symptoms were cough, nausea, diarrhea and fever. 57% of suspected people were male and 43% were female. 28% were younger than 1 years old and 72% were between 1 and 5 years old (21).

In Ontario, research was accomplished to examine hospitalization and death caused by the Omicron variant, to compare cases infected with the Delta variant. They performed a matched cohort study, examining time to hospitalization or death as the result. Cases were matched on gender, age, vaccination status, health region, and onset date. They identified 29,594 Omicron cases that met eligibility criteria, of which 11,622 could be matched with at least one Delta case (N=14,181). There were 59 (0.51%) hospitalizations and 3 (0.03%) deaths among matched Omicron cases, compared to 221 (1.6%) hospitalizations and 17 (0.12%) deaths among matched Delta cases. The risk of hospitalization or death was 65% lower among Omicron cases compared to Delta cases, while the risk of intensive care unit admission or death was 83% lower. While severity is likely to be reduced, the absolute number of hospitalizations and impact on the healthcare system may nevertheless be significant due to the increased transmissibility of Omicron (22).

Research on children under 1 years old by Clark M Et al. showed that the majority of cases with SARS-CoV-2 were seen in infants 3 months or under of those who responded, 81% of infants were admitted to hospital. The most common reason(s) for admission were fever or respiratory symptoms (86%). Only five infants (11.1% [5/45]) had co-morbidities, 1 previous bronchiolitis, 1 metabolic disorder and2 were late preterm (23). Research of Niu S et al. showed that the most frequent symptom of identified confirmed COVID-19 infection in older patients was fever and other common symptoms were cough, dyspnea and fatigue. The body temperature of 13 (21.7 %) patients was less than 37.3℃, while 24 (40.0 %) were between 37℃ to 38℃, and 23 (38.3 %) were over 38℃. There had been no remarkable differences in fever and highest temperature between the older patients and middle-aged groups ($\chi 2 = 0.006$, $p = 0.937$), however, there were notable differences in dyspnea, and respiratory rate

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[DOI: 10.22088/crms.6.2.50]

between the two groups ($\chi 2 = 14.597$, $p < 0.001$) (24). A research by Kalantari et al. of 784 naso/oropharyngeal samples of suspected patients with COVID-19 symptoms from February 24 2020, to March 24 2020, were examined by the RT-PCR method in three hospitals in Tehran, Iran. The highest prevalence of the disease was within the age group of 50–59 years, while the lowest rate was in the 0–9 years age group. patients over 80 years had the highest rate of positive samples and it was about 89%, highest death rate was in the age group range of 70-79 by 31% and over 80 by 30%. COVID-19 prevalence in lower ages (0–9 years old) is lower and the death rate is greater in older ages as a large increase in mortality was observed in those aged over 60 years old. (25).

In a study in China on 73,2314 cases, 454000 cases were positive by RT-PCR and in terms of age distribution, 1% were under 10 years old, 1% were between 10, and 19 years old, 8% were between 20 and 29 years old, 87% were between 30 and 79 years old and 3% were over 80 years old. In terms of mortality, the highest mortality rate was related to patients over 80 years of age (14.8%), while patients aged 70–79 years showed a mortality rate of 0.8% (26). One of the probable causes of high transmission of omicron and increase in the number of infections to SARS-CoV-2 might be because of vaccine low efficacy, whether the current COVID-19 vaccines can protect against the Omicron variant attracts much attention. The most recent evidence suggested that the current COVID-19 vaccines provided less immunity to the omicron variant than other VOCs (27). Prevention strategies like vaccination, masking, quarantine, and isolation are recommended to reduce transmission of SARS-CoV-2 and to protect against severe illness, hospitalization and death from COVID-19. All persons aged ≥5 years should be vaccinated against COVID-19. Persons aged ≥18 years who completed a primary mRNA COVID-19 vaccination series ≥6 months previously or who received an initial Janssen (Johnson & Johnson) vaccine dose ≥2 months previously should receive a booster dose; persons aged 16–17 years are eligible to receive a Pfizer-BioNTech COVID-19 booster dose >6 months after completion of the primary series. Booster doses are especially urgent for those at higher risk of severe diseases such as persons residing in nursing homes and long-term care facilities. In addition, CDC recommends that everyone aged ≥2 years wear masks in public indoor places or in areas where the risk of transmission is higher (28).

Conclusion

Finally, our study reports valuable information on the spread of SARS-CoV-2 during effective public health measures among symptomatic people in the community. Uncommon symptoms like diarrhea, eye redness and myalgia can be seen in elderly and it seems that different age groups show different signs following COVID-19 infection. It shows that the virus is spreading among people in the community quickly by infected people, causing an increase in morbidity and mortality. It is important to take health care protocols seriously. Moreover, since the current prevention of SARS-CoV-2 only relies on vaccine injection and supportive interventions, it is necessary to monitor its transmission dynamics continuously. The epidemic is still going on and symptomatic patients seem to play a very important role in the transmission and spread of the disease in the community.

Limitations of the study: None

Suggestions: Further research are required to be done on COVID-19 infection especially in elderly and newborns. Symptoms in these age groups may be different to other ages and due to that, we must know the differences for better diagnosis.

Authors' Contributions

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[DOI: 10.22088/crms.6.2.50]

All authors contributed equally and participated in the data collection, analysis, and interpretation. All authors critically reviewed, refined, and approved the manuscript.

Compliance with Ethics Guidelines

Letter of consent was obtained from all patients.

Competing Interests

Authors declare no conflict of interest.

Funding:

None.

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