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Age-related disparities in the severity course of COVID-19

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Abstract

COVID-19 demonstrates a different clinical severity of course in different age groups. In the present study, we present a comparative analysis regarding the risk of hospitalization and in-hospital mortality between two extreme age groups – children and young adults (0-39 years) and elderly patients (≥70 years). For the period from January to June 2022, nasopharyngeal samples of 1,611 patients at MHAT Uni Hospital (Panagyurishte, Bulgaria) were examined by PCR analysis, of which 486 had a positive result for SARS-CoV-2. From the first target group with a laboratory-confirmed diagnosis of COVID-19, there were 158 patients with an average age of 27.5 years, and only one of them was hospitalized (a 30-year-old man, unvaccinated, with bilateral pneumonia and concomitant arterial hypertension). The average age of the patients from the second target group (n=40) was 75.6 years, 29 of them were outpatients and 11 were hospitalized, among whom 5 men with an average age of 77.6 years died. The average hospital stay of the only hospitalized patient from the young age group was 6 bed days, while for patients ≥70 years of age it was 10.1 bed days. Age is among the determinants of risk of hospitalization and in-hospital mortality associated with COVID-19.

Keywords: COVID-19; Age Disparities; Children; Young Adults; Elderly patients

1. Introduction

The emergence of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) in late 2019 has become a public health emergency. SARS-CoV-2 infection can affect multiple organ systems [1]. Coronavirus disease 2019 (COVID-19) has been associated with a high rate of morbidity and mortality is featured by a variable spectrum of severity. Elderly patients with underlying chronic diseases of multi-drug regimen are more likely to develop the severe forms of COVID-19, which are observed in less than 5% of the pediatric patients [2]. A number of reports have documented the increased risks of poorer clinical outcomes in older patients with COVID-19. Age and comorbidities can influence the prognosis through immune-and inflammatory-mediated mechanisms. Age-related immune system remodeling, or immunosenescence is considered to be the major reason for developing severe COVID-19 [3]. Elderly patients have increased risk for COVID-19 associated hospitalization and in-hospital mortality. The evidence suggests that in pediatric population the clinical course of the disease differed significantly. Most pediatric patients infected with SARS-CoV-2 are asymptomatic or have mild disease [4]. Children rarely needed admission to intensive care unit (ICU) [5]. The variation in rates deaths across age and gender might be explained with immunological and genetic differences [6]. There is some evidence that age-associated and sex- associated differences in innate and adaptive immunity, as well as higher ACE2 expression in adults than in children, result in an increased risk for severe disease in older male patients [7, 8]. Several studies have demonstrated that men are at higher risk of death and severe forms of COVID- 19 than women [1]. Summarizing, SARS-CoV-2 infection is less severe in younger age-groups than it is in older age-groups.

The aim of this article is to compare severity course of COVID-19 in two age groups: 0-39 and 70+ years old patients.

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2. Materials and methods

A total of 1,611 outpatients and hospitalized patients of MHAT Uni Hospital were tested for COVID-19 by PCR (polymerase chain reaction) for the period from January 1 to June 30, 2022. There were 486 patients with a positive result for SARS-CoV-2, of which 258 (53%) were men and 228 (47%) were women. To assess the risk of hospitalization and in-hospital mortality, a comparative analysis was made between two age groups: the youngest and the oldest SARS-CoV-2 positive patients. The first target group included 158 patients (101 men and 57 women), children and young people (0-39 years) of median age (IQR 23-34). The second target group included 40 patients (20 men and 20 women) in the advanced age (≥70 years), whose median age is 74 years (IQR 72-79). Detection of SARS-CoV-2 in nasopharyngeal samples was performed with real-time PCR Kit LiliF™ COVID-19 (iNtRON, South Korea). All data were taken from the hospital information system.

Statistical methods. Results are presented as absolute and relative frequencies, arithmetic mean and standard deviation or median and interquartile range (IQR: 25th and 75th percentiles), depending on the shape of the distribution. The shape of the distribution was assessed with the Kolmogorov-Smirnov test. The means of the two groups were compared by t-test or Mann-Whitney test. The distribution of categorical variables in the two groups was compared with the Pearson chi-squared test (Fisher's exact test when applicable).

3. Results

For the selected six-month period (01.01. - 30.06.2022) of observation, the total number of positive patients for SARS-CoV-2 from both target groups constituted 41% (198/486) of all patients at MHAT Uni Hospital with a laboratory-confirmed diagnosis of COVID -19. The distribution by gender shows that of 158 children and young adults (0-39 years), 101 were male and 57 were female, while in patients ≥70 years, both sexes were equally affected (20 males and 20 females). No significant difference was found in the two groups by gender ($p>0.05$). The median age of men from the two studied groups was higher, but no significant difference was proven (table 1).

Table 1 Age of both sex in the groups 0-39 and 70+

Age groups (years)	median age, IQR (years)	males	females	p
0-39	30, 23-34	30, 24-35	30, 21-33	0.190
≥70	74, 72-79	76, 73-80	73, 71-66	0.102

There was a significant difference between the two age groups in terms of the severity of the course, as measured by the risk of hospitalization and the incidence of in-hospital mortality. Almost all pediatric and young patients were outpatients (n=157), and only one 30-year-old man was hospitalized with bilateral pneumonia and complaints of fever, cough, shortness of breath, and fatigue. The anamnestic data show that he was unvaccinated and with concomitant arterial hypertension. Of the elderly patients, 29 were outpatients (12 men and 17 women) and 11 were hospitalized (8 men and 3 women). The prevalence of most accompanying diseases was significantly more frequent among patients aged 70+: hypertension ($p<0.001$), cardiovascular disease ($p<0.001$), diabetes ($p=0.001$), chronic kidney disease ($p=0.001$), cerebrovascular disease ($p<0.001$), chronic obstructive pulmonary disease ($p=0.040$), Hashimoto's thyroiditis ($p=0.040$), oncological disease ($p=0.040$). Obesity was reported for only one patient in the 70+ group, and no significant difference was demonstrated in the young group, where there was no information on overweight patients ($p>0.05$).

All deceased patients (n=5) were male, median age 78 (IQR 72.5-82.5) years, and four of them were unvaccinated. The most commonly reported symptoms in hospitalized patients with COVID-19 included cough (n=9), fatigue (n=8), fever (n=7), shortness of breath (n=6), and difficulty breathing (n=4). Oxygen saturation (O_2Sat.) on admission was in the range of 84-95%. A total of five patients had radiographic or computed tomography evidence of pneumonia, two had pleural effusions, and two developed pulmonary thromboembolism. The most common comorbidities in hospitalized patients with COVID-19 are arterial hypertension, cardiovascular disease, diabetes mellitus, chronic obstructive pulmonary disease and cerebrovascular disease. More than half of the hospitalized patients are polymorbid. The mean hospital stay in patients ≥70 years of age was 10.1 days (SD 5.3 days), while in the 30-year-old man, was 6 days. There is limited clinical information regarding the children and young age group, as they are mainly outpatients, the majority of whom only have a PCR test done without having a recorded examination or consultation with a doctor.

Table 2 Comparison of demographic characteristics of patients from the two target groups

		0-39		70+		p
		n	%	n	%	
sex	male	101	63.9	20	50.0	0.107
	female	57	36.1	20	50.0	
ambulatory or hospitalized	ambulatory	157	99.4	29	72.5	<0.001
	hospitalized	1	0.6	11	27.5	
exitus among hospitalized	discharged	1	100.0	6	54.5	0.377
	exitus	0	0.0	5	45.5	
hypertension	no	157	99.4	18	45.0	<0.001
	yes	1	0.6	22	55.0	
cardiovascular disease	no	158	100.0	21	52.5	<0.001
	yes	0	0.0	19	47.5	
diabetes	no	158	100.0	36	90.0	0.001
	yes	0	0.0	4	10.0	
chronic kidney disease	no	158	100.0	36	90.0	0.001
	yes	0	0.0	4	10.0	
cerebrovascular disease	no	158	100.0	35	87.5	<0.001
	yes	0	0.0	5	12.5	
COPD	no	158	100.0	38	95.0	0.040
	yes	0	0.0	2	5.0	
Obesity	no	158	100.0	39	97.5	0.202
	yes	0	0.0	1	2.5	
Hashimoto’s thyroiditis	no	158	100.0	38	95.0	0.040
	yes	0	0.0	2	5.0	
oncological disease	no	158	100.0	38	95.0	0.040
	yes	0	0.0	2	5.0	

4. Discussion

Infection with SARS-CoV-2 has been reported in all age groups. A strong age gradient in the risk of death was observed among patients with COVID-19 [10]. Age is an independent prognostic factor for the clinical severity of COVID-19 [11]. Observations reveal risk factors associated with hospital mortality, such as advanced age, comorbidity and male gender [12]. The results we present are consistent with those reported in other studies. We identified older age as a determinant of adverse clinical outcomes in COVID-19-positive patients. Comparative analysis of our chosen two extreme age groups (0–39 years and ≥70 years) showed a higher number of hospitalized patients and a higher mortality among the elderly and males. The average age of hospitalized (78.09 years) and deceased (77.6 years) patients was higher than that of outpatients (74.72). The presence of comorbidities and negative vaccination status are additional risk factors for a worse prognosis [13,14]. Consistent with global data, we also found a milder course of COVID-19 in childhood and young adulthood. Of all 158 patients in the first target group, 24 were in the age range of 0-19 years and 134 were in the age group of 20-39 years, and only one was hospitalized. Reports of severe forms of the disease in the pediatric population are rare [15]. Children are less often diagnosed because they usually have milder symptoms or are

asymptomatic [16]. Among the hypotheses for the milder course of the disease in childhood, lower expression of the ACE2 receptor and a more effective innate immune response that promotes viral clearance are discussed [17]. In addition, children have a low rate of chronic diseases compared to adults, and due to the busy schedule of childhood immunizations, the protective role of vaccinations ("training immunity") is actively discussed. The possible competitive action of other respiratory viruses that colonize the nasopharyngeal mucosa in childhood is also a possibility [18]. About 20% of adult patients develop severe or critical forms of COVID-19 requiring ICU admission [19]. Most studies have shown that elderly and male patients with COVID-19 have higher mortality rates [20]. Old age is a significant risk factor for mortality from COVID-19 [21]. The immune response is dynamically remodeled with aging, a phenomenon called immunosenescence. Innate and adaptive immunity are involved in the process of control of SARS-CoV-2 infection and clinical recovery [22, 23]. Changes occurring in the aging immune system are thought to be responsible for the clinical severity and higher number of deaths in elderly patients with COVID-19 [24]. In addition, the elderly have an increased incidence of comorbidities, such as metabolic syndrome and diabetes mellitus, which is considered a risk factor for a more severe course [25,26].

5. **Conclusion**

In conclusion there were significant differences between children, young people and elderly patient in terms of inflammatory activity, severity of COVID-19 and the outcome of the disease. Age-related differences in the innate immune response can influence the clinical course of SARS-CoV-2 infection. Elderly age and male sex seem to be independent prognostic factors for increasing risk for hospitalisation and mortality. Our results may help to need for more attention and care to elderly patients with COVID-19. A deeper understanding of risk factors for COVID-19 severity among different age populations is needed.

Compliance with ethical standards

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Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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