Research Paper Clinical Manifestations, Laboratory and Imaging of COVID-19 in Children

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ABSTRACT

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Keywords:

COVID-19, Children, Hematological markers of probable, suspected, and definite patients (positive test result) (P>0.05). **Conclusion:** The result showed that the symptoms of COVID-19 in the first stage are uncommon in children and these symptoms are non-specific, also a lower percentage of tests are reported positive in children and as a result, no significant statistical difference was observed between clinical and paraclinical findings with polymerase chain reaction (PCR) test results of patients in our study.

Background and Aim: COVID-19 caused chaos in healthcare globally, particularly among

children. While they make up a smaller percentage of patients, it is essential to identify potential

prognostic factors for disease severity considering their clinical status, age, and comorbidities. This study aims to investigate the clinical, laboratory, imaging, and prognosis of COVID-19 in children. **Materials and Methods:** In this descriptive-analytical study, the clinical records of the patients were used to complete the information from the inpatient and outpatient records. Finally, the course of the disease was done by following up the patients on an outpatient basis, and the patients who suffered from the complications of COVID-19 or died were investigated. Finally, laboratory/radiology symptoms of patients were girls (38%) and 106 patients (62%) were boys. And no statistically significant difference was found between the age and sex of the patients (P=0.42). No statistical significance difference was found between lung involvement, respiratory distress, patients' fever, gastrointestinal symptoms, leukopenia and lymphopenia, high C-reactive protein (CRP) and lactate dehydrogenase (LDH), skin involvement, underlying disease, elevated liver enzymes in three groups

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Introduction

n December 12, 2019, 27 cases of pneu-

monia of unknown cause have been

reported in Wuhan City, China [1]. The

World Health Organization (WHO) in-

troduced this sickness as an acute res-

piration syndrome with the causative

agent of the coronavirus in 2019 [2].

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The sickness spread worldwide so that on March 11, 2020, the WHO declared it an endemic [3]. Near contact with symptomatic and asymptomatic cases are the primary routes of transmission in children [4]. Although the prevalence of this disorder in 18-year-olds and younger humans is incredibly low (2.4% of all suggested instances), miles are essential to test those signs in children [5, 6]. Children with this disease may have different symptoms compared to adults. Studies show that children often have more gastrointestinal symptoms and fever when infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV) [7]. Another thing to note is that babies born to mothers with COVID-19 may have problems with breathing, abnormal liver function, thrombocytopenia, and thermal instability [8]. Children with this disease are believed to be asymptomatic or eventually may show a mild form of symptoms [9]. Affected children show symptoms, such as fever, and mild respiratory symptoms, such as dry cough, distress, nasal secretions, sore throat, and fatigue [10]. In some cases, they may show digestive symptoms [11]. It is essential to know the symptoms of this disease in children. Common symptoms include fever, cough, myalgia, fatigue, nausea, diarrhea, and headache. Some patients may also experience hemoptysis [12, 13]. Children with underlying diseases have acute respiratory symptoms due to the destruction of alveoli [14]. This disease may very quickly progress to progressive multi-organ involvement (for example, shock, acute respiratory distress syndrome [ARDS], acute cardiac injury, and acute kidney injury [AKI]) and may even cause death very quickly [15]. A study found that children of any age can have COVID-19 and no difference is observed between genders. Although children's symptoms decrease faster than adults, young children, especially infants, can still get infected. Most cases of pediatric COVID-19 were in Hubei province and nearby areas. This study also confirms that the virus can be transmitted between humans. [16]. A review study found that children with COVID-19 have similar diagnostic findings to adults, with common symptoms of fever and respiratory issues. However, children tend to have less severe pneumonia. Inflammatory markers are less common in children, and lymphocytopenia is rare. Newborns can show symptoms of COVID-19, but rare evidence of transmission from mother to baby is observed during pregnancy. Treatment for children includes oxygen supply, inhalation, nutritional support, and maintaining fluid and electrolyte balance. Children have a milder disease course and better prognosis than adults, with very few deaths reported [17]. From the changes that occur in the laboratory symptoms, white blood cell counts, lymphopenia, and thrombocytopenia, and increased PT and C-reactive protein (CRP) [12-14]. Most children with COVID-19 have mild to moderate disease and recover within one to two weeks. However, severe cases are more likely in children with underlying chronic lung diseases, heart diseases, immune deficiencies, blood disorders, chronic liver and kidney diseases, and neurological diseases. This study was conducted to identify the common symptoms, radiology findings, age and gender distribution, and prognosis of COVID-19 in children under 18 years old who were treated at Bahrami Hospital.

Material and Methods

This study was conducted in a cross-sectional analytical method. The sampling method was a census and 171 children under 18 years of age who were hospitalized in Bahrami Hospital in Tehran Province, Iran with symptoms of COVID-19 between March 2018 and January 2019.

The inclusion criteria included children with symptoms of COVID-19 or multisystem inflammatory syndrome in children (MISC) manifestations, including (rejecting other differential diagnoses and evidence in favor of COVID-19 infection) proven fever above 38 degrees for more than 24 hours, involvement of two or more organs, including cardiovascular (such as shock, increased troponin, B-type natriuretic peptide (BNP), abnormal echo and arrhythmia, >45% E.F), respiratory involvement (such as pneumonia, ARDS, pulmonary embolism, kidney involvement (such as AKI and renal failure), nerve involvement (convulsions, aseptic meningitis, decreased level of consciousness and stroke), hematological, such as coagulopathy, gastrointestinal involvement (such as increased liver enzymes, jaundice, diarrhea and vomiting, ileus, acute abdomen, gastrointestinal bleeding, and signs and symptoms related to pancreatitis) and skin (such as erythroderma, mucositis, and other rashes) and the exclusion criteria included children with a diagnosis other than COVID-19 and their symptoms were consistent with that disease. After recording the information in the checklist, the patients were divided into 3 groups (definite, probable, and suspected) according to the cri-

Group	Definition
Definite	For patients who have pulmonary and gastrointestinal symptoms consistent with COVID-19 and their PCR are positive.
Probable	The result of the person's PCR test is unknown or reported as negative. But one of the following points is relevant for the patient: Have radiological manifestations that are strongly suggestive of COVID-19 from the radiologist's point of view. A person with pneumonia who, despite proper treatment, has an inappropriate clinical response and the patient's clinical condition becomes more acute and serious or dies in an unusually and unexpectedly. Death in a suspected patient with COVID-19 (the above criteria) that cannot be justified by another reason.
Suspected	In a patient who presents with a sudden onset of fever and cough or at least three or more symptoms, such as weak- ness and lethargy, headache, muscle pain, sore throat, runny nose, shortness of breath, anorexia, nausea, vomiting, and diarrhea, the diagnosis of COVID-19 is discussed.

Table 1. Examining definite, probable, and suspected definition of COVID-19 disease

PCR: Polymerase chain reaction.

teria announced by the Ministry of Health and Medical Education (Table 1). Finally, the course of the disease was done by following up the patients on an outpatient basis, and the patients who suffered from the complications of the COVID-19 disease or died were investigated. Finally, the laboratory/radiological symptoms of the patients were compared between the three groups. To analyze the relationships, all the information was entered into SPSS software, version 26 and analyzed using chi-square statistical tests. The significant level for all tests was considered 0.05%.

Results

In this study, 17 patients (9.9%) were <1 year old, 71 patients (41.5%) were between 1 and 3 years old, 20 patients (11.7%) were 3 to 5 years old, 43 patients (25.1%) were 5 years old. They were up to 10 years old and 20 patients (11.7%) were >10 years old. The age distribution was the same in three groups, probable, definite (positive test result), and doubtful, and no statistically significant difference was observed (P=0.42). In all three definite, probable, and doubtful groups, the gender distribution of patients is uniform, and no statistically significant relationship was found between patients' gender and PCR results (P=0.67).

The PCR results indicated that in 64 patients (37.4%), PCR results were definite (positive test result), in 63 patients (36.8%), probable (diagnosis in favor of CO-VID-19), and in 44 patients (25.7%), the results were doubtful. Based on the results of the chest computed tomography (CT) scan, 29 patients (17%) had lung involvement and 142 patients (83%) had no lung involvement. Twenty-three patients (13.5%) had MIS criteria and 148 patients (86.5%) had no MIS criteria. Of the 171 Journal of Vessels and Circulation Qom University of Medical Sciences

patients studied, death was reported in 7 cases (4.1%) and 164 patients (95.9%) survived.

Regarding the laboratory, clinical and paraclinical conditions of the patients between body mass index (BMI) (P=0.78), underlying disease (P=0.79), fever (P=0.23), respiratory distress (P=0.56), gastrointestinal symptoms (P=0.31) skin involvement (P=0.24), lung involvement (P=0.12), and laboratory findings of lymphopenia (P=0.41), leukopenia (P=0.85), lactate dehydrogenase (LDH) (P=0.68), CRP (P=0.72), disorders of liver enzymes (P=0.23), no statistically significant difference was found between the three groups of probable, definite and suspected patients (Table 2).

Discussion

Panahi et al. conducted a study to review the published articles on the clinical manifestations and characteristics of children and infants with COVID-19. Clinical manifestations in children may be mild (72%), moderate (22%), or severe (6%) and the most common symptoms include dry cough (91%) and fever (96%) [1]. In our study, fever was one of the vital initial symptoms in patients, so that this symptom was identified in 117 patients (68.4%). Similar to the results of our study, this study found no difference between male and female children regarding the incidence of COVID-19. Infected children have relatively mild clinical symptoms compared to infected adults [18]. In our study, the symptoms in children were mild and non-specific. However, special attention should be paid to early diagnosis and early treatment in children with COVID-19. Preliminary epidemiological data have shown that the involvement of symptoms of COVID-19 in children is rare. According to a study reported in China in March 2020, only 2% of children had symptomatic disease [19]. Due to the constantly chang**Table 2.** Review of demographic, clinical, and paraclinical findings of confirmed, probable, and suspected patients with CO-VID-19 in the studied children

	No. (%)					
	Variables	_	PCR			Р
			Definite	Probable	Suspected	
	Gender	Воу	37(21.6)	41(24)	28(16.4)	0.42
		Girl	27(15.8)	22(12.9)	16(19.4)	
Demographic	Age (y)	<1	5(2.9)	5(2.9)	7(4.1)	
		1-3	28(16.4)	31(18.1)	12(7)	
		3-5	6(3.5)	9(5.3)	5(2.9)	0.42
		5-10	17(9.9)	12(7)	14(8.2)	
		>10	8(4.7)	6(3.5)	6(3.5)	
	BMI (kg/m²)	Low	17(9.9)	16(9.4)	13(7.6)	
		Normal	38(22.2)	37(21.6)	21(12.3)	0.78
		Overweight	9(5.3)	10(5.8)	10(5.8)	
	Underlying disease	Positive	26(15.2)	22(12.9)	17(9.9)	0.70
		Negative	38(22.2)	41(24.0)	27(15.8)	0.79
	Fever	Positive	44(25.7)	47(27.5)	26(15.2)	0.23
		Negative	20(11.7)	16(9.4)	18(10.5)	
	Respiratory distress	Positive	25(14.6)	20(11.7)	18(10.5)	0.56
		Negative	39(22.8)	43(25.1)	26(15.2)	
Sign and	GI symptom	Positive	4(2.3)	9(5.3)	4(2.3)	0.31
symptom		Negative	60(35.1)	54(35.6)	40(23.4)	
	Skin involve- ment	Positive	3(1.8)	5(2.9)	6(3.5)	0.24
		Negative	61(35.7)	58(33.9)	38(22.2)	
	Lung diserder	Positive	10(5.8)	15(8.8)	4(2.3)	0.12
	Lung disorder	Negative	54(31.6)	48(28.1)	40(23.4)	
	Leukopenia	Positive	11(6.4)	11(6.4)	6(3.5)	0.85
		Negative	53(31.0)	52(30.4)	38(22.2)	
	Lymphopenia	Positive	15(8.8)	9(5.3)	8(4.7)	0.41
		Negative	49(28.7)	54(31.6)	36(21.1)	
Labaratari i data	LDH	Normal	39(22.8)	42(24.6)	26(15.2)	0.68
Laboratory date		Abnormal	25(14.6)	21(12.3)	18(10.5)	
	CRP	Normal	41(24.0)	44(25.7)	28(16.4)	0.72
		Abnormal	23(13.5)	19(11.1)	16(9.4)	
	Liver enzyme	Normal	63(36.8)	58(33.9)	41(24.0)	0.23
		Abnormal	1(0.6)	5(2.9)	3(1.8)	

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Abbreviations: CRP: C-reactive protein; LDH: Lactate dehydrogenase; BMI: Body mass index; GI: Gastrointestinal.

ing nature of COVID-19, it has been observed that the disease can worsen the condition of young patients in future peaks and with new strains. The American Academy of Pediatrics (AAP) reports that the incidence rate is 11% and the death rate is 0%-0.23% of total cases. A total of 3.5%-14.5% of PCR tests for children are positive [12]. In our study, the deaths of these children were reported in 7 cases (4.1%) and 164 patients (95.9%) survived. Also, the results of our study showed that the tests were positive in a smaller percentage of these patients. This recent study showed the higher involvement of children compared to previous studies. In children, the most common method of virus transmission and contamination is through family contacts, but compared to adults, their laboratory tests are less positive [20]. In children, no difference is observed in the viral load between symptomatic and asymptomatic patients, and asymptomatic patients can still infect a large number of people [21]. It is reasonable to have an exact count of infected people to prevent transmission by following health and personal protection principles. Radiological methods, such as chest x-ray (CXR) or CT scan are used for diagnosis, with peribronchial cuffing and ground glass opacity being common in infected children. Imaging methods should be used for patients with positive test results or respiratory symptoms. However, the American College of Radiology (ACR) does not recommend using imaging methods for screening or first-line diagnosis, and x-rays should only be used for moderate to severe involvement in patients with underlying diseases or risk factors requiring hospitalization [22]. As was shown in our study, lung involvement is much less observed in radiographs, and no significant statistical relationship was observed between lung involvement and the COVID-19 test. According to the opinion of this college, it is better to limit the CT scan of the lung only to specific clinical conditions or severe respiratory symptoms and laboratory disorders, such as increased D-dimer or evaluation of patients who do not respond to appropriate treatment. According to the latest edition of the diagnosis and treatment flowchart of the Ministry of Health and Medical Education CXR is not sensitive to show pulmonary involvement in the early stages of the patient, but in emergency cases, it can be used as a diagnostic tool to monitor pulmonary involvement, especially in patients hospitalized in pediatric intensive care unit (PICU). CXR sensitivity is low in the early stages of the disease or mild disease. As the disease progresses, up to 70% of patients at the beginning of hospitalization and up to 80% during hospitalization have abnormal CXR. Gastrointestinal involvement and abdominal pain are more common in MIS-C patients than in Kawasaki patients [23]. While gastrointestinal involvement was rarely observed in our patients. In the laboratory examination, evidence of inflammation is observed in the form of increased CRP in 58 patients (33.9%) and high erythrocyte sedimentation rate (ESR) in 64 patients (37.4%). However, leukocytosis and thrombocytosis are more common in Kawasaki. Liver involvement is observed as an increase in transaminases. Elevation of ferritin, fibrinogen, and D-dimer confirm inflammation. Increased troponin is observed in myocarditis [24]. Also, high liver enzymes were rarely reported. The complications and symptoms of COVID-19 are increasing, which can be a result of non-specific complications of systemic diseases or the direct effect of the virus itself, or as a result of inflammation of the nervous and vascular system [23].

Conclusion

The result of our study showed that the symptoms of COVID-19 in the first stage are uncommon in children and these symptoms are non-specific, also a lower percentage of tests are reported positive in children and as a result, a significant statistical difference is observed between the clinical findings and paraclinical with PCR test results of patients.

Ethical Considerations

Compliance with ethical guidelines

This article has been approved by the Ethics Committee of Tehran University of Medical Sciences (Code: IR.TUMS.CHMC.REC.1400.043).

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Authors' contributions

All authors participated equally in the design, execution, and writing of all parts of this research.

Conflict of interest

The authors declared no conflict of interest.

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