

Clinical and laboratory findings of children with Coronavirus Disease 2019 (COVID-19) in Mashhad, Iran: An observational study.

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Abstract

Background: The novel Coronavirus Disease 2019 (COVID-19) is a cause of respiratory/systemic disorder which is spread in the world since September 2019 and is now a serious pandemic. To date, there is limited data on children available in the literature especially in Middle East.

Objective: In this article, we aimed to provide an overview of clinical and laboratory data in children with COVID-19 admitted in Mashhad, Iran.

Methods: This was a cross sectional study that was related to the Registry of COVID19 Pediatric patients in Mashhad (RCPM), from 20 February 2020 to 5 August 2020 in Akbar and Dr. Sheikh Hospitals, the tertiary referral centers of pediatric COVID19 patients in Northern East of Iran. Demographic information, clinical symptoms, laboratory results, management, and outcome data from each patient's medical records were recorded.

Results: In this period, from 1245 patients referred to our center, 97 patients were positive for COVID19 with PCR or serologic test. Majority of them were male (58, 59.8%).

The median age of patients was 5.5 years old. The mean time from beginning the symptoms to hospitalization was 6.72 ± 9.02 days. The most age groups were 1-5 years old (28.9%)

Twenty patients lead to pneumonia (20.6%), eight of them lead to Multi-Inflammatory Syndrome Of Children (MISC) (8.2%), Kawasaki disease was seen in 4 patients (4.1%), myocarditis in 4 patients (4.1%) and 14 patients were died (14.4%).

Conclusion: The existence of asymptomatic cases indicates the difficulty in identifying pediatric patients without clear epidemiological information. This finding suggests a dangerous situation if community acquired infections occur.

Keywords: SARS-CoV2, Novel coronavirus, Pediatric, Clinical manifestation, Viral infection, Children.

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Introduction

The novel Coronavirus Disease 2019 (COVID-19) is a cause of respiratory/systemic disorder which became a pandemic since September 2019 [1]. The COVID-19 disease can affect all age groups, but children and/or adolescents seem to be less susceptible [2]. Furthermore, the reports of severe COVID-19 infection in pediatrics are rare [3]. In a large-scale report of laboratory-confirmed COVID-19 cases, only 2.1% aged less than 19 years old [4]. Similar to both Severe Acute Respiratory Syndrome (SARS) and the Middle Eastern Respiratory Syndrome (MERS), milder symptoms and less hospitalization rates are reported in children compared to adults [5,6]. Although a severe infection have been reported in 2.5% of pediatric patients leading to mortality in some [7].

Preliminary data focused on severe respiratory manifestations, seen predominantly in adults, with scant initial data on the burden of COVID-19 in children. Signs and symptoms in children might be different from adults. In an investigation, 13% of virologic confirmed cases had asymptomatic infection. Among symptomatic children, 5% had dyspnea or hypoxemia and 0.6% progressed to Acute Respiratory Distress Syndrome (ARDS) or multi-organ system dysfunction, which is also lower than adults [8]. In some studies, preschool-aged children and infants were more likely to have severe clinical manifestations than older children [2,8,9].

Laboratory data offers more than etiological diagnosis and disease surveillance, and may provide insights into evaluating the disease severity, assessing prognosis and decision making [10-12]. Moreover, laboratory data may provide hints to underlying pathophysiology and the immunological responses.

To date, there is limited data in children regarding COVID-19 infection, especially in the Middle East. In this article, we aimed to provide an overview of clinical and laboratory data in children with COVID-19 infection admitted to some hospitals in Mashhad, Iran.

Methods

This was a cross-sectional study according to the Registry of COVID-19 Pediatric Patients in Mashhad (RCPM), from 20 February 2020 to 5 August 2020. Patients who admitted to

Akbar and Dr. Sheikh Hospitals, the tertiary referral centers of pediatric COVID-19 patients in Northern East of Iran were evaluated.

Real-time reverse-transcriptase Polymerase Chain Reaction (PCR) was performed in children aged 18 years or below who were suspicious to COVID-19 infection according to the Iranian society of pediatric national guideline for COVID-19 or a family or social history of COVID-19 exposure. Subsequently, these patients underwent diagnostic and therapeutic assessments. The therapeutic principles included general support, respiratory and cardiac monitoring, liver and renal function tests, controlling high fever and oxygen therapy if necessary.

Demographic information, clinical symptoms, laboratory results, management, and outcome were recorded. Clinical outcomes were followed till August 5, 2020. PCR confirmation of COVID-19 was performed at central referral institution in Imam Reza hospital, Mashhad, Iran. Discharge criteria were normal body temperature, stable clinical vital sign for at least 24 hours, or resolution of all clinical symptoms. Patients who were discharged from hospital had to be quarantined for 2 weeks.

Statistical analysis

We presented continuous variables as mean (SD) and categorical variables as number (%). Means of continuous variables between the groups were compared using independent t tests when values were normally distributed; otherwise, Mann-Whitney U test was used. Categorical variables between the groups were compared using Fisher's exact test. P value less than 0.05 was considered as statistically significant. All data analyses were performed by SPSS version 20 (SPSS Inc. Chicago, IL, The USA).

Results

In the study period, from 1245 patients referred to our center, 97 had a positive result for COVID-19 infection using PCR or serologic test. Most were males (58%, 59.8%). Other demographic data is shown in Table 1.

Feature			
Residency (n, %)		Urban (84, 86.6)	Rural (13, 13.4)
Age group (n, %)	<1 year	20, 20.6	
	1-5 years	28, 28.9	
	5-10 years	22, 22.7	
	10-15 years	25, 25.8	
	≥ 15 years	2, 2.1	
Positive family history		12, 12.4	
Hospital stay (mean ± SD) day		7 ± 5.89	

Table 1. Demographic data of positive pediatric patients.

The median age of patients was 5.5 years old. The mean time from beginning of symptoms to hospitalization was 6.72 ± 9.02 days. The most common age groups were 1-5 (28.9%) and

10-15 years old (25.8%). Thirteen patients (13.4% were asymptomatic in our study. Signs and symptoms of patients are listed in Table 2.

Signs or symptoms	%
Fever	68.04
Cough	47.42
Abdominal pain	23.71
Irritation	12.37
Breath shortening	26.8
Cyanosis	9, 9.27
Sore throat	8.24
Headache	13.4
Vomiting	32.98
Nasal congestion	8.24
Diarrhea	23.71
Hemoptysis	5.15
Chest pain	6.18
Myalgia	8.24
Chills	11.34
Runny nose	8.24

Table 2. Signs and symptoms of pediatric patients.

The mean of vital signs at admission is listed in Table 3. The mean of laboratory findings is shown in Table 4. Forty-seven patients had at least an underlying disorder (48.45%. Nine of

them had cerebral palsy (9.27%). Six patients had a definite immune system deficiency (6.18%). Other underlying disorders are listed in Table 5.

Characteristics	Minimum	Maximum	Mean	Std. Deviation
RR	20	70	42.848	16.0276
HR	80	201	137.788	26.3851
T	36.8	40.2	38.103	0.9603
SPO2	75	99	90.032	6.5038
SBP	50	120	91.87	15.8782
DBP	50	90	66.7	11.7254

Table 3. Primary vital signs of positive pediatric patients.

Characteristics	Minimum	Maximum	Mean	Std. Deviation
WBC	200	65300	11931.183	8372.0936
Hb	6.5	17.9	11.639	2.115

plt	7	1111	293.717	198.6013
pmn	17	98	63.859	20.5071
L	2	68	27.761	18.2187
RDW	11.4	22	14.127	2.1271
MCV	52.3	103.9	79.484	8.5247
CRP	3	351.4	50.2384	70.35459
ESR	2	151	34.474	31.716
AST	8	314	39.245	47.4102
ALT	3	193	31.283	39.7702
ALP	121	1420	439.163	247.9525
PT	13	60	16.909	9.2424
PTT	1	120	40.876	27.3311
INR	0	49	3.9496	9.80989
BS	30	438	109.167	56.4309
Urea	6	113	25.217	16.4809
Cr	0.3	6.8	0.73	0.6974
Na	124	189	140.765	8.8381
K	2.7	6.6	4.1295	0.73931
LDH	245	1260	527.367	228.721
CPK	19	931	208.686	240.2137
BilT	0.1	31.4	5.7589	10.88088
BilD	0.18	19.4	3.7289	7.03587
Ca	5.9	11	8.6005	0.9924
Mg	1.7	2.6	2.098	0.27718
PCT	1.04	30	12.4133	15.44748
pH	7.06	7.59	7.3536	0.09585
HCO3	8.4	35.9	20.848	5.3488
PCO2	11.4	105.6	35.016	12.3506
O2Sat	22.8	99.8	74.0843	19.5472
PO2	10	221.9	48.18	29.477

Table 4. Laboratory data of positive pediatric patients.

Underlying disease	N	%
Known immune deficiency	6	6.2
Down syndrome	8	8.2
Known cardiac disease	4	4.1
Gastro-intestinal disease	3	3.1
Neurologic disorders	9	9.3
Cystic fibrosis	4	4.1

Hematologic/oncologic disorder	5	5.2
Surgical disorder	1	1
Endocrine disorder	2	2.06
Renal disorder	1	1

Table 5. Underlying disease in positive pediatric patients.

Twenty patients had pneumonia (20.6% and eight had Multi-Inflammatory Syndrome of Children (MISC (8.2%. Besides, Kawasaki disease was seen in 4 (4.1% and myocarditis in 4 patients (4.1%. Finally, 14 patients died (14.4%. There was no significant association between mortality and age group (P=0.857. Four dead patients were under one year old, four 1-5 years old, four 10-15 years old and two 5-10 years old. In admission laboratory data, MCV (P=0.001 and RDW (P=0.016 were significantly higher in dead patients versus recovered ones. It was shown that previous underlying disease had a significant association with mortality (11/14, P=0.015.

Therapeutic management options for patients are listed in Table 6. Eighty-five patients had a positive COVID-19 PCR (87.6% and 12 (12.4% positive serologic tests. Laboratory data according to the age groups is listed in Table 7. Median of admission hemoglobin level (P=0.003, platelet count (P=0.005, neutrophil count (P<0.001, lymphocyte count (P=0.003, RDW (P=0.006, MCV (P=0.001, ESR (P=0.011, blood sugar (P=0.039, creatinine (P=0.011 and potassium (P=0.006 were significantly different according to the age group.

Treatment options	N	%
O2 Therapy	69	71.1
Antibiotic	83	91.2
Intubation	14	15.6
HFNC	1	1
ICU admission	28	28.9
Oseltamivir	4	4.1
IVIG	14	14.4
Hydroxychloroquine	23	23.7
Kaletra	1	1
Corticosteroid	28	28.9

Table 6. Treatments used in positive pediatric patients.

Age group		Minimum	Maximum	Mean	Std. deviation
<1yr	CRP	3	90	20.7	26.08
	WBC	5600	65300	15635	12812.09
	PMN	17	77	44.15	17.7
	L	15	68	46.3	16.17
	RDW	11.8	22	15.97	2.78
	MCV	59.8	103	78.72	9.02
1-5	CRP	3	351.4	85.56	97.1
	WBC	4300	31300	12768	7469.19
	PMN	32	88	65.52	15.81
	L	8	55	26.44	14.82
	RDW	11.9	15.9	13.49	1.18

	MCV	66.5	92.2	75.29	5.48
5-10	CRP	3	161	41.88	49.87
	WBC	200	20300	9304.76	5850.93
	PMN	20	91	68.66	19.93
	L	6	66	22.09	16.32
	RDW	11.6	15.8	13.36	1.26
	MCV	72.9	103.9	81.03	7.2
10-15	CRP	3	249	48.21	66.06
	WBC	3100	23000	10708	5653.9
	PMN	32	98	73.24	17.73
	L	2	54	19.56	14.67
	RDW	11.4	19	13.88	2.1
	MCV	52.3	100	83.23	10.07
>15	CRP	3	16	9.5	9.19
	WBC	4000	10600	7300	4666.9
	PMN	81	81	81	.
	L	14	14	14	.
	RDW	14.9	14.9	14.9	.
	MCV	74.5	74.5	74.5	.

Table 7. Admission laboratory data according to age group in positive pediatric patients.

Discussion

In this study, we reported a range of signs and symptoms in SARS-CoV-2 infection in children. In contrast to adults, most infected children appeared to have a milder clinical course. Mild or asymptomatic infections are more common in lower age groups. Determining the transmission potential of these asymptomatic patients is important for controlling the development of disease in the ongoing pandemic.

The ability of SARS-CoV-2 to cause infection is very high in all age groups. Perception of clinical manifestations of COVID-19 infection in children is of high importance in a proper diagnosis and management [13]. Our findings showed that most patients who died had an underlying disease and only three of them did not have any medical history. The main clinical features of COVID-19 in our study population were fever (68.04%), cough (47.42%) and abdominal pain (23.71%).

Documented positive family history of COVID-19 was reported in 12.4% of cases. However, in COVID-19 pandemic, determining patients with COVID-19 is difficult, because some people refuse that they are infected. Finding transmission route in pediatric patients is not well known, because some parents do not care about their children, such as wearing facemasks, not participating in crowded places or epidemic area, travelling and etc.

In our study, 13 patients were asymptomatic and others had at least one symptom at admission. Eighty three patients (85.56%) were cured and discharged and follow-up is continuing. Children are less probable to become severely ill than adults and there are sub-populations of children with an increased risk for critical infection. Younger age, underlying pulmonary pathology, and immune compromising conditions have been associated with more severe outcomes with non-COVID-19 coronavirus infections in children [14].

Prior studies have shown that children with COVID-19 infection of the respiratory tract have viral co-infections in up to two-thirds [15]. Children may play a major role in community-based viral transmission. They may have more upper respiratory tract and nasopharyngeal microbial colonization, rather than lower respiratory tract involvement [16]. There is also evidence of fecal shedding in the stool for several weeks after infection [17], leading to concern about fecal-oral transmission of the virus, particularly for infants and children who are not toilet-trained [18].

The results of our study showed that the spectrum of clinical manifestations in children with COVID-19 infection can be very different. Moreover, classic pattern of laboratory findings in adults is not compatible with children, and we had patients with normal range of all laboratory data at admission, who were then deteriorated during the hospitalization. Therefore, in COVID-19 pandemic, notifying different signs and symptoms and close follow-up should be considered. Multi-Inflammatory Syndrome of Children (MISC) was detected in 8 patients in our

study leading to mortality in three without any underlying disease. Attention to this syndrome and its fast progression is necessary in pediatric patients admitted to hospitals for better management.

Conclusion

Pneumonia was the most common complication of COVID-19 in our study population. However, respiratory symptoms subsided by time, and non-specific symptoms appeared. Pediatric population becomes infected by either close contact with diseased adults or exposure in epidemic areas. Although fever and cough are common manifestations, some patients did not have obvious symptoms or abnormal radiological findings. The existence of asymptomatic cases indicates the difficulty in identifying pediatric patients without clear epidemiological information.

Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee of Mashhad University of Medical Sciences (IR.MUMS.REC.1399.032).

Human and Animal Rights

This study was performed according to the Declaration of Helsinki principles.

Consent for Publication

Written informed parental/guardian consent were obtained prior to enrollment in the study at admission.

Availability of Data and Materials

The data supporting the findings of the article is available and will be introduced by a formal and reasonable request.

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Conflict of Interest

There is no conflict of interest.

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