

# Clinical, laboratory and imaging characteristics, and outcomes of hospitalized children with suspected COVID-19 infection: A report from Isfahan-Iran

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**Background:** The aim of this study was to evaluate the clinical, laboratory and imaging characteristics, and outcomes of hospitalized children with suspected COVID-19 infection in Isfahan. **Materials and Methods:** In this cross-sectional study, all children aged < 15 years, who hospitalized as suspected case of COVID-19 were enrolled. During this study, all demographic, clinical, laboratory, and imaging characteristics as well as follow-up data and outcomes of the hospitalized children were recorded by pediatric residents using a questionnaire. The findings of studied populations in the two groups of definite/or suspected and negative COVID-19 patients were compared. **Results:** During 6 months' period, 137 children with suspected COVID-19 infection were evaluated. Mean age of studied population was 4.3 (0.38) years. The most common symptoms in order were fever, cough, dyspnea and diarrhea. The most common computed tomography scan findings were bilateral ground glass and subpleural involvements. The rate of mortality was 7.3%. COVID-19 polymerase chain reaction test was positive in 22% of the patients. Based on the specialist's diagnosis, 30/25 patients were definite/or suspected to COVID-19 and reminder (79) were negative. O2 saturation <90%, was significantly higher in children with definite/or suspected diagnosis for COVID-19 (46.7% vs. 22.4%,  $P < 0.05$ ). Dyspnea and shivering were significantly higher in children with definite/or suspected diagnosis for COVID-19 than those negative for COVID-19 ( $P < 0.05$ ). Mean duration of hospitalization was significantly associated with level of lactate dehydrogenase ( $P < 0.05$ ). **Conclusion:** The clinical, laboratory, and imaging findings of our studied population were similar to other studies, but outcome was not similar which may be due to our studied population (inpatients cases). It is suggested that a better understanding of the infection in children may give important insights into disease pathogenesis, health-care practices, and public health policies.

**Key words:** COVID-19, child, symptom assessment, medical laboratory science

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## INTRODUCTION

During last decades, outbreaks of three beta coronaviruses, severe acute respiratory syndrome coronavirus (SARS-CoV) in 2002–2003, Middle East respiratory syndrome-CoV (MERS-CoV) in 2012 and SARS-CoV-2 have caused deadly pneumonia, with

mortality rates of 10% for SARS-CoV, 36% for MERS-CoV and 4% for SARS-CoV-2.<sup>[1]</sup> Comparing with SARS-CoV and MERS-CoV, the novel coronavirus appears to have a higher transmissibility and lower mortality rates.<sup>[2]</sup> On March 11, 2020, the World Health Organization announced that the COVID-19 epidemic was upgraded to the pandemic.<sup>[3]</sup> The pandemic has already affected many people worldwide (270 million) including children.<sup>[4]</sup>

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Evidences about COVID-19 infection in children revealed that 1%–5% of diagnosed cases of COVID-19 were children.<sup>[5]</sup> The rate was 1.2% in Italy, 2% in China, and 5% in the United States.<sup>[6]</sup>

Results of a systematic review study regarding the characteristics of the infection among children demonstrated that children have milder form of the disease with lower rate of mortality.<sup>[7]</sup> Although the clinical and radiologic findings of the disease in children were similar to adults, there were few cases of severe pneumonia in children. Laboratory findings such as elevated inflammatory markers and lymphocytopenia were less common in children than adults.<sup>[8]</sup>

Some expert consensus statements have been developed in different countries for the management of COVID-19 in children. Most of them were upgraded based on the reported epidemiological findings in this high-risk population.<sup>[9]</sup> The Iranian protocol for COVID-19 management in children have been developed also.<sup>[10]</sup>

The results of different studies regarding the epidemiologic findings of COVID-19 in children indicated that despite the worldwide spread, the epidemiological and clinical patterns of the COVID-19 remain largely unclear, particularly among children.<sup>[5]</sup> The aim of this study was to evaluate the clinical, laboratory and imaging characteristics, and outcomes of hospitalized children with suspected COVID-19 infection in Isfahan. However, these findings would be helpful for better management of the disease in children.

## MATERIALS AND METHODS

In this cross-sectional study, all children aged <15 years, who referred to Imam Hossien Children's, hospital and Amin hospital, affiliated to Isfahan University of Medical Sciences, and hospitalized as suspected case of COVID-19 were enrolled.

The protocol of the study was approved by ethics committee of Isfahan University of Medical Sciences with a research project number of 198264 and ethics code of IR.MUI.MED.REC.1399.525.

The suspected cases were those children who initially diagnosed with COVID-19 cases based on their clinical manifestations and history of exposure.

History of exposure was defined as exposure of a child with a COVID-19 case, or lived in an epidemic area or community where COVID-19 case (s), within the last 2 weeks.

Clinical manifestations of suspected COVID 19 cases were defined as follows; fever or respiratory symptoms or

digestive symptoms (e.g., vomiting, nausea, and diarrhea) or fatigue; (2) laboratory test: Normal or decreased white blood cell count with lymphocytopenia or increased level of C-reactive protein (CRP); (3) abnormal chest X-ray imaging.<sup>[10]</sup>

During this study, all demographic, clinical, laboratory, and imaging characteristics as well as follow-up data and outcomes of the hospitalized children were recorded by pediatric residents using a questionnaire.

The questionnaire was validated by experts in pediatric infectious disease specialists and the items were according to the diagnostic and follow-up chart of COVID-19 which was developed by experts in pediatric infectious disease.

### Statistical analysis

Data were analyzed using the SPSS software for Windows version 23 (SPSS Inc., Chicago, IL). Continuous and categorical variables were reported as mean standard deviation and number (%), respectively. Clinical, laboratory and imaging characteristics, and outcomes of the studied populations in the two groups of definite/or suspected and negative COVID-19 patients were compared using Chi-square and student *t*-test.  $P < 0.05$  was considered statistically significant.

## RESULTS

In this study, during 6 months period (From March 2020 to August 2020), 137 children with suspected COVID-19 infection were evaluated. The characteristics of studied patients are presented in Table 1. Mean age of studied population was 4.3 (0.38) years. Most of the patients aged 1–4 years old. The most common symptoms in order were fever, cough, dyspnea and diarrhea. The most common CT scan findings were bilateral ground glass and sub pleural involvements.

The rate of mortality in all suspected children to COVID-19 was 7.3%.

COVID-19 polymerase chain reaction (PCR) test was positive in 22% of the patients. Based on the specialist's diagnosis, 31/26 patients were definite/or suspected to COVID-19 and reminder (80) were negative.

Comparison of the characteristics of studied population in the two groups indicated that there was not significant differences between groups except for the rate of low O<sub>2</sub> saturation (<90%), which was significantly higher higher in children with definite/or suspected diagnosis for COVID-19 (46.7% vs. 22.4%,  $P < 0.05$ ). Clinical manifestations of the two groups are presented in Figure 1. Dyspnea and shivering were significantly higher in children with

**Table 1: The characteristics of studied patients**

Variables	n(%) /mean(SD)
Demographic characteristics	
Age (years)*	4.3 (0.38)
Female/male (%)	44.4/56.6
Prematurity (%)	5.3
History of chronic disorders (%)	7
Age groups (%)	
Infant	11.8%
<1 years old	15.8%
1-4 years old	57.5%
>4 years old	14.9%
COVID-19 related data	
COVID-19 PCR test positive/negative (%)	21.9%/78.1%
History of exposure with a COVID-19 patient	32.1%
Mean duration of symptoms before admission* (days)	3.86 (2.53)
Mean duration of hospitalization* (days)	4.81 (3.53)
Clinical manifestations (%)	
Fever	84.4
Cough	47
Dyspnea	30.7
Diarrhea	23.7
Vomiting	21.5
Rash	15.3
Productive cough	14.8
Anorexia	10.4
Fatigue	8.9
Shivering	7.4
Rhinorrhea	5.9
Seizure	3.7
Abdominal pain	3.7
Headache	3.7
Sore throat	3
Myalgia	3
Chest pain	0.7
Anuria	0.7
Biochemical findings	
WBC	9533.85 (13,218.93)
Lymphocytes	36.86 (21.16)
Neutrophils	54.14 (21.84)
Platelet	251,664.59 (146,598.87)
Hemoglobin	11.86 (2.09)
PCT	4.63 (5.33)
LDH	613.15 (345.44)
CRP positive	52.8%
CT scan findings (%)	
No findings	16.1
Bilateral involvement	29.9
Unilateral involvement	6.6
Lobular involvement	1.5
Multinodular involvement	5.8
Sub pleural involvement	16.8
Pleural effusion	3.6
Grand glass pattern involvement	27
Reversed Halo sign involvement	7.3
Crazy paving pattern involvement	1.5

\*Mean (SD), PCT: Procalcitonin, CRP: C-reactive protein, CT: Computed tomography, LDH: Lactate Dehydrogenase, PCR: Polymerase Chain Reaction, WBC: White Blood Count

definite/or suspected diagnosis for COVID-19 than those negative for COVID-19 ( $P < 0.05$ ).

Characteristics of patients with definite/or suspected diagnosis for COVID-19 than negative ones are presented in Table 2.

Regression analysis indicated that from prognostic factors, mean duration of hospitalization was significantly associated with level of lactate dehydrogenase (LDH) ( $P < 0.05$ ).

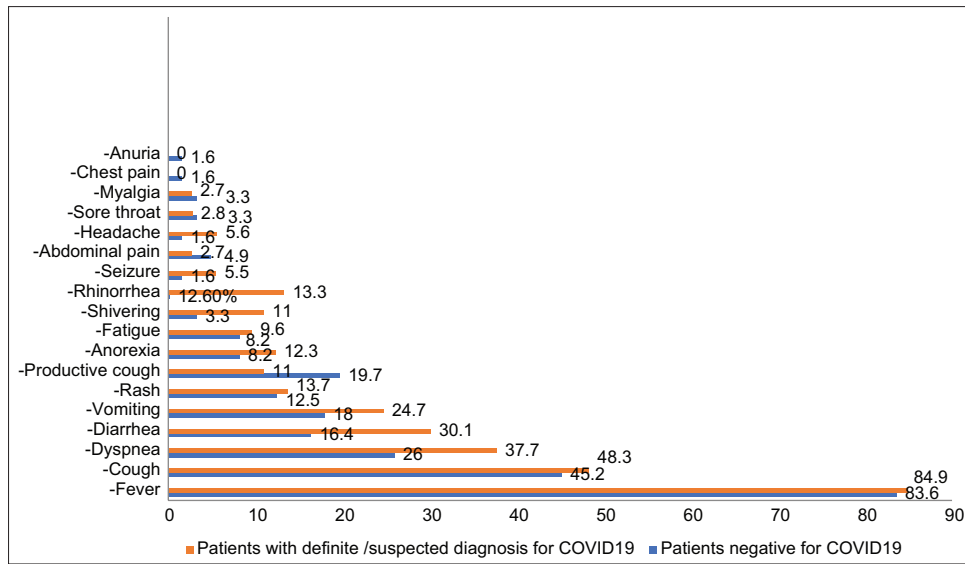
## DISCUSSION

In this study we presented the epidemiologic findings and outcomes of hospitalized children with suspected COVID-19 infection in Isfahan during a 6-month period. Our findings regarding demographic, biochemical and radiologic findings were similar to that reported by other studies from different parts of the world. Comparison of children negative for COVID-19 with those with positive or/and suspected to COVID-19 indicated that in children with definite and/or suspected COVID-19 diagnosis, symptoms such as diarrhea and shivering were more prevalent than those negative for COVID-19. Regarding biochemical indexes, in those who were definite and/or suspected for COVID-19, mean of WBC and platelets were lower than non-COVID-19 cases and lymphopenia was higher than COVID-19 group. There was significant association between mean duration of hospitalization and level of LDH.

Several studies from different countries have been reported their epidemiological findings for COVID-19 in children.<sup>[11-15]</sup>

Results of recent systematic review studies and meta-analyzes indicated that hospitalization and severe cases of COVID-19 in children are less than adults.<sup>[16]</sup> Current evidence suggests that children with certain medical conditions and infants may be at risk for severe disease.<sup>[17]</sup> Considering that the findings of the studies were almost similar, recent studies have suggested that future studies should focus on the risk factors that cause severe disease or those factors which are useful in early diagnosis of COVID-19 in children.<sup>[12]</sup> However, results from South Korea and Italy indicated that early diagnosis of COVID-19 cases in children would result in better outcome.<sup>[18,19]</sup>

The findings of this study regarding epidemiologic findings of children with suspected COVID-19 were similar to that reported by other studies worldwide. Our results indicated that there was not significant difference in clinical presentations of the patients with definite/or suspected diagnosis for COVID-19 than those negative for COVID-19 except for symptoms such as diarrhea and shivering. Results of another recent systematic review indicated that



**Figure 1:** Clinical manifestations of children with definite/or suspected diagnosis for COVID-19 and negative for COVID-19

the clinical presentations of COVID-19 in children are not similar to adults (including fever, cough, and dyspnea) and it could be present by different presentations.<sup>[20]</sup>

The most common clinical presentations of COVID-19 in order were fever, cough, dyspnea, and diarrhea. In a study in Korea, the most common clinical presentations were fever (58%), cough (52%), and fatigue or myalgia (19%).<sup>[21]</sup>

In this study regarding demographic characteristics, although number of children with prematurity, history of chronic disease and male patients were higher in positive/suspected group than negative group, but there were not significant differences between groups.

It seems that the proportion of patients with positive/suspected COVID-19 infection aged <1 year old is higher than negative group, but the difference was not significant.

Considering that in most previous reports, mean age of children was higher than our study.<sup>[11-15]</sup> It is suggested that in our community familiar transmission is more prominent than social contacts. In addition, it may be due to that age <1 year old can be a risk factor for hospitalization due to COVID-19.

Regarding COVID-19-related factors, patients with positive/suspected infection had higher rate of exposure with COVID-19 patients and longer duration of hospitalization. This finding was similar to reported studies.<sup>[11-15]</sup> Hence, it is important to ask about the history of exposure in cases with suspected clinical presentations for COVID-19.

In the current study, there was no significant difference between the two studied groups regarding their biochemical

findings, but the mean of WBC and platelets has trend to be lower in positive/suspected cases than negative patients. Dong *et al.* found that children with suspected COVID-19 had more severe disease than those with laboratory-confirmed disease.<sup>[22]</sup> This suggests that a number of suspected COVID-19 cases may have been caused by other pathogens. Our findings were similar to the mentioned study.

In the current study, high CRP, lymphopenia, and increased level of procalcitonin were reported in 63.3%, 56.6%, and 54.5% of the positive/suspected cases. The findings of a study in Korea showed lower rate of lymphopenia (2.5%, *n* = 2) and increased CRP (16%, *n* = 13) and procalcitonin (3.7%, *n* = 3).<sup>[21]</sup> The difference may be due to the early diagnosis of the infection in Korea.

In a study in Morocco, 68 children with COVID-19 infection were investigated. Based on their study, level of inflammation and coagulation biomarkers and LDH were normal in majority of the cases. In their study, most of the cases had milder form of the infection. The rate in our study was higher which may be due to that we evaluated only inpatients children with COVID-19.<sup>[23]</sup>

In a study in UK, 45 children with COVID-19 infection were studied. Our findings were similar to their study, regarding the rate of high CRP (69%), but the rate of mortality was 0%.<sup>[24]</sup>

Results of a multicenter European study from 25 countries indicated that during April 1 to April 24, 2020, information of 582 patients with positive PCR COVID-19 test with median age of 5 years have been evaluated. Male to female ratio, history of underlying chronic diseases and

**Table 2: Characteristics of patients with definite/or suspected diagnosis and negative for COVID-19**

Variables	Patients negative for COVID-19	Patients with definite/suspected diagnosis for COVID-19	P
Demographic characteristics			
Age (years)*	3.8 (3.2)	4.7 (4.2)	0.25
Female/male	49.2/50.8	41.1/58.9	0.23
Prematurity (%)	4.9	5.6	0.58
History of chronic disorders (%)	28.2	34.4	0.41
Age groups (%)			
Infants	3.4	10.3	0.9
<1 year old	22.1	32.2	
1-4 year old	33.8	32.2	
>4 year old	33.8	32.2	
COVID-19 related data			
History of exposure with a COVID-19 patient (%)	23.0	41.1	0.02
Mean duration of symptoms before admission* (days)	3.79 (2.34)	3.93 (2.70)	0.70
Mean duration of hospitalization* (days)	4.05 (2.01)	5.73 (4.30)	0.00
Biochemical findings			
WBC*	9300.00 (5919)	7797.9 (4139)	0.08
Lymphocytes*	35.02 (18.51)	38.66 (23.26)	0.33
Neutrophils*	57.10 (21.90)	51.42 (23.40)	0.15
Platelet*	291,568.96 (163,143.04)	247,041.66 (120,637.10)	0.07
Hemoglobin* (g/dl)	11.01 (2.21)	11.81 (2.61)	0.80
PCT* (ng/dL)	5.67 (6.68)	4.29 (4.78)	0.42
LDH* (U/L)	588.52 (204.59)	604.00 (176.12)	0.77
CRP positive (>10 mg/L) (%)	60.4	63.3	0.40
CT scan findings (%)			
Bilateral involvement	48.3	70.0	<0.001
Unilateral involvement	42.5	26.5	0.14
Lobular involvement	0	8	<0.001
Multinodular involvement	5	14.3	0.17
Sub pleural involvement	20	44.1	0.24
Pleural effusion	5.9	12.0	0.34
Grand glass pattern involvement	32.5	70.6	<0.001
Reversed Halo sign involvement	7.5	20.6	0.09
Crazy paving pattern involvement	2.5	2.9	0.71
Treatments (%)			
No medication	1.8	0	0.10
Only medication	35.1	32.4	
O2 therapy	42	31.0	
Ventilation	21.1	36.6	
Outcomes (%)			
Death	5.0	10.5	0.26
Discharge	95.0	89.5	

\*Mean (SD). PCT: Procalcitonin, CRP: C-reactive protein, CT: Computed tomography, LDH: Lactate Dehydrogenase, WBC: White Blood Count

mechanical ventilation were 1.15, 45% and 4% in their study, respectively.<sup>[25]</sup> In our study, the rates were 1.43, 34.4%, and 36.6%, respectively. The difference between our study and European study regarding the high rate of using mechanical ventilation may be due to that most of our patients did not diagnosis in the early stage of the disease or the quality of care in the centers was different.

The comparison of performed treatments in the two groups demonstrated that though the difference was not significant, but using mechanical ventilation was higher in positive/

suspected cases and no medication or drug treatment was higher in cases negative for COVID-19.

In our experience, COVID-19-related radiologic findings in positive and/or suspected to COVID-19 group were significantly higher than negative group. Bilateral grand glass findings were significantly higher in positive/suspected group.

An experience from Korea indicated that in the early stages of the disease, the radiologic findings are not observed in the

first stages of the disease. They reported that abnormalities in computed tomography were reported in 63.0% of cases. The most prevalent abnormalities were ground-glass opacities, patchy shadows, and consolidations.

In this study, there was significant relationship between the duration of hospitalization and LDH level at admission time. Considering that hospitalization period was significantly longer in positive/susceptible cases of COVID-19, it is suggested that the level of LDH could be predict the disease course in this group of patients.

In this study, the rate of mortality was high in comparison to reported rates. It may be due to that we only studied inpatients cases.

The limitations of current study were as follows: small sample size and inclusion of only inpatients cases.

## CONCLUSION

The clinical, laboratory, and imaging findings of our studied population were similar to other studies, but outcome was not similar which may be due to our studied population (inpatients cases). It is suggested that a better understanding of the infection in children may give important insights into disease pathogenesis, health-care practices, and public health policies.

Further evaluation of the findings for longer time would be helpful for developing guidelines or questionnaire for the preview and triage of the suspected cases of COVID-19 which consequently result in appropriate early diagnosis, isolation, and management of the disease.

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Nil.

## Conflicts of interest

There are no conflicts of interest.

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