# Demographic, clinical, and paraclinical characteristics of COVID-19 pediatric cases in Zahedan, Iran

Gholamreza Soleimani[1], Fatemeh Akbarirad[1], Elham shafighi shahri[1], and Seyyed Masoud Sajjadi[1]

[1]Zahedan University of Medical Sciences

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**Abstract**

Background Even though children seem to be less vulnerable to the COVID-19 infection, still a diverse range of clinical presentations and symptoms have been reported. We therefore aimed to have a comprehensive study on the evaluation of clinical and paraclinical characteristics of infected children. Methods We included all likely, suspected, and confirmed cases of COVID-19 referred to the Ali-ibn-Abitaleb Hospital of Zahedan. Patients were evaluated at admission time and during hospitalization. Clinical, imaging, and laboratory results were collected and statistically analyzed using SPSS version 23.0. Results Out of the 42 studied children, 32 cases (76% of patients) developed pneumonia. Fever (39 cases, 92.9% of patients), cough (26, 61.9%), tachypnea at admission (24, 57.1%), and pharyngeal erythema (22, 52.4%) were the most common clinical presentations seen in more than 50% of patients. Regarding the imaging findings, ground-glass opacity, seen in CT scan, was the most common (23, 54.8%). Chest X-ray also showed bilateral haziness in 19 patients (45.2%). The mean hospitalization duration was 7.55 nights, and patients on average had fever for 5.55 days. In laboratory findings, anomaly was more noticeable for CRP (79% of patients) and ESR (69% of patients). Conclusion Even though our population was small, most of the findings matched other studies conducted on pediatric cases in Iran or other countries. It was also found that some clinical features such as pneumonia, cough, diarrhea, and tachycardia at admission time were statistically different among age groups.

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Gholamreza Soleimani[1], Fatemeh Akbarirad[2], Elham shafighi shahri[3], Seyyed Masoud Sajjadi[4]

1. Associate Professor of Pediatric Infectious Disease, Department of Pediatrics, School of Medicine, Children and Adolescents Health Research Center, Ali-Ibn-Abitaleb Hospital, Zahedan, Iran
2. MD, Pediatrics assistant, Department of Pediatrics, Ali-ebne abitaleb hospital, Zahedan University of Medical Sciences, Zahedan, Iran
3. MD, Assistant professor, Department of Pediatrics, School of Medicine, Zahedan University of Medical Sciences, Zahedan, Iran
4. MD., Assistant Professor, Department of Cardiovascular Disease, Faculty of Medicine, Zahedan University of Medical Sciences, Zahedan, Iran

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Keywords: COVID-19, Pediatrics, SARS-CoV-2, Clinical presentations

Introduction

The cases of pneumonia associated with what was called later the novel coronavirus first reported in Wuhan, China in December 2019 (1). The virus was formally named SARS-CoV-2 due to its similarities with SARS which emerged in 2003 (2). Later, the disease was officially named COVID-19 (coronavirus disease 2019) by the World Health Organization (WHO). It was then spread to the whole world such that in March 2020, WHO declared it a pandemic. Despite all efforts, the disease is still spreading and has expanded to almost the whole world. Until 28 July 2020, more than 16 million people have contracted the virus, and around 650, 000 cases lost their life (3).

COVID-19 has been found to cause a very diverse range of symptoms and consequences, if any, from very mild ones, such as sore throat and runny nose to very severe ones such as pneumonia, respiratory distress, and death (4-6). In the first few months after the emergence of the virus, COVID-19 was known more as an adult disease with very few pediatric cases reported and very few mild symptoms in children (7-9). For example, in the first published reports from Wuhan, no confirmed pediatric case was mentioned (10), and by January, less than one percent of the patients in Wuhan were reported to be children (4). A similar trend has been seen in Italy where till 21 July 2020, 1% and 1.7% of 244,708 confirmed cases have been children respectively in the age range of 0-9 and 10-19 years, with 4 death (11).

However, later and especially after March 2020, some children infected with COVID-19 presented with severe clinical symptoms similar to the diagnosis of Kawasaki disease (KD), which was termed as multisystem inflammatory syndrome in children (MIS-C) (12). More research showed that the clinical presentations of COVID-19 in children were not consistent either and may include a diverse range (13, 14).

Iran was one the first countries badly hit by the virus, and despite all efforts, is unfortunately still the top state in the Middle East with more than 293,000 confirmed cases and around 16,000 death by 28 January 2020 (3). There have been some studies on the epidemiological analysis of COVID-19 in the Iranian population (15, 16), but to the best of our knowledge, very few comprehensive studies (19, 20) on the clinical presentations of this disease especially among children have been conducted. We therefore aimed to have a comprehensive study on the evaluation of clinical and paraclinical characteristics of infected children in Zahedan, in the southeast of Iran, to provide insights for the early diagnosis and efficient management of the infection.

Methods

Study design and population

We recruited pediatric patients (under the age of 18 years) admitted between 21 March and 21 July 2020 as suspected, likely, and confirmed cases of COVID-19 to the Ali-ibn-Abitaleb Hospital of Zahedan, affiliated to the Zahedan University of Medical Sciences.

A suspected case was defined as a patient with dry cough, chills, or sore throat with difficulty breathing, and with or without fever with no other known etiology for the symptoms. Besides, a patient with fever and shortness of breath, diarrhea, nausea and vomiting, headache, abdominal pain, with or without having symptoms similar to Kawasaki disease who had been in close contact with a suspected or confirmed case of COVID-19 in the previous 14 days was also considered as a suspected case.

A likely case was defined as a patient having imaging findings corresponding to COVID-19. In addition, patients with pneumonia who did not respond to treatments and whose clinical conditions deteriorated rapidly or resulted in death were also considered as likely cases. The third group of patients categorized as likely cases were patients whose polymerase chain reaction (PCR) test was unclear and inconclusive (neither positive, nor negative). Finally, a patient with some of the symptoms discussed above whose PCR test was positive was defined as a confirmed case.

Children who met the inclusion criteria were included in the study. At the admission time, a laboratory test, an X-ray imaging, and a chest computerized tomography (CT) scan were done, and all findings along with clinical features of the patients were recorded. Accordingly, a questionnaire was completed by the care team with the participation of the patient and their parents which also included the demographic information and questions about potential exposure and source of transmission, and if anyone else in the family had been a confirmed or suspected case of COVID-19.

Inclusion and exclusion criteria

As discussed, children (0-18 years) who were admitted from March 21$^{st}$ to July 21$^{st}$, 2020 as a suspected, likely, or confirmed case of COVID-19 were included. The patients for whom the final confirmed diagnosis was something else than COVID-19 were excluded.

Ethical considerations

A written informed consent form was signed by the parents if they were willing to participate. This study was approved by the Ethics Committee of the Zahedan University of Medical Sciences.

Statistical analyses

We have used SPSS software version 23.0 for statistical analysis. The frequency distribution of features versus the age groups was compared using the Fisher exact test. A P-value $< 0.05$ was considered statistically significant. For quantitative metrics, mean and standard deviation (SD) are provided, and categorial metrics are presented with count and percentage.

Results

We included 42 pediatric patients, from a few months ($<$ 1 year) to 18 years old; 27 of them were confirmed cases with a positive PCR test. The patients were divided into four groups of age as follows: <1 year (N=6, percentage =14.3%), 1-5 years (10, 23.8%), 6-10 years (16, 38.1%), and 11-18 years (10, 23.8%). The sex distribution was 18 males and 24 females. All clinical and paraclinical findings are summarized in Table 1, and Table 2 provides more details about the feature of fever. Laboratory findings along with the duration of hospitalization (quantitative features) are presented in Table 3 for the whole 42 patents, and in Table 4 per age group.

As can be seen in Table 1, regarding the infection diagnosis, patients were evaluated to diagnose whether they had an asymptotic infection, suffered from an upper respiratory tract infection (URTI), and had pneumonia or not. Pneumonia was diagnosed in 76.2% of patients (N=32). Fever and cough were the most common symptoms seen in more than 60% of patients while vomiting was the least frequently seen, only in 28.6% of patients.

Regarding the source of contracting the virus or being exposed to it, as can be seen in Table 1, the source was unknown in most of the patients (42.9%, N = 18), followed by having a confirmed (21.4%, N = 9) or suspected (21.4%, N = 9) case in the family.

As presented in Table 2, patients' fever was monitored during the hospitalization period, and the fever duration (how many days) and the highest value were also recorded. In around 50% of patients, fever lasted for 5 days or more. Also, in 66.7% of patients, the highest value recorded was in the range of 38.1 °C and 39 °C. Note that, considering the number of days with fever as a quantitative feature, its descriptive statistics are provided in Table 3 where it can be seen that on average, fever lasted 5.55 days.

Applying Fisher's exact test, we compared the clinical symptoms and signs among different age groups. The population was small, so the results may be approached by caution. As you could see in Table 1 (only the number of positive cases is shown), pneumonia and cough occurrence were significantly higher in older children compared to infants. In addition, diarrhea and tachycardia at admission were significantly less common in the age range of 1-5 years.

In Table 3, we can also see the statistics for the duration of hospitalization where on average, a patient spent 7.55 nights in the hospital. Laboratory results are also summarized in Table 3 for the whole studied population, and in Table 4, the mean and median per age group are provided. Note that two complete blood cell (CBC) tests were taken: one on at admission and one later during hospitalization. Considering the normal (reference) range for each laboratory feature, we also calculated the number of cases which had an abnormal result. Features with the most anomaly among the whole population were the level of hemoglobin (Hb), platelets (Plt), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), lymphocyte, and white blood cells (WBC).

Discussion

In this study, 42 COVID-19 pediatric patients (suspected, likely, and confirmed) were evaluated, and their clinical and paraclinical features including symptoms at admission, imaging findings, and laboratory analysis results along with the demographic information and potential source of exposure were collected and analyzed. It what follows, we first compare our results with other studies conducted also on children (8,9, 11, 19-21), then with some any-age studies, if applicable (4-6).

The sex distribution was almost balanced in our patients even though our group was small. However, looking at the reports from different countries, we can see likewise that among children, no substantial difference is seen between the number of male and female cases (51% boys in Italy until 21 July 2020 (11), 57% in the US (21), and 56.6% boys in China reported by Dong et al. (9)). In another study on Iranian children by Soltani et al. (19), there were also 46.7% male out of 30 children (19).

Fever was found to be the most common symptom (in 92.9% of cases) followed by cough (61.9%), tachypnea (57.1%), and pharyngeal erythema (52.4%). In the study by Lu et al. on 171 confirmed pediatric cases of COVID-19 in Wuhan (8), cough (48.5%), erythema (46.2%), and fever (41.5%) were the most frequent symptoms, which are analogous to our findings. However, fever was much more frequent among our cases. Besides, 70% of our patients had a fever of $> 38$ °C compared to only 32.1% in the study of Lu et al. (8). In the Centers for Disease Control and Prevention (CDC) report (21), fever (56%) and cough (54%) were the most common symptoms too, among 291 American pediatric patients (21). Our results are however also aligned with two other studies done in China and reviewed by Ludvigsson where 60.0% of 10 and 76.1% of 134 pediatric patients had a fever (14).

In the US, among pediatric cases with known information on each symptom, 56% of cases had fever, and 54% reported cough (21). In Iranian children, in the Soltani et al.'s study, fever was reported for 76.7% of 30 patients, followed by tachypnea (76.7%), dyspnea (66.7%), and cough (53.3%) (19), which are consistent with our results. The same three symptoms and signs of fever, cough, and tachypnea reported in all 9 Iranian patients by Rahimzadeh et al. (20)

One of the potential reasons for difference in fever frequency in different studies can be reporting the fever

at admission time versus during hospitalization. Note that in most studies with any-age patients (mostly adults), fever was usually the most common symptom with high percentages such as 98.6% of 138 patients (6), 77% of 94 cases (5), 71% of 10944 US cases (21), and 88.7% of 1099 Chinese patients (4).

Considering the least frequent symptoms, our findings correspond to most other studies which reported diarrhea and vomiting as the least common ones. However, while respectively 35.7% and 28.6% of our patients experienced diarrhea and vomiting, close to what reported by Soltani et al. (19), Lu et al. reported respectively 8.8% and 6.4% among 171 patients (8), and in the US, 13% and 11% of 291 pediatric patients had respectively diarrhea and vomiting (21). The difference can probably be due to the small size of our population. Guan et al. also indicated that vomiting ($< 5.0\%$) and diarrhea (3.8%) were uncommon among 1099 any-age patients (4), and Li et al. mentioned diarrhea as an infrequent feature in only 13 out of 94 (14%) any-age cases (5).

Our patients were hospitalized on average 7.55 nights with 50% more than 7 nights. Even though the duration of hospitalization has not been mentioned in many articles, the percentage of hospitalized cases in our study ($> 90\%$) seems higher than other studies. While the size of population could be an impacting factor, it is worth reminding that reports such as the one by CDC (21) include aggregated data mostly from walk-in COVID-19 test centres, but in our study, patients referred to the hospital which usually occurs when the symptoms are more advanced.

While the potential source of exposure was unknown in 42.9% of our patients and was a suspected or confirmed family member in 42.8% of them, in the Lu et al.'s study, a family member (suspected or confirmed) accounted for 90.1% of 171 patients, and in only 8.8%, the source was unknown (8). However, in the report by CDC (21), the exposure information was only known for 184 out of 2572 pediatric patients (7.2%), which was exposure in the family or community (21). In Soltani et al.'s report, the source of exposure has been reported only for 11 cases (36.7%), which had been a close contact with a suspected or confirmed case of COVID-19 (19). While, by nature, it is difficult to have accurate data for the source of exposure, the size of studied population and the social conditions (whether schools and playgrounds were closed, travel was allowed, and businesses were open or not) all affect the frequency distribution of potential sources of exposure. Note that there was no significant difference between different age groups in terms of the source of exposure.

Regarding the imaging findings, CT scan revealed ground-glass opacity in 54.8% of cases, which matches the findings of Xia et al. with ground-glass opacity seen in 60% of 20 patients (17) and Lu et al. with 32.7% out of 171 patients (8), also of the Soltani et al. study with 73.1% of 19 patients (19). Local and bilateral patchy shadowing were not very frequent neither in our work (respectively 14.3% and 14.3%) nor in the Lu et al.'s work (18.7% and 12.3%). Among the any-age population, the percentage of cases with ground-glass opacity was similar, for example, 56.4% in Guan et al., but their number of cases with bilateral patchy shadowing was high (51.8%) compared to our study (4).

Laboratory tests were done at the admission, however the CBC test was repeated later during hospitalization, for most of the patients (shown with suffix -1 and -2 in Tables 3 and 4). Even though, on average, the number of while blood cells (WBC) and platelets were lower in the second test, the Wilcoxon signed-rank test showed no significant difference between the paired samples of any of the CBC metrics, before and during treatment. The difference that can be seen should mainly be due to the patients who were released without having the second test.

In the last column of Table 3, it can be seen that the most percentage of anomaly among patients is for hemoglobulin in 90% of patients (normal range: $> 13.6$ g/dL), followed by CRP in 79% of patients (normal range: $> 6$ mg/L), and ESR in 69% of them (normal range: $<20$ mm/h). The number of cases with abnormal levels of WBC, platelets, and lymphocyte was also considerably high. The low hemoglobulin level indicates anemia in most of our patients. It would be difficult to interpret it and associate it with their infection as we did not have any background information. However, high levels of CRP and ESR should be associated with the COVID-19 infection, as reported in other works too. In the study by Cai et al. (22) on 10 Chinese children, 6 children had high CRP level even though the maximum level they reported was 35 mg/L while

50% of our patients had a CRP level higher than 90 mg/L. In the work by Soltani et al. (19) on 30 Iranian children, positive CRP was reported for 23 out of 30 cases (77%) and abnormal ESR was seen in 11 out of 25 cases (44%), which match our findings. However, only 5 patients in their study (17%) had an abnormal platelet count while in our work 45% were abnormal. Besides, 100% and 90% of 10 patients in the study by Rahimzadeh et al. (20) also had positive CRP and elevated ESR respectively (20).

In Table 4 and using the Kruskal–Wallis test (non-parametric ANOVA) to compare some of the quantitative features among age groups, C-reactive protein (CRP) was the only metric which was statistically different among four age groups (P: 0.020), as can be seen that it is lower in the 1-5 years age range, implying that CRP for diagnosis of COVID-19 could be more reliable in the higher ages.

In Dong et al. retrospective study on 2143 Chinese children, they concluded that children of all ages are susceptible to be infected with COVID-19, and even though their clinical manifestations are generally milder, younger children especially infants are at risk (9). The mechanism of action of SARS-CoV-2 has become more clear thanks to its resemblance to SARS and a lot of ongoing research (18). However, the reason of children being less prone to COVID-19, what Cristiani et al. (7) call it the "secret" of children, is not still very clear, but they concluded that it should be due to the interaction between the children's immunological response and the virus pathogenetic mechanisms (7). They discussed that as children show elevated expression of angiotensin-converting enzyme 2 (ACE2) and lymphocyte count, and since their immune system experiences frequent viral infections and thus becomes more trained and adaptive, they have milder symptoms compared to adults (7).

The main limitation of this study is that the data were collected from a single center, so the population was small. Limited population and some missing data prevent us from confidently associating the observations with the COVID-19 infection.

## Conclusion

Children at any age seem to be susceptible to COVID-19, and even though their symptoms are milder, they still present a diverse range of clinical presentations. This study provided a comprehensive report of demographic, clinical, imaging, and laboratory findings of 42 children as suspected, likely, or confirmed cases of COVID-19 in Zahedan, Iran. Even though our population was small, most of the findings matched other studies conducted on pediatric cases in other countries. It was also found that some clinical features such as pneumonia, cough, diarrhea, and tachycardia at admission time were statistically different among age groups. In terms of laboratory findings, CRP, ESR, lymphocyte, platelets, and WBC had more abnormal cases. While we hope that no larger population of patients will be seen, further studies may be conducted by aggregating data from different centers and regions to have more conclusive insights.

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## Conflict of interest

No conflict of interest to declare.

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