Comparison of RT-PCR, lung CT Scan, and Anti-COVID-19 Antibody Results in Hospitalized Children Suspected for COVID-19

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Abstract

Background: Mild symptoms of COVID-19 in children may lead to delayed or misdiagnosis. Reverse transcription polymerase chain reaction (RT-PCR) is an approved laboratory method for detecting COVID-19 virus. Given that COVID-19 is considered an emerging disease, its diagnostic methods in children have not yet been well compared. Therefore, this study was designed to compare RT-PCR, lung CT scan, and anti-COVID-19 antibody results in hospitalized children suspected for COVID-19.

Methods: This cross-sectional study was conducted on patients less than 18 years of age, suspected fot COVID-19, and admitted to Shahid Sadoughi Hospital in Yazd, Iran, from February 2020 to February 2021. All hospitalized children who had suspected COVID-19 based on their initial clinical symptoms or signs, and had undergone RT-PCR were included in the study. Demographic data such as age, sex, contact history with COVID-19 patients, clinical manifestations, outcome, comorbidities, and information on other paraclinical procedures were collected by checklist.

Results: In total, 53.3% of the patients were male, and 59% were under five years old. The most common symptom was fever (81%), followed by respiratory distress (34.3%) and diarrhea (26.7%), and cough (19%). Additionally, a significant relationship was observed between respiratory symptoms and a positive PCR test (P = 0.020) and positive lung CT findings (P = 0.017). This study failed to find a significant association between PCR, chest CT scan, and anti-COVID-19 antibody results with ICU admission, endotracheal intubation, and death (P>0.05).

Conclusions: Our findings showed a significant association between respiratory symptoms, positive RT- PCR, and positive CT findings. But ICU admission, endotracheal intubation, and death were not significantly correlated with PCR, chest CT scan, and anti-COVID-19 antibodies.

Key Words: COVID-19; Computed Tomography, Hospitalized Children, Polymerase Chain Reaction, Reverse Transcriptase.

1- INTRODUCTION

The novel coronavirus, or severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was first appeared in Wuhan, China, in December 2019 and declared a pandemic by the World Health Organization (WHO) due to its widespread transmission. It is still propounded a serious threat to the health of the people of the world. (1-3).

The most common manifestations of COVID-19 in patients are fever, cough, and fatigue, while other symptoms include headache, diarrhea, abdominal pain, and vomiting (3, 4). Considerable evidence shows that children and adolescents are less susceptible to infection and less likely to develop severe illness after infection (5-7). Even though the symptoms of COVID-19 in children are similar to those in adults, they often show milder symptoms or even are asymptomatic. Out of the common symptoms, gastrointestinal complaints have been reported more in children. In addition, it is difficult to diagnose children with COVID-19 who have no or mild respiratory symptoms (3, 8, 9). The deceptive nature of gastrointestinal symptoms compared to respiratory symptoms in COVID-19 leads to delay or no diagnosis. Also, some patients excrete the virus only in the stool during the disease without any respiratory symptoms and have negative respiratory samples (10). Since early detection of COVID-19 is essential in preventing and controlling this pandemic, clinical signs and symptoms alone cannot confirm the diagnosis of COVID-19, especially for patients who show early symptoms (11).

Using reverse transcription polymerase chain reaction (RT-PCR) is one of the most widely used and accurate laboratory methods for detecting COVID-19 virus. Moreover, specific IgM and IgG antibodies and radiological examinations, including chest radiography and chest computed tomography (CT), are other COVID-19 diagnostic tests (11, 12). Low sensitivity of RT-PCR leads to a relatively high number of false-negative results that can mistakenly show a patient with COVID-19 without infection and continue the undetectable transmission of the virus (13).

Radiological manifestations of COVID-19 vary between age groups, and High-resolution computed tomography (HRCT) findings may be milder in younger patients (14). Numerous studies in children have reported normal chest CT in a large percentage of children with asymptomatic or mild COVID-19. Due to the unacceptable percentage of false-negative cases in children, chest CT scan is not considered appropriate as a screening tool to rule out COVID 19 in pediatric patients with few or no symptoms (8, 12, 15).

In addition to viral nucleic acid assays, detecting specific antibodies can be beneficial in diagnosing COVID-19, including subclinical cases (16, 17). A positive result portends that the person has been exposed to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The presence of IgM antibodies may indicate an active or recent infection; on the other hand, IgG antibodies can often indicate a past infection, although it does not rule out a recent disease, especially when IgM antibodies are detected simultaneously (18).

A noteworthy point about real-time RT-PCR testing is the risk of eliciting false negatives and false positives. There are many reports of undiagnosed suspected cases with typical clinical manifestations of COVID-19 and dedicated computed tomography images. (11)

Given the emergence of this disease and the limited experience with diagnostic methods, the report of our experience in diagnostic tests for children may share helpful information with others. Therefore, this study aimed to explore and compare the results of RT-PCR (the gold standard for diagnosis of COVID-19 in this study), lung CT scan, and specific antibodies in the diagnosis of hospitalized children with suspected COVID-19. Furthermore, the relationship between different diagnostic methods with the course and outcome of patients was evaluated.

2- METHODS

This descriptive, cross-sectional study was conducted on 105 patients less than 18 years old, suspected of having COVID-19 infection, who were admitted to Shahid Sadoughi Hospital in Yazd, central Iran, from February 2020, to February 2021. The ethics committee of Shahid Sadoughi University of Medical Sciences approved this study protocol. (Ethics Code: IR.SSU.REC.1399.076).

All hospitalized children who were suspected of having COVID-19 based on their initial clinical symptoms or signs and had undergone RT - PCR to confirm the diagnosis were included in the study. We used a checklist to collect data. At the beginning, patient demographic information such as age, sex, and history of contact with suspected COVID-19 patients was recorded. Then, information about patients' clinical symptoms at the time of referral, outcome, history of previous diseases and comorbidities, and information about other paraclinical procedures were collected in the next section. A chest HRCT scan was performed for subjects who had respiratory symptoms such as tachypnea, respiratory distress, or oxygen saturation below 95% at the time of admission or during hospitalization. COVID-19 IgM and IgG were tested for suspected cases by negative RT-PCR during hospitalization. In other

cases, the antibodies were measured within one month.

All analyses were done using SPSS software (SPSS 25, SPSS Inc., Chicago, IL, USA). The level of statistical significance in all tests was considered at 0.05.

3- RESULTS

In this study, the results of RT-PCR test, chest CT scan, and COVID-19 specific antibodies tests were compared in 105 children hospitalized with probable COVID-19.

Out of 105 cases, 56 (53.3%) were male, and 49 (46.7%) were female. More than half of the patients were under five years old (59%). About 36.2% of participants had an underlying disease, with chronic kidney disease and epilepsy being the most common. Only 36 patients (36.2 %) had a history of contact with a suspected COVID-19 patient. See details in **Table 1**. The most frequent complaint in this study was fever (81%). Other clinical manifestations were respiratory distress (34.3%), diarrhea (26.7%), and cough (19%), respectively.

RT-PCR test was positive in 61.9% of participants. Moreover, 41% of patients had positive chest CT findings, including unilateral or bilateral peripheral ground-glass opacities or other findings indicating SARS-CoV-2. Serum-specific antibodies were detected in 26.7% of cases.

Of the 40 patients suspected of COVID-19 and negative PCR, 30 and 27 underwent lung CT and specific antibodies, of which 23 and only 10 had positive findings confirming SARS-CoV-2, respectively.

In this study, there was a significant relationship between the presence of respiratory symptoms and a positive PCR test (P=0.020) as well as positive findings of lung CT (P=0.017). Nevertheless, no relationship was found between respiratory symptoms and anti-COVID-19 antibody

positivity (P>0.05). Our study did not find any association between other symptoms (gastrointestinal, neurological, etc.) with RT-PCR, lung CT scan, and anti–SARS-CoV-2 antibodies.

The relationship between PCR test, chest CT scan, and specific serum antibody results with the patients' clinical outcomes was insignificant (P>0.05) (**Table 2**).

47(44.8 %) 47 patients were admitted to the ICU. But ICU admission, endotracheal intubation, and death were no significantly correlated with PCR, chest CT scan, and anti-COVID-19 antibodies (P>0.05).

Table-1: Demographic information and underlying diseases of children with suspected COVID-19

Variables	No. of Children	% of Children
Gender		
Male	49	46.7
Female	56	53.3
Age group		
≤1 month	13	12.4
>1 month – 1 year	26	24.8
>1 year- 5 year	23	21.8
>5 year-12 year	36	34.3
>12year	7	6.7
Underlying disease		
Yes	38	36.2
No	67	63,8
Total	105	100

Table-2: Frequency distribution of PCR, chest CT scan, and antibody results according to patient's clinical outcome

variable		Discharge (Good)	Death	Total	P-value
PCR	Positive	57(62.6%)	8(57.1%)	65(61.9%)	0.693
	Negative	34(37.4%)	6(42.9%)	40(38.1%)	
	Total	91(100%)	14(100%)	105(100%)	
CT scan	No CT	35(38.5%)	5(35.7%)	40(38.1%)	0.282
	Positive	35(38.5%)	8(57.1%)	43(41%)	
	Negative	21(23.1%)	1(7.1%)	22(21%)	
	Total	91(100%)	14(100%)	105(100%)	
Antibody	Not checked	29(31.9%)	7(50%)	36(34.3%)	0.343
	Positive	26(28.6%)	2(14.3%)	28(26.7%)	
	Negative	36(39.6%)	5(35.7%)	41(39%)	
	Total	91(100%)	14(100%)	105(100%)	

4- DISCUSSION

The outbreak of Coronavirus disease 2019 is an unprecedented global public health challenge. However, reports to date indicate that COVID-19 is less common in children than in adults (19, 20).

According to our study, RT-PCR test was positive in 61.9% of hospitalized patients

suspected of having COVID-19. Numerous studies still recommend RT-PCR as the first tool to diagnose the disease. Furthermore, RT-PCR is mentioned as the preferred diagnostic test for SARS-CoV-2 (21, 22).

The results of the present study showed that the ratio of males to females was 1.14. Some studies reported equal gender ratios in children, while others described the preference of one gender over the other (20, 23, 24). In general, it seems that, at least in children, there is no gender preference for COVID-19. About 12.4% of the admitted cases in this study were newborns, and 59% of the patients were under five years. Shahbaznejad et al. reported that 3% and 34% of the patients in their study were newborns and under five years, respectively (24). Based on the study of Dong et al., 40% of cases were under five years old (25). Qiu et al. and Shekerdemian et al. declared that 28% and 30% of the cases were younger than five years, respectively (26,27). This study revealed that, as in many studies, the most common complaints of patients at the time of referral were fever and respiratory problems (28-31). It should also be noted that Wang et al. have identified fever and cough as the most common symptoms in children (32). A systematic review and meta-analysis study indicated that fever, cough, and tachypnea were the most common clinical signs of COVID-19 (33). However, de Souza et al. have stated that fever and respiratory manifestations should not be considered a COVID-19 hallmark in children, and a high level of clinical suspicion is necessary for pediatricians to diagnose children infected with SARS-Cov-2 (19).

More than 75% of children with COVID-19 respiratory symptoms and their PCR was negative showed abnormal CT findings on the chest, indicating SARS-CoV-2 infection. It seems that in cases where PCR is negative despite considerable clinical suspicion of COVID-19, performing a CT scan of the lung is very contributory in diagnosis. One study noted that chest CT might prepare useful information for diagnosis and management in cases with high clinical suspicion and negative RT-PCR results. However, the final diagnosis is still based on RT-PCR (34). A systematic review provides similar results, suggesting that computed tomography may be helpful in cases where the results of the PCR test are false negative while the patient is clinically symptomatic (35). Moreover, other studies have justified the use of chest CT in patients with typical clinical symptoms in highly infected areas or in close contact with COVID-19-infected patients who tested negative for RT-PCR (36).

The present study's findings showed that, apart from respiratory symptoms, other manifestations of COVID-19, such as gastrointestinal and neurological symptoms, were not significantly associated with a positive RT-PCR test and positive findings of chest CT. Sinha IP recommended that chest CT may not be helpful for children with COVID-19 infection with few or no respiratory symptoms, and CT changes cannot instruct clinical decisions well (37). The results of another study showed that in COVID-19-positive children with mild upper respiratory symptoms, chest CT might be normal in 35-50% of the cases (8).

The recent study did not find a significant relationship between results of RT-PCR test, chest CT scan, and specific serum antibodies with the frequency distribution of ICU admission, endotracheal intubation, and mortality rate in the participants (P>0.05). Thus, it can be said that physicians cannot predict their patient's prognosis solely based on radiological findings or RT-PCR and antibody results and should determine the treatment plan based on various factors, especially the clinical course of patients.

5- CONCLUSION

More than two-thirds of patients had positive RT-PCR tests. The results revealed a significant relationship between the presence of respiratory symptoms and positive PCR test and positive lung CT findings. ICU admission, endotracheal intubation, and death were not significantly correlated with PCR test, chest CT scan, and anti-COVID-19 antibody results.

6- CONFLICT OF INTEREST: None.

7- ACKNOWLEDGMENTS

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9- REFERENCES

1. Ornell F, Schuch JB, Sordi AO, Kessler FHP. "Pandemic fear" and COVID-19: mental health burden and strategies. Braz J Psychiatry. 2020; 42(3):232-5.

2. Ren L-L, Wang Y-M, Wu Z-Q, Xiang Z-C, Guo L, Xu T, et al. Identification of a novel coronavirus causing severe pneumonia in human: a descriptive study. Chin Med J (Engl). 2020; 133(9):1015-24.

3. Rajapakse N, Dixit D. Human and novel coronavirus infections in children: a review. Paediatr Int Child Health. 2021; 41(1):36-55.

4. Yasuhara J, Kuno T, Takagi H, Sumitomo N. Clinical characteristics of COVID-19 in children: A systematic review. Pediatr Pulmonol. 2020; 55(10):2565-75.

5. Viner RM, Mytton OT, Bonell C, Melendez-Torres G, Ward J, Hudson L, et al. Susceptibility to SARS-CoV-2 infection among children and adolescents compared with adults: a systematic review and meta-analysis. JAMA Pediatr. 2021; 175(2):143-56.

6. Davies NG, Klepac P, Liu Y, Prem K, Jit M; CMMID COVID-19 working group, Eggo RM. Age-dependent effects in the transmission and control of COVID-19 epidemics. Nat Med. 2020; 26(8):1205-11.

7. Forbes H, Morton CE, Bacon S, McDonald HI, Minassian C, Brown JP, et al. Association between living with children and outcomes from covid-19: OpenSAFELY cohort study of 12 million adults in England. BMJ. 2021; 372:n628.

8. Merkus P, Klein WM. The value of chest CT as a COVID-19 screening tool in children. Eur Respir J. 2020; 55(6):2001241.

9. Pouletty M, Borocco C, Ouldali N, Caseris M, Basmaci R, Lachaume N, et al. Paediatric multisystem inflammatory syndrome temporally associated with SARS-CoV-2 mimicking Kawasaki disease (Kawa-COVID-19): a multicentre cohort. Ann Rheum Dis. 2020; 79(8):999-1006.

10. Yang L, Tu L. Implications of gastrointestinal manifestations of COVID-19. Lancet Gastroenterol Hepatol. 2020; 5(7):629-30.

11. Tahamtan A, Ardebili A. Real-time RT-PCR in COVID-19 detection: issues affecting the results. Expert Rev Mol Diagn. 2020; 20(5):453-4.

12. Bayramoglu Z, Canıpek E, Comert RG, Gasimli N, Kaba O, Sarı Yanartaş M, et al. Imaging Features of Pediatric COVID-19 on Chest Radiography and Chest CT: A Retrospective, Single-Center Study. Acad Radiol. 2021; 28(1):18-27.

13. Karam M, Althuwaikh S, Alazemi M, Abul A, Hayre A, Alsaif A, et al. Chest CT versus RT-PCR for the Detection of COVID-19: Systematic Review and Meta-analysis of Comparative Studies. JRSM Open. 2021; 12(5):20542704211011837.

14. Chen Z, Fan H, Cai J, Li Y, Wu B, Hou Y, et al. High-resolution computed tomography manifestations of COVID-19 infections in patients of different ages. Eur J Radiol. 2020; 126:108972.

15. Steinberger S, Lin B, Bernheim A, Chung M, Gao Y, Xie Z, et al. CT features of coronavirus disease (COVID-19) in 30 pediatric patients. AJR Am J Roentgenol. 2020; 215(6):1303-11.

16. Xiang F, Wang X, He X, Peng Z, Yang B, Zhang J, et al. Antibody detection and dynamic characteristics in patients with coronavirus disease 2019. Clin Infect Dis. 2020; 71(8):1930-4.

17. Guo L, Ren L, Yang S, Xiao M, Chang D, Yang F, et al. Profiling Early Humoral Response to Diagnose Novel Coronavirus Disease (COVID-19). Clin Infect Dis. 2020; 71(15):778-85.

18. Mathur G, Mathur S. Antibody Testing for COVID-19. Am J Clin Pathol. 2020; 154(1):1-3.

19. de Souza TH, Nadal JA, Nogueira RJ, Pereira RM, Brandão MB. Clinical manifestations of children with COVID-19: a systematic review. Pediatr Pulmonol. 2020; 55(8):1892-9.

20. Zare-Zardini H, Soltaninejad H, Ferdosian F, Hamidieh AA, Memarpoor-Yazdi M. Coronavirus disease 2019 (COVID-19) in children: prevalence, diagnosis, clinical symptoms, and treatment. Int J Gen Med. 2020; 13:477-82.

21. Poortahmasebi V, Zandi M, Soltani S, Jazayeri SM. Clinical performance of RT-PCR and chest CT scan for COVID-19 diagnosis; a systematic review. Front Emerg Med. 2020; 4(2s):e57-e.

22. Sankar J, Dhochak N, Kabra SK, Lodha R. COVID-19 in Children: Clinical Approach and Management. Indian J Pediatr. 2020; 87(6):433-42.

23. Jiehao C, Jin X, Daojiong L, Zhi Y, Lei X, Zhenghai Q, et al. A Case Series of Children with 2019 Novel Coronavirus Infection: Clinical and Epidemiological Features. Clin Infect Dis. 2020; 71(6):1547-51.

24. Shahbaznejad L, Rouhanizadeh H, Navaeifar MR, Hosseinzadeh F, Movahedi FS, Rezai MS. Clinical characteristics and outcomes of COVID-19 in children in northern Iran. Int J Pediatr. 2021; 2021: 5558287.

25. Dong Y, Mo X, Hu Y, Qi X, Jiang F, Jiang Z, et al. Epidemiology of COVID-19 among children in China. Pediatrics. 2020; 145(6):e20200702.

26. Qiu H, Wu J, Hong L, Luo Y, Song Q, Chen D. Clinical and epidemiological features of 36 children with coronavirus disease 2019 (COVID-19) in Zhejiang, China: an observational cohort study. Lancet Infect Dis. 2020; 20(6):689-96.

27. Shekerdemian LS, Mahmood NR, Wolfe KK, Riggs BJ, Ross CE, McKiernan CA, et al. Characteristics and outcomes of children with coronavirus disease 2019 (COVID-19) infection admitted to US and Canadian pediatric intensive care units. JAMA Pediatr. 2020; 174(9):868-73.

28. Zimmermann P, Curtis N. COVID-19 in children, pregnancy and neonates: a review of epidemiologic and clinical features. Pediatr Infect Dis J. 2020; 39(6):469-77.

29. Hoang A, Chorath K, Moreira A, Evans M, Burmeister-Morton F, Burmeister F, et al. COVID-19 in 7780 pediatric patients: a systematic review. EClinicalMedicine. 2020; 24: 100433.

30. Parri N, Lenge M, Buonsenso D; Coronavirus Infection in Pediatric Emergency Departments (CONFIDENCE) Research Group. Children with Covid-19 in pediatric emergency departments in Italy. N Engl J Med. 2020; 383(2):187-90.

31. Derespina KR, Kaushik S, Plichta A, Conway Jr EE, Bercow A, Choi J, et al. Clinical manifestations and outcomes of critically ill children and adolescents with coronavirus disease 2019 in New York city. J Pediatr. 2020; 226:55-63.e2.

32. Wang Z, Zhou Q, Wang C, Shi Q, Lu S, Ma Y, et al. Clinical characteristics of children with COVID-19: a rapid review and meta-analysis. Ann Transl Med. 2020; 8(10):620.

33. Gholami A, Hemati R, Khorshidi A, Borji M, Kafashian M, Kalvandi G, et al. The Prevalence of Clinical Symptoms in Children and Adolescents with Covid-19: A Systematic Review and Meta-Analysis Study. Int J Pediatr. 2020; 8(10):12177-88.

34. Duan Y-n, Zhu Y-q, Tang L-l, Qin J. CT features of novel coronavirus pneumonia (COVID-19) in children. Eur Radiol. 2020; 30(8):4427-33.

35. Jahangir M, Nawaz M, Nanjiani D, Siddiqui MS. Clinical manifestations and outcomes of COVID-19 in the paediatric population: a systematic review. Hong Kong Med J. 2021; 27(1):35-45.

36. Kovács A, Palásti P, Veréb D, Bozsik B, Palkó A, Kincses ZT. The sensitivity and specificity of chest CT in the diagnosis of COVID-19. Eur Radiol. 2021; 31(5):2819-24.

37. Sinha IP, Kaleem M. The role of pulmonary CT scans for children during the COVID-19 pandemic. BMC Med. 2020; 18(1):171. Doi: 10.1186/s12916-020-01647-1. [PubMed: 32498685]. [PubMed Central: PMC7272233].