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Original Article

An Examination of the Laboratory Data of Paediatric COVID-19 Cases

Pediatrik COVID-19 Olgularında Laboratuvar Verilerinin İncelenmesi

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Abstract

Background: Aim: The aim of this study was to investigate abnormalities in the laboratory tests of children with COVID-19 disease.

Material and Method: The study included 71 pediatric cases infected with SARS-CoV-2 virus, and a control group of 60 healthy children. A retrospective examination was made of age, gender, clinical findings and laboratory data.

Results: The patients comprised 39 males and 32 females and the control group comprised 30 males and 30 females with. The clinical characteristics of the patient group were fever in 36.6%, cough in 12.7%, and respiratory problems in 7%. When the laboratory test results were examined, the leukocyte and lymphocyte levels in the patient group were found to be statistically significantly lower than those of the control group ($p=0.01$, $p<0.001$). No significant difference was determined between the groups in respect of neutrophil and thrombocyte counts ($p>0.05$, $p>0.05$). The median C-reactive protein measurement was found to be statistically significantly higher in the patient group than in the control group ($p<0.001$).

Conclusion: The results of this study showed that lymphocyte levels were significantly low and C-reactive protein levels were significantly high in children with COVID-19 infection, and these two findings could have significant predictive value for COVID-19 disease. Therefore, the evaluation of lymphocytes and C-reactive protein together in children infected with SARS-CoV-2 virus could increase diagnostic success in COVID-19 cases.

Key Words: Pediatric, COVID-19, laboratory parameters

ÖZ

Amaç: Bu çalışmada, COVID-19 hastalığı olan çocuklarda laboratuvar tetkiklerindeki anormallikleri araştırmayı amaçladık.

Materyal ve Metod: Bu çalışmaya, SARS-CoV-2 virüsü ile enfekte 71 olgu ve 60 sağlıklı çocuktan oluşan kontrol grubu dahil edildi. Tüm olguların yaş, cinsiyet, klinik bulguları ve laboratuvar verileri retrospektif olarak incelendi.

Bulgular: Hastalar 39 erkek ve 32 kadın, kontrol grubu ise 30 erkek ve 30 kadından oluşuyordu. Hasta grubunun klinik özellikleri; vakaların %36,6'sında ateş, %12,7'sinde öksürük ve %7'sinde solunum sıkıntısı vardı. Laboratuvar bulguları incelendiğinde; hasta grubunda lökosit ve lenfosit düzeyleri kontrol grubuna göre anlamlı olarak düşük bulundu ($p = 0.01$ ve $p <0.001$). Nötrofil ve trombosit sayıları açısından gruplar arasında anlamlı fark saptanmadı ($p> 0.05$ ve $p> 0.05$). Medyan C-reaktif protein ölçümü hasta grubunda kontrol grubuna göre istatistiksel olarak anlamlı derecede yüksek bulundu ($p <0.001$).

Sonuç: Bu çalışma, COVID-19 hastalığı olan çocuklarda lenfosit düzeylerinin anlamlı derecede düşük olduğunu, C-Reaktif Protein düzeylerinin ise anlamlı derecede yüksek olduğunu ve bu iki bulgunun COVID-19 hastalığı için önemli prediktif değer olduğunu göstermiştir. Bu nedenle SARS-CoV-2 virüsü ile enfekte çocuklarda lenfosit ve C-Reaktif Protein düzeylerinin birlikte değerlendirilmesi, COVID-19 vakalarında tanısal başarıyı artırabilir.

Anahtar Kelimeler: Pediatrik, Covid-19, laboratuvar parametreleri

Introduction

The novel coronavirus disease caused by SARS-CoV-2 virus was first determined in December 2019 in Wuhan, China. The disease was named COVID-19 and on 11 March 2020, was declared a global pandemic by the World Health Organisation (1). The first cases were in the adult age group, but following the first pediatric case infected with SARS-CoV-2 virus in Shenzhen on 20 January 2020, cases reported in the pediatric population have shown an increase (2). The clinical and laboratory characteristics of the pediatric age group differ from those of adults and generally there is a milder prognosis (3). After two years, despite all the precautions taken around the world and the advances in vaccination programs, spread of the SARS-CoV-2 virus continues with mutations, the COVID-19 pandemic is still ongoing and pediatric cases are frequently reported.

Recently study, it was determined that CRP, WBC, Glucose, urea and creatinine values in the patient group increased significantly compared to the control group (4). In studies of pediatric COVID-19, some results have been obtained related to laboratory data, and these have focussed on the lower incidence of leukocytosis (neutrophilia and/or lymphocytosis) and especially that there may be a precursor of bacterial infection in thesse patients (5). It has also been emphasized that neutrophilia in COVID-19 could be a marker of cytokine storm and hyperinflammatory status (6). The aim of this study was to investigate changes in leukocyte (WBC), lymphocyte (LYM), neutrophil (NEU), thrombocyte (PLT), and C-reactive protein (CRP) levels in pediatric COVID-19 infection.

Material and Method

This retrospective study included 71 pediatric COVID-19 cases confirmed by real-time reverse transcription polymerase chain reaction (rRT-PCR) testing and a control group of 60 healthy children. Nasal and pharyngeal smear samples or blood samples were tested for the determination of SARS-CoV-2 virus specific RNA using the rRT-PCR test, and confirmed when necessary with the nucleic acid series analysis method. A 2 ml blood sample was taken for complete blood count during first presentation at the hospital before any treatment of all the cases with an rRT-PCR-confirmed COVID-19 diagnosis who were included in the study. complete blood count was performed on the blood samples taken using an automatic blood count device (Abbott Celldyn 3500, IL, USA). The WBC (10^3/uL), LYM (10^3/uL), NEU (10^3/uL), and PLT (10^3/uL) levels were examined with complete blood count. A 2cc venous blood sample was taken into a gel biochemistry tube for CRP measurement (mg/dL) using a spectrophotometric chemical analysis device (Architect C16000, Abbott Daignostics, Abbott Park, IL, USA). The laboratory data of complete blood count and CRP were also obtained from the 60 control group subjects who had blood samples taken for another reason and had no history or findings of COVID-19 infection.

The complete blood count and CRP data, age, gender, and findings on presentation were compared in all the cases in the patient and control groups.

Permission for this scientific research was obtained from the Turkish Republic Ministry of Health and approval for the study was granted by the Clinical Research Ethics Committee of Harran University (decision no:21, session no:11, dated:15.06.2020). All procedures were applied in compliance with the Helsinki Declaration.

Study Inclusion Criteria: Cases aged <18 years with rRT-PCR test positivity for COVID-19 infection were included in the study.

Study Exclusion Criteria: Patients aged >18 years, or with a negative rRT-PCR test result despite a history of contact and/or clinical suspicion of COVID-19 were excluded from the study.

Statistical analysis

Data obtained in the study were analysed statistically using SPSS vn. 24.0 software (SPSS Inc., Chicago, IL, USA). Descriptive statistics were stated as mean ± standard deviation (SD), median (minimum-maximum) values or number (n) and percentage (%). Conformity of the data to normal distribution was assessed with visual tests (histogram and probability graphs) and the Kolmogorov-Smirnov test. In the comparisons between the groups of variables not showing normal distribution, the Mann Whitney U-test was used. The Pearson Chi-square test was applied in the comparisons of qualitative data.

Multivariate linear regression analysis was performed to determine independent predictors of COVİD-19. Receiver operating characteristic (ROC) curve analysis was used to determine the optimum cut-off value of CRP level for predicting the COVİD-19. A value of $p<0.05$ was accepted as statistically significant.

Results

Evaluation was made of 131 cases, as a patient group of 71 cases with rRT-PCR test positivity for COVID-19 and a control group of 60 healthy children. The patients comprised 39 males and 32 females with a mean age of 9.77±5.35 years, and the control group comprised 30 males and 30 females with a mean age of 9.45±3.75 years. The demographic characteristics of the study population are shown in Table 1. No significant difference was determined between the groups in respect of median age and gender distribution ($p>0.05$).

The clinical characteristics of the patient group with rRT-PCR test positivity for COVID-19 were fever in 36.6%, cough in 12.7%, and respiratory problems in 7% (Table 1).

Table 1. Demographic and clinical characteristics of the study population

Parameters	**COVID group (n = 71)**	**Control group (n=60)**	***P***
Age, years	11(0-17)	9(1-17)	0.394
Gender, *(%)* *Male* *Female*	 39(54.9) 32(45.1)	 30(50) 30(50)	0.573
Fever,(>38.5 ^{0}C) Yes/No,*(%)*	26(36.6/)/45(63.4)	-	
Cough *Yes/No, (%)*	9(12.7)/62(87.3)	-	
Respiratory distress *Yes/No, (%)*	5(7)/66(93)	-	

The control group was formed of healthy children and there were no clinical pathological findings. When the laboratory test results were examined, the WBC and LYM levels in the patient group were found to be statistically significantly lower than those of the control group (p=0.01, p<0.001). No significant difference was determined between the groups in respect of NEU and PLT counts (p>0.05, p>0.05). The median CRP measurement was found to be statistically significantly higher in the patient group than in the control group (p<0.001) (Table 2). Multivariate linear regression analysis was used to assess the independent predictors of COVİD-19. It was found that CRP was the independent predictor of COVİD-19 (β=0.60, P<0.001) (Table 3). Also, ROC curve analysis was used to determine the optimal cut-off value of CRP for predicting the COVİD-19. CRP sCD40L ≥0.255 mg/l predicted the COVİD-19 with a sensitivity of 79% and specificity of 75% (AUC: 0.821, 95% CI: 0.748–0.893, p<0.001) (Figure-1) Also, ROC curve analysis was used to determine the optimal cut-off value of CRP for predicting the COVİD-19. CRP sCD40L ≥0.255 mg/l predicted the COVİD-19 with a sensitivity of 79% and specificity of 75% (AUC: 0.821, 95% CI: 0.748–0.893, p<0.001) (Figure-1)

Table 2. Analysis of total blood count and biochemical parameters in the study population

Parameters	**COVID group (n = 71)**	**Control Group (n = 60)**	**P**
WBC (10e3/uL) LYM (10e3/uL)	6 (2,8-22,6) 2.11 (0,6-12.04)	7.1 (3.59-10.52) 3.07 (1.5-7.04)	0.01 <0.001
NEU (10e3/uL) PLT (10e3/uL) CRP (mg/dL)	3.03 (1.04-20,6) 261(113-644) 1 (0.01-44.17)	2.85 (1,4-6.74) 290.9 (92-525.7) 0.15 (0.01-1.9)	0.773 0.133 <0.001

Abberations: WBC: White blood cells counts; LYM: Lymphocyte; NEU: Neutrophil; PLT: Platelet; CRP: C-reactive protein

Table 3. Multivariate linear regression analysis showing independent predictor of the COVİD-19

	Unstandardized coefficients		**Standardized coefficients**		
	B	**SE**	**β**	**t**	**P**
CRP	2.819	0.664	0.60	18.022	<0.001
WBC	1.108	0.844	3.027	1.723	0.189
Neutrophil	1.150	0.890	0.317	1.670	0.196
Lymphosit	0.666	0.894	0.514	0.555	0.456

Aberrations: B. Unstandardized regression coefficient; SE. Standard error; β. Standardized β coefficient; CRP. C reactive protein. WBC: white blood count

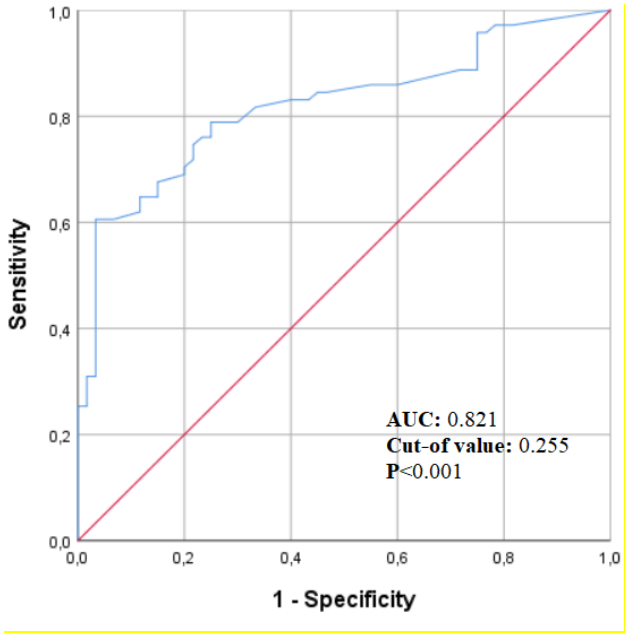

Figure 1: Receiver operating characteristic curve analysis CRP and COVİD-19.

Discussion

In previous studies of pediatric COVID-19 disease, there have been determined to be several changes in laboratory parameters and it has been suggested that these changes could be useful in the diagnosis of COVID-19 disease (7). In the laboratory findings of 10 pediatric patients reported by Cai et al (8), median WBC was 7.35 x 109/L. In a study of 20 children by Xia et al (9), the WBC level was found to be normal in 14 (70%), low in 4 (20%) and increased in 2 (10%). A meta-analysis in literature showed that leukocytosis was determined in 11.4% of patients with severe disease compared to 4.8% of patients with mild and moderate disease (10). Leukocytosis (neutrophilia and/or lymphocytosis) is seen less in COVID-19 patients and there are publications reporting that this is a precursor of bacterial infection (5). Henry et al (7) examined laboratory abnormalities in children with COVID-19, and while WBC was found to normal at the rate of 69.6%, leukocytosis was determined in 15.2% and leukopenia in 15.2%. In a study of 31 cases by Wang et al (11), there was determined to be a decrease in total WBC in peripheral blood in the early stage in 2 (6%) cases. In the current study, the WBC levels were determined to be significantly low (p=0.01).

Although there are reports of lymphopenia rate of around 9.8% (12-15), Wang et al (11) determined this rate as 6%. In another study, the LYM percentage was determined to be decreased in 7 patients (7/20, 35%), and increased in 3 patients (3/20, 15%) (9). That the LYM count is normal in most children has been associated with less immune suppression in some studies in literature (16, 17). In a review by Henry et al (7) of 12 studies conducted in China, which included 66 pediatric patients, lymphopenia was determined in only 3% of cases. Gumus et al (18) found a significant decrease in lymphocyte count in their study in children infected with COVID-19. Unlike these findings in literature, the LYM levels in the current study were determined to be significantly low (p<0.001). Therefore, low LYM levels should be accepted as a parameter worthy of attention.

There are different opinions in literature about NEU and PLT counts. Neutrophilia is thought to reflect a hyperinflammatory state and cytokine storm, although there are insufficient data on this (6). Studies have generally shown lymphocytosis and/or neutrophilia in a status of bacterial infection (5). In the literature related to thrombocytopenia, there are also different opinions. In one study, thrombocytopenia was determined in 57,7% of patients with severe infection and in 31,6% of patients with less evident symptoms (10). However, there are also studies showing the contrary. In studies of 1099 children, Guan et al (19) determined thrombocytopenia in 36% and stated that this laboratory finding was more evident in severe cases than in less severe cases. Wang et al (11) observed that thrombocyte count was increased in 6% of cases (2/31). Despite the different results and opinions, thrombocytopenia is accepted as a marker of poor prognosis in COVID-19 patients (20, 21). In the current study, no significant difference was determined between the patient and control groups in respect of NEU and PLT counts (p>0.05).

In a report by Cai et al (8), median CRP was determined as 7.5mg/L. The CRP value was seen to be increased in 9 of 20 patients (45%) in a study by Xia et al (9), and Wang et al (11) determined increased CRP in 10% of cases (3/31). Henry et al (7) reported increased CRP, which is an inflammatory marker, in 13.6% of cases. In the study by Cai et al (8), 2 of the 4 patients with radiological anomaly were determined to have significantly elevated CRP. In the current study, the CRP measurements of the COVID-19 patients were determined to be statistically significantly high (p<0.001). In contrast to previous literature, the predictive value of CRP in this study was concluded to be higher than had been estimated. Therefore, it is important that the CRP value is examined, as the diagnostic value can be considered to be higher than previously assumed.

Conclusion

It can be recommended that the CRP levels are investigated in children being examined in respect of COVID-19 infection.

Limitation

The number of cases in our study was low, since the clinical findings in the pediatric age group were milder than adults, and the hospitalization rates due to Covid-19 were lower.

References

1. Adhikari SP, Meng S, Wu YJ, et al. Epidemiology, causes, clinical manifestation and diagnosis, prevention and control of coronavirus disease (COVID-19) during the early outbreak period: a scoping review. Infect Dis Poverty. 2020;17;9(1):29.
2. Chan JF, Yuan S, Kok KH, et al. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. Lancet. 2020; 15;395:514-23.
3. Ludvigsson JF. Systematic review of COVID-19 in children shows milder cases and a better prognosis than adults. Acta Paediatr. 2020;109(6):1088-95.
4. OCAK, Metin, et al. A new predictor for indicating clinical severity and prognosis in COVID-19 patients: Frontal QRS-T angle. The American Journal of Emergency Medicine, 2021, 50: 631-635.
5. Lippi G, Plebani M. The critical role of laboratory medicine during coronavirus disease 2019 (COVID-19) and other viral outbreaks. Clin Chem Lab Med. 2020;58(7):1063-69.
6. Mehta P, McAuley DF, Brown M, et al. HLH Across Speciality Collaboration, UK. COVID-19: consider cytokine storm syndromes and immunosuppression. Lancet. 2020;395(10229):1033-34.
7. Henry BM, Lippi G, Plebani M. Laboratory abnormalities in children with novel coronavirus disease 2019. Clin Chem Lab Med. 2020 ;58(7):1135-38.
8. Jiehao C, Jin X, Daojiong L, et al. A Case Series of Children With 2019 Novel Coronavirus Infection: Clinical and Epidemiological Features. Clin Infect Dis. 2020;71(6):1547-51.
9. Xia W, Shao J, Guo Y, et al. Clinical and CT features in pediatric patients with COVID-19 infection: Different points from adults. Pediatr Pulmonol. 2020;55(5):1169-74.
10. Lippi G, Plebani M. The critical role of laboratory medicine during coronavirus disease 2019 (COVID-19) and other viral outbreaks. Clin Chem Lab Med. 2020;58(7):1063-69.
11. Wang D, Ju XL, Xie F, et al. [Clinical analysis of 31 cases of 2019 novel coronavirus infection in children from six provinces (autonomous region) of northern China]. Zhonghua Er Ke Za Zhi. 2020;58(4):269-74.
12. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020 ;395(10223):497-506.
13. Guan WJ, Zhong NS. Clinical Characteristics of Covid-19 in China. Reply. N Engl J Med. 2020;382(19):1861-62.
14. Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet. 2020;395(10223):507-13.
15. Wang D, Hu B, Hu C, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. JAMA. 2020;323(11):1061-69.
16. Liu J, Liu Y, Xiang P, et al. Neutrophil-to-lymphocyte ratio predicts critical illness patients with 2019 coronavirus disease in the early stage. J Transl Med. 2020;18(1):206.
17. Cao Q, Chen YC, Chen CL, et al. SARS-CoV-2 infection in children: Transmission dynamics and clinical characteristics. J Formos Med Assoc. 2020;119(3):670-73.
18. Gumus H, Demir A, Yükkaldıran A. Is mean platelet volume a predictive marker for the diagnosis of COVID-19 in children? Int J Clin Pract. 2021; 75(4): e13892.
19. Guan WJ, Ni ZY, Hu Y, et al. China Medical Treatment Expert Group for Covid-19. Clinical Characteristics of Coronavirus Disease 2019 in China. N Engl J Med. 2020;382(18):1708-20.
20. Lippi G, Plebani M, Henry BM. Thrombocytopenia is associated with severe coronavirus disease 2019 (COVID-19) infections: A meta-analysis. Clin Chim Acta. 2020; 506:145-48.
21. Perlman S. Another Decade, Another Coronavirus. N Engl J Med. 2020;382(8):760-62.