OTJHS
Online Turkish Journal of Health Sciences

e-ISSN: 2459-1467

OTSBD
Online Türk Sağlık Bilimleri Dergisi

Online Turkish Journal of Health Sciences 2020;5(3):503-509 *Online Türk Sağlık Bilimleri Dergisi 2020;5(3):503-509*

COVID-19 Şüphesi Olan Çocuklarda Gastrointestinal Sistem Tutulumu: Türkiye' den Tek Merkez Deneyimi

Gastrointestinal System Involvement in Children suspected for COVID-19: A Single Tertiary Center Experience from Turkey

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ÖZ

Amaç: Çalışmanın amacı pediyatrik COVİD-19 hastalarının klinik olarak sadece gastrointestinal semptomlar sergileyebileceğine dikkat çekerek, gastrointestinal sistem ile solunum sistemi tutulumu arasındaki ilişkiyi ortaya koymaktır.

Materyal ve Metot: Çalışmaya 1-18 yaş arasında 300 hasta dahil edildi. Hastalar semptomlarına göre; gastrointestinal semptomları, solunum semptomları ve gastrointestinal semptomları ile solunumsal semptomları olanlar şeklinde 3 gruba ayrıldı. PCR testi pozitif hastalar COVID -19 tanısı aldı. PCR negatif saptanan hastaların tanısı klinik semptomlara ve temas öyküsüne göre konuldu. Hastalar demografik özellikler, laboratuvar ve görüntüleme bulguları açısından analiz edildi.

Bulgular: COVID-19 tanısı alan 300 hastanın 29' unda PCR pozitif saptandı. Sadece gastrointestinal semptomları olan 58 hastanın tümünde yakın temas öyküsü vardı, ellisekiz hastanın 24'ünde PCR pozitifliği (%41.3) saptandı. Yedi hastanın ikisinde (%12) görüntüleme bulguları COVID ile uyumluydu, 7 hastanın ikisinde PCR negatifti. Medyan nötrofil lökosit oranı ve CRP gastrointestinal semptomları olan grupta solunum semptomları olan gruba göre daha yüksek bulundu (sırasıyla p = 0.034, p = 0.028).

Sonuç: Solunumsal şikayetler içermeyen, sadece gastrointestinal semptom bulguları olan ve PCR testi negatif saptanan hastalar, olası COVİD-19'un erken solunum tutulumu açısından dikkatle değerlendirilmelidir.

Anahtar Kelimeler: COVID-19, çocuk, gastrointestinal semptom

ABSTRACT

Objective: The aim of our study is to present the association between respiratory system disorders and gastrointestinal system involvement through showing that pediatric COVİD 19 patients can only display gastrointestinal symptoms.

Materials and Methods: Three hundered COVID-19 patients between 1-18 years of age were included into the study. The patients were divided into 3 groups according to symptoms which are classified gastrointestinal, respiratory and gastrointestinal and respiratory groups. Diagnosis of COVID-19 were made by PCR testing. In patients with negative PCR testing, diagnosis was made according to clinical symptoms and contact history. Patients were analyzed in terms of demographic features, laboratory and imaging findings.

Results: There were 300 patients diagnosed with COVID-19. PCR testing was positive in 129 of 300 children. All patients with only gastrointestinal symptoms had close contact history, 24 of 58 patients had PCR positivity (41.3%) and in 7 patients (12%), chest X- Ray findings were compatible with COVID-19. Two of 7 patients had negative PCR testing. Median NRL and CRP was higher in gastrointestinal group than respiratory group (p=0.034, p=0.028 respectively).

Conclusions: Patients with gastrointestinal symptom and negative PCR testing should be evaluated carefully for early respiratory involvement without symptoms.

Keywords: COVID-19, children, gastrointestinal symptom

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Yayın Bilgisi / Article Info:
Gönderi Tarihi/ Received: 24/06/2020
Kabul Tarihi/ Accepted: 02/09/2020
Online Yayın Tarihi/ Published: 30/09/2020

Atıf / Cited: Polat E et al. Gastrointestinal system involvement in children suspected for COVID-19: A single tertiary center experience from Turkey. *Online Türk Sağlık Bilimleri Dergisi* 2020;5(3):503-509. doi: 10.26453/otjhs.757053

INTRODUCTION

Coronavirus disease 2019 (COVID-19) pandemia continues unabated all over the world. It was known that adult patients were more affected at the beginning of the outbreak, and there was insufficient data on pediatric patient group. Diagnosis of COVID-19 in children based on the epidemiological features, clinical symptoms, laboratory, and imaging findings. Criteria for testing and treatment COVID-19 vary geographically. According to the largest meta-analysis reporting clinical characteristics of the infection, disease mainly causes respiratory system symptoms (like cough, expectoration, shortness of breath etc…) [1] Although the virus mainly affects respiratory system, different system involvements have been reported [2, 3]. There are some publications in the literature that refer to cardiovascular, urinary, neurological, ocular, cutaneous, and hematological involvement. The gastrointestinal system (GI) involvement of the virus in adult patients were declared [4].

However, the association between GI and respiratory findings is limited in childhood. In our study, we compared the clinical and laboratory findings by grouping COVID-19 pediatric patients according to their respiratory and gastrointestinal system symptoms and both. We also investigated the positivity of pulmonary imaging and Polymerase chain reaction (PCR) tests only in the presence of gastrointestinal symptoms.

MATERIALS AND METHODS

Five hundred and eighty-one children aged 1 to 18 years with suspected COVID-19 referred to the Pediatric Department at Sancaktepe Training & Research Hospital Istanbul, Turkey, from March 16, 2020 to April 26, 2020 were enrolled to the study. The study was approved by the ethics committee of University of Health Sciences, Ümraniye Training and Research Hospital (Date: 28/04/2020, No: 139). The study was conducted in accordance with the international Helsinki declaration and ethical standards.

All of the patients were evaluated according to their symptoms. Of 581 children, 300 had GI symptoms, respiratory symptoms and both GI symptoms and respiratory symptoms with or without fever, loss of smell and taste and constitutional symptoms. Three hundred patients' management was based on national COVID-19 diagnosis and treatment strategies. The first national strategy was testing children who have contact with a person infected with COVID-19 or who have travel history and at least one symptom of fever, cough, shortness of breath. Subsequently, all children with symptoms and signs of COVID-19 regardless of contact or travel history began to be tested. All children with contact history, signs, and symptoms suggested to COVID-19, together with abnormal chest computed tomography (CT) scans and positive PCR tests, were diagnosed as a confirmed case of COVID-19.

Symptomatic children with close contact history and negative PCR test results were defined as a suspected case of COVID-19. Confirmed and suspected children for COVID-19 were treated regardless of the severity of their clinical status.

We divided the patients into three groups according to their symptoms. Newborn patients were excluded from the study. Symptoms like vomiting and diarrhea were classified as GI symptoms; symptoms like cough and shortness of breath were grouped into respiratory symptoms; the third group was constituted by both GI and respiratory symptoms. All patients in each group were presented with or without fever, fatigue, loss of taste, or smell. According to the PCR test results, demographic characteristics, laboratory findings, and chest X-Ray, CT images of all groups were evaluated.

Informed consents were obtained from all patients for follow-up and treatment procedures. The study protocol was approved by the local ethical committee.

The data was analyzed using SPSS 22 software package (IBM Corp., Armonk, NY, USA). The distribution of normality was analyzed using Kolmogorov- Smirnov test. Data were expressed as median and range for non-parametricvariables; number and percentages (%) were expressed for categorical variables. Ki square test for categorical variables and Mann Whitney U test were used for comparison of nonparametric variables. Statistical significance was considered as $p\text{-value} < 0.05$.

RESULTS

Five hundred eighty-one children with suspected COVID-19 were enrolled in the study. There were 300 patients with GI and respiratory or both GI and respiratory symptoms. Of the 581, 300 children assessed, 129 (43%) had positive, and 171 (57%) negative PCR test results.The mean age of children was 10.2±5.5 years of age, and there were 139 female, 161 male patients (p=0.51). No patients died during

the follow-up period of the patients.

The age, laboratory findings, and hospitalization times of the children from 3 groups are shown in Table 1.

Patients with GI symptoms

There were 58 patients with GI symptoms (vomiting, diarrhea). The mean age of the patients was 10±5.2 years. Twenty-four of 58 patients had PCR positivity (41.3%). Of 58 patients with GI symptoms only 32 had chest X-Ray evaluation, and 7 of them (21.8%) were compatible with COVID-19. One patient had PCR testing negative but CT findings compatible with COVID-19. All of the patients with GI symptoms (100%) had contact history with one or 2 infected people. Conversely, 210 of 242 patients (patients with respiratory symptoms and patients with both respiratory and GI symptoms) had contact history (p=0.01). In laboratory evaluation; median Neutrophil Lymphocyte Ratio (NLR) was higher in GI symptoms group (2.2; 0.20-6.04) than in the respiratory group (median 1.43; 0.22-8.1) (p=0.034). Median serum C- reactive protein (CRP) level 0.07 mg/dl (0-23.7 mg/dl) in GI group higher than serum CRP level in the respiratory group (median 0.01; 0-1.28) (p=0.028). Median eosinophil count was 170 U/l (range: 10-350 U/l) and lower than in the respiratory group (median 200; 20-3100) (p=0.05). Three patients (5%) were followed at the hospital or were hospitalized.

Patients with GI and Respiratory symptoms

One hundred and eighty five patients presented with cough and shortness of breath. The mean age of the patients was 12.4±4.6 years. Patients in this group were older than patients with GI symptoms (p=0.014) and patients with respiratory symptoms (p=0.001). Eighty-eight of 185 patients had PCR positivity (41.3%). Fifty-seven patients had both GI and respiratory symptoms, and seventeen of 65 patients had PCR positivity (29.8%). Thirty-seven patients with GI and respiratory symptoms had chest X-Ray evaluation, and in 10 of 37 patients, chest X-ray findings were compatible with COVID-19 infection (27%). PCR results of these 10 patients were negative.

In laboratory evaluation; median White blood cells (WBC) count was 10400 (range; 4800-26500) and was higher than in the respiratory group (median 8050; range 3900-20300) (p=0.047). The median neutrophil count was 7690 (range; 2930-19960) and was higher than in the respiratory group (median 4185; range: 860-10030) (p=0.003). Median NLR was 3.8 (1.1-5.79) and higher than in the respiratory group (median 1.43, range: 0.22-8.1) (p=0.004). Median monocyte count was 680 (330-2220) higher than in the respiratory group (median 555, range: 10 -2510) (p=0.04). Median serum CRP levels 0.66 mg/dl (0.01-12.2) were also higher than in the respiratory group (median 0.01; 0-1.28) (p=0.001). Seven patients (12%) from this group were hospitalized during follow up.

Patients with Respiratory Symptoms

The mean age of these patients was 9.6±5.7 years. Chest X-Ray was performed in 129 patients in the respiratory group. Forty-six of 129 (35.6%) chest X-Ray evaluation were compatible with COVID-19 infection in the respiratory group. Twenty (10.8%) patients were hospitalized, and one of them admitted to the intensive care unit due to the severity of symptoms.

DISCUSSION AND CONCLUSION

Studies about clinical features have been increasing in children with COVID-19 recently. The respiratory system is not only affected by severe acute respiratory syndrome coronavirus 2 (SARS–CoV–2) infection; it has been shown that other systems (cardiovascular, urinary, neurological, ocular, cutaneous, and hematological) can also be affected and symptoms according to the affected system may be seen.[5-10] One of the most frequently affected systems is the gastrointestinal tract, and patients may experience different digestive system symptoms. A meta-analysis evaluating 60 studies and 4234 patients gives the frequency of GI findings as 17.6%[11]. The GI system involvement mechanism has been described as the primary functional receptor of the Sars-CoV-2 virus ACE2 receptors, outside the respiratory system, in the digestive system, epithelial cells.[12, 13] Unlike adult patients, the number of studies in pediatric patients is limited; few studies among children have been reported about GI tract involvement of COVID-19 in the literature.[14-17]

The present study is the largest single-center study evaluating GI symptoms of COVID-19 in children to date. Among 581 suspected COVID-19 cases, 300 patients had GI and/or respiratory symptoms. We found that 9.9 % (58/581) of the children had only GI symptoms. Wang et al., reported that 16.1% of 31 pediatric patients, Xia et al. stated that 25% of 20 pediatric patients had GIS symptoms.[14, 18] In a study evaluating 168 COVID-19 pediatric patients in Italy, it was stated that 18.5% of patients had GI symptoms.[16] In a single-center study evaluating 50 children and adolescent patients diagnosed with

COVID-19 in the USA, it was stated that 3 (6%) of 50 patients had GI symptoms.[15]

Close contact history is more frequent in patients with GI symptoms.[19, 20] Ping et al. reported nine adult patients with only GI symptoms, and all of nine patients had a history of exposure confirmed or suspected SARS–CoV–2 infected patient.[21] The data of the contact history in children infected with COVID-19 with GI symptoms are deficient. In our study, all patients with GI symptoms had one or two close contacts. This ratio was 87% in children without GI symptoms.

Besides, 24 of 58 patients with GI symptoms were negative PCR for COVID-19. Therefore, patients with contact history and an initial sign of GI symptoms should be carefully evaluated for early diagnosis of COVID-19, especially in PCR negative patients. There were 32 patients with GI symptoms evaluated with chest X-Ray; it was founded that 7 of 32 patients were compatible with COVID-19 radiologically. Two of 7 patients had a negative PCR result.

It is known that pediatric COVID-19 patients had milder and have a better prognosis than adults. It is not clear why the disease is milder compared to adults in the childhood age group. Different theories on this subject are emphasized. The first was explained as that ACE expression was less in children than in adults, the second was that the immunological response was different in pediatric patients, and the third was that other viral agents in the upper respiratory tract in children may be competing with SARS-CoV-2.[12]

In our cohort, there was no death, and patients with older age and patients with respiratory symptoms were hospitalized. Also, a significant relationship was reported between GI involvement and infection severity according to published articles and meta-analyses. However, in our patient group, the patients with GIS involvement did not show a more serious clinical course.

The age of patients with GI and respiratory symptoms was older than the GI group and respiratory group. We could not fully understand the cause of this condition, but as age grows, it can be considered as a possible ACE expression with possible GI and respiratory tract maturation.

It is noteworthy that chest X-Ray in 7 (21.8%) patients of the GI group were pathological. Two of them had negative PCR testing. Therefore, pulmonary system evaluation is critical in patients presented with only GI symptoms, even if PCR testing is negative. It is known that careful assessment should be made in children before radiological imaging, but in COVID-19 patients, this requires individual assessment.

Laboratory findings in COVID-19 disease are known as lymphopenia and high inflammatory markers, high AST, ALT, and abnormal coagulation parameters.[22, 23] In a study by Zhang et al., laboratory values of 164 COVID-19 adult patients with GI symptoms were compared with those without GI symptoms, CRP and LDH levels were significantly higher in GI groups than the non-GI group. Four pediatric studies with 227 patients analyzed by Mao et al., children with COVID-19, had a lower risk of increased ALT concentrations than adults. However, gastrointestinal symptoms were similar between children and adults.[4] In our study, we did not detect significant AST and ALT elevation in our patients. NLR and CRP levels were higher in the GI symptoms than in the respiratory group, besides eosinophil count was lower than the respiratory group. The median WBC count, median ANC count, median NLR, median monocyte count, and median serum CRP level in GI and the respiratory group was higher than in the respiratory group. The increase in leukocytosis and polymorphonuclear cell numbers will provide an advantage in terms of cellular response, as well as facilitating the spread of the virus to different tissues. It can be thought that severe inflammation causes more than one system involvement.

Our study's limitation was that we could not study PCR in stool samples to assess the excretion time and viral load of the virus with feces in patients with GI symptoms (with or without respiratory symptoms). Future studies on this subject are needed.

It should never be forgotten that GI problems may also be seen with COVID-19, especially in pediatric patients. Detailed evaluation of pulmonary system involvement is fundamental in patients who have only GI symptoms.

Ethics Committee Approval: Our study was approved by the University of Health Sciences Umraniye Training and Research Hospital, Researchs Ethics Committee (Date: 28/04/2020, Decision no: 139)

Conflict of Interest: No conflict of interest was declared by the authors.

Author Contributions: Concept – EP, ŞG; Supervision – ŞG; Materials – GZ, AZG, AB, İS, GY; Data

Collection and/ or Processing – GZ; Analysis and/ or Interpretation – EE, EP; Writing -, EP, EE.
Peer-review: Externally peer-reviewed.

REFERENCES

1. Li LQ, Huang T, Wang YQ, et al. COVID-19 patients' clinical characteristics, discharge rate, and fatality rate of meta-analysis. J Med Virol. 2020;92(6):577-583. doi: 10.1002/jmv.25757
2. Lee IC, Huo TI, Huang YH. Gastrointestinal and liver manifestations in patients with COVID-19. J Chin Med Assoc. 2020:83(6):521-523. doi: 10.1097/JCMA.0000000000000319
3. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020;395:497-506.
4. Mao R , Qiu Y, He JS, et al. Manifestations and Prognosis of gastrointestinal and liver involvement in patients with COVID-19: A systematic review and meta-analysis. Lancet Gastroenterol Hepatol. 2020;5(7):667-678. doi: 10.1016/S2468 -1253(20)30126-6
5. Inciardi RM, Lupi L, Zaccone G, et al. Cardiac involvement in a patient with coronavirus disease 2019 (COVID-19). JAMA Cardiol. 2020 doi: 10.1001/jamacardio.2020.1096
6. Xu XW, Wu XX, Jiang XG, et al. Clinical findings in a group of patients infected with the 2019 novel coronavirus (SARS-CoV2) outside of Wuhan, China: retrospective case series. BMJ. 2020;368:m606. doi: 10.1136/bmj.m606
7. Ye M, Ren Y, Lv T. Encephalitis as a clinical manifestation of COVID-19. Brain Behav Immun. 2020;S0889-1591(20)30465-7. doi: 10.1016/j.bbi.2020.04. 017
8. Wu P, Duan F, Luo C, et al. Characteristics of ocular findings of patients with coronavirus disease 2019 (COVID-19) in Hubei Province, China. JAMA Ophthalmol. 2020;138:575–8. doi: 10.1001/jamaophthalmol.2020. 1291
9. Recalcati S. Cutaneous manifestations in COVID -19: a first perspective. J Eur Acad Dermatol Venereol. 2020 34(5):212-213. doi: 10.1111/jdv. 16387
10. Rotzinger DC, Beigelman-Aubry C, von Garnier C, Qanadli SD. Pulmonary embolism in patients with COVID-19: time to change the paradigm of computed tomography. Thromb Res. 2020;190:58–59. doi: 10.1016/ j.thromres.2020.04.011
11. Zhang C, Shi L, Wang FS. Liver injury in COVID-19: management and challenges. Lancet Gastroenterol Hepatol. 2020;5:428-30. doi: 10.1016/ S2468-1253(20)30057-1
12. Yuki K, Fujiogi M, Koutsogiannaki S. COVID-19 pathophysiology: A review. Clin Immunol. 2020;215:108427. doi: 10.1016/ j.clim.2020.108427
13. Lai CC, Ko WC, Lee PI, Jean SS, Hsueh PR. Extra-respiratory manifestations of COVID-19. Int J Antimicrob Agents. 2020:106024. doi: 10.1016/j.ijantimicag.2020.106024
14. Wang D, Ju X, 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):269-274. doi: 10.3760/ cma.j.cn112140-20200225-00138
15. Zachariah P, Johnson CL, Halabi KC, et al. Epidemiology, clinical features, and disease severity in patients with coronavirus Disease 2019 (COVID-19) in a children's hospital in New York City, New York. Columbia Pediatric COVID-19 Management Group. JAMA Pediatr. 2020;e202430. doi: 10.1001/ jamapediatrics.2020.2430
16. Garazzino S, Montagnani C, Donà D, et al. Multicentre Italian study of SARS-CoV-2 infection in children and adolescents, preliminary data as at 10 April 2020. The Italian SitipSip Pediatric Infection Study Group. Euro Surveill. 2020;25 (18):2000600. doi: 10.2807/1560-7917.ES.2020.25.18.2000600
17. Nicoletti A, Talarico V, Sabetta L, et al. Screening of COVID-19 in children admitted to the hospital for acute problems: preliminary data. Acta Biomed. 2020;91(2):75-79. doi: 10.23750/ abm.v91i2.9607
18. 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):1169-1174. doi: 10.1002/ ppul.24718
19. Tian Y, Rong L , Nian W , He Y. Review Article: Gastrointestinal features in COVID-19 and the possibility of faecal transmission. Alient Pharmacol Ther. 2020;51(9):843-851. doi: 10.1111/apt.15731
20. Ng SC, Tilg H. COVID-19 and the gastrointestinal tract: more than meets the eye. Gut. 2020;69 (6):973-974. doi: 10.1136/gutjnl-2020-321195
21. Ping A, Hongbin C, Xiaoda J, Honggang Y.

Clinical features of 2019 novel coronavirus pneumonia presented gastrointestinal symptoms but without fever onset. Lancet. 2020. https://ssrn.com/abstract=3532530. Accessed March 15, 20020.

22. Dong Y, Mo X, Hu Y, et al. Epidemiology of COVID-19 among children in China. Pediatrics. 2020;145(6): e20200702. doi: 10.1542/peds.2020-0702
23. 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;S1473-3099(20)30198-5. doi: 10.1016/S1473-3099(20)30198-5
24. Drescher B, Bai F. Neutrophil in viral infections, friend or foe?. Virus Res. 2013;171(1):1-7. doi: 10.1016/j.virusres.2012.11.002

Table 1. The age, contact history, laboratory findings and hospitalization times of the children.

	GI	**GI +R**	**R**	**P***	**P****	**P*****
Number of Patients	58	57	185	NS	NS	NS
Age	10±5.2 years	12.4±4.6	9.6±5.7	NS	**0.014**	**0.001**
Contact History n, %	58 (100)	42 (73)	180 (97)	NS	NS	NS
PCR positivity	24 (41.3)	17(29.8)	88 (47.5)	NS	NS	0.01
Laboratory Findings						
WBC (U/l)	10400(4800-26500)	10.350(4800-26.500)	8050 (3900-20300)	NS	NS	**0.047**
Neutrophils (U/l)	4520 (1330-9710)	7690 (2930-19960)	4185 (860-10030)	NS	NS	0.003
Lymphocytes (U/l)	2220 (970-8110)	2450 (750-5890)	2310 (690-13.250)	NS	NS	NS
NLR	2.2 (0.20-6.04)	3.8 (0.79-5.9)	1.43 (0.22-8.1)	**0.034**	NS	**0.004**
Eosinophils (U/l)	170 (10-350)	35 (10-100.2)	200 (20-3100)	**≤0.05**	NS	NS
Monocytes (U/l)	550 (50-1080)	680 (330-2220)	555 (10-2510)	**0.04**	NS	0.04
Platelets (U/l)	281.000 (163.000-422.000)	289.000 (178.000-411.000)	254.000 (123.000-512.000)	NS	NS	NS
Hemoglobin (gr/dl)	13.1 (10-17)	12.8 (10.6-16.6)	13 (10.5-16)	NS	NS	NS
CRP (mg/dl)	0.07 (0-23.7)	0.66 (0.01-12.2)	0.01 (0.0-1.28)	NS	NS	**0.001**^{S}
AST (U/l)	31.6 (12-163)	21 (10-31)	24 (14-117)	NS	NS	NS
ALT (U/l)	11.7 (9-57)	13 (8-49)	16 (9-310)	NS	NS	NS
LDH (U/l)	211 (158-306)	235 (164-342)	217 (143-357)	NS	NS	NS
Troponin (ng/ml)	0.7 (0.0-5.9)	0.6 (0-5)	0.7 (0.0-5.2)	NS	NS	NS
D-Dimer (ng/ml)	0.3 (0.09-2.14)	0.27 (0.15-3.15)	0.29 (0.0	NS	NS	NS
Follow-up						
Hospitalization	3 (5)	7(12)	20 (10.8)	**0.045**	NS	NS

Abbreviations: GI: Gastrointestinal symptoms; PCR: Polymerase chain reaction; WBC: White blood cells; NLR: Neutrophil lymphocyte ratio; CRP: C- reactive protein; AST: Aspartate transaminase; ALT: Alanine Transaminase; LDH: Lactate Dehydrogenase; P*: GI vs respiratory symptoms; p**:GI +respiratory symptoms vs GI symptoms; p***: GI+ respiratory symptoms vs respiratory symptoms, NS: p>0.05,^{S}: p<0.05.