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ASYMPTOMATIC, MILD AND MODERATE COVID-19 IN CHILDREN: EPIDEMIOLOGICAL, CLINICAL AND LABORATORY FINDINGS, GEORGIAN EXPERIANCE

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ასიმპტომური, მსუბუქი და საშუალო მიმდინარეობის COVID-19-ის ეპიდემიოლოგიური, კლინიკური და ლაბორატორიული თავისებურებები ბავშვთა ასაკში, საქართველოს გამოცდილება

[1]თბილისის სახელმწიფო სამედიცინო უნივერსიტეტის ინფექციურ დაავადებათა დეპარტამენტი; [2]თსსუ ბავშვთა და მოზარდთა მედიცინის დეპარტამენტი; [3]თსსუ ფიზიკის, ბიოფიზიკის, ბიომექანიკისა და საინფორმაციო ტექნოლოგიის დეპარტამენტი; [4]აკად. ვ. ბოჭორიშვილის კლინიკის პედიატრიული დეპარტამენტი, [1]საქართველოს ფიზიკური აღზრდისა და სპორტის სახელმწიფო სასწავლო უნივერსიტეტი;

რეზიუმე

შრომის მიზანი: ბავშვთა ასაკში COVID-19-ის ეპიდემიოლოგიური, კლინიკური და ლაბორატორიული თავისებურებების დადგენა საქართველოში.

მეთოდოლოგია: რეტროსპექტულად გაანალიზებულ იქნა 0-18 წლის ასაკის 44 პაციენტის სამედიცინო ბარათი, რომლებიც მკურნალობდნენ COVID-19-ის დიაგნოზით აკად. ვ.ბოჭორიშვილის კლინიკაში.

შედეგები: ყველა პაციენტის ინფიცირების წყაროს წარმოადგენდა ოჯახის წევრი, საშუალო ასაკი იყო 9 წელი. უხშირესად COVID-19 გამოვლინდა 7-15 წლის ასაკში (57%). პაციენტთა 50%-ში დაავადება მიმდინარეობდა მსუბუქად, 14%-ში საშუალო სიმძიმით, რომელიც გართულებული იყო პნევმონიით. მათ შორის 33%-ში გამოვლინდა ე.წ. დაბურული მინის ფენომენი, ქვედა წილებში. პაციენტთა 36%-ში დაავადება მიმდინარეობდა ასიმპტომურად. უხშირესად პაციენტებს აღენიშნებოდათ ცხელება (36%). ასიმპტომურ პაციენტებში ლეიკოპენია გამოვლინდა 40%-ში, მონოციტოზი 20%-ში, ც-რეაქტიული ცილა>10მგ/ლ-46% და დ-დიმერი>0.5მგ/ლ-53% შემთხვევებში.

მსგავსი ტენდენცია აღინიშნა საშუალო და მსუბუქი მიმდინარეობისას. დადგინდა კორელაციური კავშირი პაციენტის ასაკსა და სისხლის მაჩვენებლებს შორის, ასაკი უკუპროპორციულ კავშირშია ლეიკოციტებისა და თრომბოციტების რაოდენობასთან.

დასკვნა: პანდემიის დასაწყისში ბავშვთა ასაკში COVID-19 მიმდინარეობდა მსუბუქი ან ასიმპტომური ფორმით, ლაბორატორიული ცვლილებები აღინიშნა ასიმპტომურ პაციენტებშიც. კლინიკურად უხშირესად ვლინდება სუბფებრილიტეტი, პნევმონია ძირითადად ცალმხრივია.

Introduction. COVID-19 caused by SARS-CoV-2 is a significant challenge of the XXI century. Infection was emerged in Wuhan (China) in December 2019 and spread throughout the world. The first case of coronavirus infection in Georgia was registered on February 26, 2020.

On March 11, 2020, the World Health Organization declared a new coronavirus (COVID-19) outbreak a global pandemic. Globally there have been 11,588,427 confirmed cases of COVID-19, including 535,388 deaths, reported WHO [1].

As of July 6, 2020, according to the National Center for Disease Control [2], there were 953 registered cases and 15 deaths in Georgia. Consequently, lethality rate was 1.57% that is significantly lower compared to the incidence rates both cumulative (4.6%) as well as in other countries. The low morbidity and mortality rate of COVID-19 in Georgia is mainly due to the timely and effective implementation of epidemiological measures. Georgian governmental bodies have been informed about the spread of a new coronavirus infection in China since January 6, 2020. Imposing land and air travel restrictions with high-risk countries (China, Italy, Iran, etc) started on January 29. From March 2, 2020, the study process was

stopped and events drawing crowds were banned. From March 21 to May 22, 2020, Georgia declared a state of emergency and curfew throughout the country.

Methods and Materials: A retrospective analysis of the medical histories for 44 COVID-19 confirmed patients, 0 to 18 years of ages, who were treated at Acad. V. Bochorishvili Clinic. In addition, 284 adults were treated in the above-mentioned clinics; therefore, the morbidity rate of children in this group was 13.4%. According to the protocol, patients underwent laboratory and radiological examinations at the clinic. In all cases, nasopharyngeal swab test on SARS-CoV-2 was performed by RT-PCR, both for the first time and in dynamics. The criterion for hospitalization was a positive result for SARS-CoV2 and criterion to discharge - two negative responses for SARS-CoV-2 at 24-hour intervals and clinical recovery, respectively.

Results: Epidemiological characteristics - Due to the epidemiological situation in Georgia, it was possible to monitor all confirmed cases, including asymptomatic patients, in special boxes at the hospital.

All the children belonged to the family clusters. No sporadic cases have been reported on our material. 16 of 44 patients (36.4%) lived in the capital - Tbilisi, approximately the same number of patients from large clusters were - Bolnisi, and single cases from different cities of Georgia, 1 child was from a neighboring state (Armenia). 6 patients had travel history to different countries (USA, Turkey, Armenia and Russia). Most patients had contact with someone with recent travel history. Grandparents, mothers, fathers and cousins were often infected in the family (as it is a tradition of different generations to live together in Georgia). The studied patients were divided into age groups as follows: 2 patients <1 year - 8 and 3 months (4.5%), 1–5 years were 10 (22.7%), 6–10 years 13 (29.5%), 11–15 years 13 (29.5%) and 6 patients over>15 years of age (13.8%), respectively. However, there was an increase in the number of people aged 7-15 (57%). The distribution rate by gender was equal - 22 girls (50%) and 22 boys (50%).

The minimum length of hospital stay was 2 weeks; according to the protocol, 2 weeks after the positive test result, re-testing scheduled. The individuals negative twice at a 24-hour interval were required to self-isolate or keep quarantine at home or other residential premises for 2 weeks. 12 patients (27%) were positive for the virus up to 3 weeks, 20 (46%) to 4 weeks and 4 (9%) over a month. On average, the negative test result was achieve in 24.6 days. The maximum length reported was 42 days (Table 1).

Table 1: Sars CoV2 excretion rate according to clinical types (n=44)

Excretion days	Asymptomatic (n=16)	Mild cases (n=22)	Moderate cases (n=6)
Min.	15	13	18
Max.	29	35	42
Average	20	21	29

Patients were divided into 3 groups according to their clinical manifestations. First group included asymptomatic patients (n = 16), the second group - patients with mild course (n = 22) and patients with moderate course (n = 6) who developed pneumonia, respectively.

All patients were vaccinated by age, according to the national calendar. Namely, BCG at birth in the maternity unit; At 2, 3, 4 months and 18 months of age - DTaP diphtheria-tetanus-pertussis vaccine; At 1 year of age - MMRV vaccine which protects against measles-rubella-mumps.

Clinical characteristics: Patients admitted to the clinic 1-2 days after the onset of symptoms (54%), or positive results after contacts testing. The disease course was asymptomatic in 16 individuals (36.4%); as for the rest of cases, clinical symptoms were as follows: disease started with a high temperature > 38 in 2 patients for 3 days. They also had a sore throat and dry cough. 5 patients (11.5%) had only low-grade fever at the beginning of the disease and lasted approximately 5 days. 9 patients (20.5%) reported sub febrile and general weakness. Simultaneously 3 symptoms - general weakness, sub febrile and cough were revealed in 7 patients (16%). 4 symptoms - general weakness, fever, cough and sore throat in 2 (4.5%) patients. 1 patient 16 years of age had a loss of smell and taste. Only 4 patients had intestinal dysfunction, 2 of them with other symptoms, 2 with only diarrhea, manifested in defecation with yellowish liquid consistency masses 2-3 times a day for 2 days (Table 2). 6 patients (13.8%) developed pneumonia, CT imaging revealed changes characteristic for COVID-19, as shown in Table 3. 2 children had urticarial rash on the body for a short period - 3 days, which disappeared without any signs.

Table 2: Clinical types of COVID-19 disease in children

Symptom / Symptoms	Total (n=44)
Asymptomatic	16 (36.4%)
Only low-grade fever	5 (11.4%)
Low grade fever and weakness	9 (20.5%)
Weakness, low grade fever and cough	7 (15.9%)
High grade fever, weakness, dry cough and sore throat	2 (4.5%)
Weakness and diarrhea	1 (2.3%)
Low grade fever and diarrhea	1 (2.3%)
Only diarrhea	2 (4.5%)
Anosmia and disguise	1 (2.3%)

Table 3: Abnormalities on chest CT in case of pneumonia caused by COVID-19

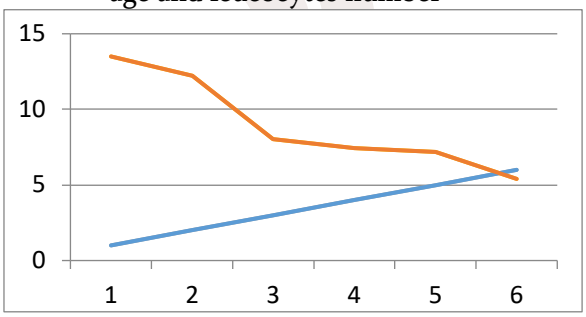
CT	Total (n=6)	Age (year)
Ground-glass opacity in right middle lobes	1(16.6%)	13
Ground-glass opacity in left lower lobe	1(16.6%)	6
Ground-glass opacity in lower lobes of both lungs	2(33.3%)	10, 18
Ground-glass opacity in left middle lobes	1(16.6%)	9
Local patchy shadowing in right lower lobes	1(16.6%)	17

Treatment and outcome: Patients were treated symptomatically. Unlike other respiratory viral infections, the patients were not administered inhalation therapy. Fluids were administered orally taking into consideration the electrolyte balance. Antiviral medications (Plaquenil, Ritonavir / Lopinavir, Remdesivir) were not included in the treatment process for none of the cases. In every case, the positive outcome achieved. All the children recovered completely with no residual changes.

Laboratory findings in children with confirmed COVID-19: At the clinic, the patients underwent laboratory tests - minimum, maximum and average rates in accordance with clinical form of the disease where statistical analyses were performed, have been shown.

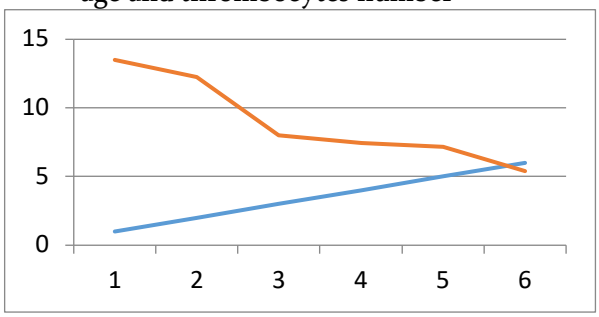
Statistical analysis: Patients who treated in the clinic were divided into three groups: patients with mild severity (n = 22), moderate severity (n = 6), and patients with asymptomatic disease (n = 16). Each patient underwent appropriate laboratory tests several times, and therefore the average value was taken. The data obtained because of observation has given in the form of a table (as a range). For statistical studies, laboratory results are compared between the following groups: 1. Patients with mild and moderate severity, 2. Patients with mild severity and asymptomatic patients, 3. Patients with moderate severity and Patients without symptoms. The statistical study used the Manna-Whitney test. In each group for each component there were no differences in the two samples, which indicates that the course of the disease in all three groups was the same, according to the data that are available to us.

Figure 1: Correlation between patients age and leucocytes number



Abscissa (OX): Patients age groups.
Ordinate (OY): Leucocytes number

Figure 2: Correlation between patients age and thrombocytes number



Abscissa (OX): Patients age groups
Ordinate (OY): Thrombocytes number

Studies have also been conducted to determine the correlation between the age of patients and blood-forming elements (leukocytes, platelets, monocytes). Since the law of sample distribution is

unknown, a nonparametric method was used to determine the relationship between the two indicators. In particular, the Spearman rank correlation coefficient was determined. The null hypothesis has been verified. A correlation was found between age and white blood cell count, as well as age and platelet count. The correlation between age and monocyte count has not been confirmed (Figure 1, 2).

A statistical study performed between the group of patients infected with COVID-19 and the control group on the following blood elements: hemoglobin, white blood cells, platelets, monocytes. The data of healthy patients are taken for the control group (normal). Wilcoxon's U-test is used for statistical studies. The null hypothesis has been verified. It was found that the difference between the two samples was significant in two indicators: white blood cells and monocytes.

Statistical data processing was carried out using the statistical program SPSS. A 95% confidence interval was considered statistically reliable.

Discussion. Currently, the global spread of a new coronavirus infection and investigation of its clinical and laboratory features are considered an urgent problem worldwide, the rising rates of morbidity and mortality every day [1,5]. Rise in new coronavirus cases have been reported in almost every country throughout the world. Active research studies are conducted in different countries to study the course of the disease. Basing on the systematic analysis of literary data, it was found out that most often the studies were performed using open, prospective-retrospective methods. The results obtained make it possible to study the disease peculiarities in different countries and compare the findings. In this regard, the study and analysis of pediatric cases is of great importance [2,3,4,6]. The morbidity rate of the novel coronavirus in the pediatric population is lower, with moderate severity and low lethality rate [7,9,10].

A thorough study of the clinico-epidemiological and laboratory features of pediatric cases can reveal the approaches that will maintain the optimization of new coronavirus infection management in children [6]. In a number of countries, due to the wide prevalence of the disease, less attention was paid to asymptomatic and mild patients, most of the COVID infected ones in Georgia. A median age of pediatric patients infected with the new coronavirus in our clinic was 9.7 years.

Most detected cases (30.0%) were fixed in patients, 11-15 years of age. The lowest incidence rate - 4.5% was revealed in patients under 1 year. Similar tendency have been revealed in European countries, America and China, average age - 5-12 years [1,4,5]. In all cases described above, children were infected from household exposure and source of infection were either family members of close relatives. Having studied a family history it turned out that in 34.0% of hospitalized children at least 1 family member was infected as well. SARS CoV 2 infection was confirmed in all hospitalized patients with PCR test.

As for the clinical course can range from mild to severe, 50.0% of the studied patients had mild clinical course while asymptomatic course was observed in 36.3%, respectively. Fever (36.6%) and general weakness/tiredness (34.0%) were most common symptoms reported in hospitalized patients. Other symptoms characteristic for coronavirus (cough, loss of smell or taste, diarrhea, sore throat) were less common. Similar trends have also been observed in European countries, America and China. In these countries, coronavirus in pediatric patients was most often manifested by fever [10].

According to the results of the study, a new coronavirus infection with complicated pneumonia was detected in 13.6% of cases. All cases were confirmed by CT examination. In 83.3% of the cases of pneumonia, so-called "frosted glass" lung areas were detected, while in 50.0% - pulmonary infiltrates were observed bilaterally, that is consistent with the results of studies conducted by other countries [8,9].

The variability of the laboratory findings in all mild, moderate, and asymptomatic patients were studied. Leukopenia occurred in 40.0% of asymptomatic patients (<6X109), monocytosis (>10%) in 20.0%, elevated CRP (>10mg/l) - 46.6% and D-dimer (>0.5mg/L) - 53.3% , respectively. In 80.0% of asymptomatic patients an increase in lactate (>2.2 mmol/l) was observed. Similar trends were observed in patients with mild course of disease. In addition, an increase in ferritin and procalcitonin levels was observed in 9.0% of cases. In 33.3% of patients diagnosed with pneumonia neutrophilosis was revealed. Tendency of such nature were reported in Europe, USA and China as well [7]. According to the results obtained, in the majority of pediatric patients the new coronavirus infection is mostly asymptomatic or mild symptomatic, the incidence of complication with pneumonia is low, despite shortage, lack of symptoms, significant changes have been found in the findings of laboratory studies.

References:

1. National Center for Disease Control and Public Health. COVID 19 statistic date: URL: https://www.ncdc.ge/Pages/User/LetterContent.aspx?ID=161b884d-ef3c426c-9ddc
2. Wenliang Song, Junhua Li, Ning Zou, Wenhe G, Jiali Pan, Wei Xu. Clinical features of pediatric patients with coronavirus diseases (COVID 19). Journal of Clinical Virology; June 2020; 127: 104377.
3. Jun Zhang, Miao Yu, Song Tong, Lu-Yu Liu, Liang-V. Tang, Predictive factors for disease progression in hospitalized patients with coronavirus disease 2019 in Wuhan, China. Journal of Clinical Virology; June 2020; 127: 104392.
4. Haiyan Qiu, Junhua Wu, Liang Hong, Yunling Luo, Qifa Song, Dong Chen. Clinical and epidemiological features of 36 children with coronavirus disease 2019 (COVID-19) in Zhejiang, China: an observational cohort study. The Lancet Infectious Disease; Vol 20, Issue 6, June 2020, 689-696.
5. World Health Organization Coronavirus disease (COVID-19) Situation Report – 153. Data as received by WHO from national authorities by 10:00 CEST, 21 June 2020. URL: https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200621-covid-19-sitrep153.pdf?sfvrsn=c896464d_2
6. İlker Devrim, Nuri Bayram. Infection control practices in children during COVID-19 pandemic: Differences from adults. American Journal of Infection Control; 2020, May 26; In Press, doi: https://doi.org/10.1016/j.ajic.2020.05.022
7. C. Dolores De Luca, E. Esposito, L. Cristiani, E. Mancino, R. Nenna, E. Cortis, F. Midulla, Covid-19 in children: A brief overview after three months experience, Paediatric Respiratory Reviews (2020), doi: https://doi.org/10.1016/j.prrv.2020.05.006.
8. Huanhuan Liu, Fang Liu, Jinning Li, Tingting Zhang, Dengbin Wang, Weishun Lan. Clinical and CT imaging features of the COVID-19 pneumonia: Focus on pregnant women and children. J of Infection; 80 (2020): 7–13.
9. M. Oualha, M. Bendavid, L. Berteloot et al. Severe and fatal forms of COVID-19 in children. Archives de Pédiatrie; Volume 27, Issue 5, July 2020: 235-238.
10. Brandon Michael Henry, Stefanie W. Benoit, Maria Helena Santos de Oliveira, et al. Laboratory abnormalities in children with mild and severe coronavirus disease 2019 (COVID-19): A pooled analysis and review. Clinical Biochemistry; Volume 81, July 2020: 1-8.

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SUMMARY

Aim of our study was to detect epidemiological, clinical and laboratory findings in asymptomatic, mind and moderate COVID-19 cases in children. Due to the epidemiological situation in Georgia, it was possible to monitor all confirmed cases, including asymptomatic patients.

Methods: A retrospective study of the medical histories for 44 confirmed patients, 0 to 18 years performed in Acad.V. Bochorishvili clinic, Pediatric department.

Results: All patient belonged to the family clusters and average age was 9 year. The highest rate performed in 7-15 (57%) of age. 50% of patients had mild clinical type, 14% moderate type complicated with pneumonia. 33% had ground-glass opacity in lower lobes of both lungs on CT. Asymptomatic was 36%. Fever (36%) was the most common symptom. Leukopenia (40%) and monocytosis (20%) occurred in asymptomatic patients. Also, elevated CRP (>10 mg/L) - 46% and D-dimer (>0.5 mg/L) - 53%. Similar tendency presented in patients with mild and moderate cases. A correlation found between age and white blood cell count, as well as age and platelet count. It turned out that older the infected patient is, the less white blood cells and platelets are in the blood.

Conclusion: Children mostly are mild or asymptomatic. Laboratory changes were found in asymptomatic patients as well. Low-grade fever and general fatigue are the most common manifestation. Pneumonia in children appears most commonly as unilateral.

Keywords: COVID-19, SARS COV2, children, epidemiology, laboratory