ORIGINALNI RAD – ORIGINAL ARTICLE

What is about Covid Pneumonia in Children?

Covid pneumonija kod dece?

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Summary The authors present clinical symptoms, laboratory findings, radiographic pictures and the most important clinical data and outcomes of patients admitted to Medical Center „Dr Dragiša Mišović“, Children's Hospital for Lung Diseases and Tb, Belgrade, Serbia during the SARS COV2 pandemic from March 2020 to March 2021. Overall number of children hospitalized due to Covid19 infection was 734 from 16th of March 2020. until 8th of April 2021. Not all of them present with symptoms and signs of viral pneumonia due to corona viurs. We will describe clinical features and caracteristics of Covid pneumonia in 67 children hospitalized during autumn – winter season 2020/2021. The age range was from 2 to 18 years. The complete number of respresentative cases were confirmed by biochemical and heamatological markers, and positive PCR test respectivelly. During autumn winter season 2020/2021 Chest X ray and/or computerasied tomography (CT Scan) were performed in almost all children and remarkable results were obtained. Our experience was in accordance with worldwide data about risk factors for moderate to severe Covid pneumonia in children. Obesity, morbid obesity and comorbidities were verified as the most prominent risk factors. Speaking about the Covid pneumonia not mentioning multisystem inflammatory syndrome in children (MISC) it is imprtant to emphasize that all our patients recovered successfully with very mild protracted symptoms ocasionally.

Key words: Covid19, pneumonia, children

Sažetak Autori iznose podatke o kliničkoj slici, laboratorijskim nalazima, radiografskoj slici i kliničkom toku pacijenata lečenih hospitalno u Kliničko bolničkom centru „Dr Dragiša Mišović“, Dečja bolnica za plućne bolesti i tuberkulozu, u Beogradu, u periodu od marta 2020. do marta 2021. godine tokom pandemije SARS COV 2. Ukupan broj dece hospitalizovane zbog Covid 19 infekcije je 734 od 16. marta 2020. do 8. aprila 2021. Nisu svi pacijenti imali simptome virusne pneumonije na terenu infekcije korona virusom. U radu su opisane kliničke karakteristike Covid pneumonije kod 67-oro dece, u periodu oktobar 2020. do početka aprila 2021.. Uzrast je bio od 2 do 18 godina. Svi pacijenti su obrađeni laboratorijski, bioemijski i hematološki markeri kao i pozitivan PCR test su učinjeni. Tokom jeseni zime 2020/2021. radiografija grudnog koša i /ili kompjuterizovana tomografija grudnog koša su učinjene i vrlo upečatljive promene su detektovane. Naše iskustvo je sasvim u saglasnosti sa podacima širom sveta u vezi faktora rizika za razvoj srednje teške i teške pneumonije kod Covid19 infekcije u dečjem uzrastu. Preuhranjenost, gojaznost i ekstremna gojaznost, kao i udružene bolesti su najznačajniji faktori rizika. Kada govorimo o Covid19 pneumoniji kod dece, ne uzimajući u razmatranje multisitemski inflamatorni sindrom kod dece, svi naši pacijenti su se opravili uspešno, dok su po neki imali produžene blage simptome bolesti.

Ključne reči: Covid 19, pneumonije, deca

Introduction

A new coronavirus was identified in Wuhan, a city in the Hubei province of China at the end of 2019. It swiftly spread, throughout China and began to spread rapidly throughout the world. From the beginning of 2020 this new virus was labeled as Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) . SARS-CoV-2 is the etiologic agent of the disease Covid19, an acronym made by the World Health Organization (WHO). The WHO declared Covid19 a pandemic on March 11, 2020 . Serbia went on lockdown due to Covid19 on March 15th 2020 (Vesna Vekovic's son Marko's birthday) (1,2). Soon after the first reports from China, paediatric cases have been described all over the world. Close personal contact is labeled as the main mode for virus transmission. The respiratory route of viral spreading was suspected the most evident although other ways were described later on, as well, like subject's

contaminated hands or by touching contaminated surfaces and then touching one's eyes, nose, or mouth. Period of incubation is roughly two weeks. Covid19 might have been spread within the whole age spectrum and children of all ages can get Covid19 infection. The vast majority of paediatric Covid19 cases resulted from house exposure or peer gathering particluarly in adolescent group (3.4). Extremely important is to emphasize that confirmed Covid19 infection in children doesn't mean serious or any troublesome clinical condition. In a case-control study, close contact with persons suffering from Covid19 (typically a household member), visitors and attending gatherings with persons outside the household, social activities with other children definitely were associated with SARS-CoV-2 infection in children and adolescents (5). Children of all ages can transmit SARS-CoV-2 to another person. However, the rate of transmission by young children is uncertain. Older children and adolescents have been the major source of Covid19 infection in household and in community settings (6.7).

Clinical findings

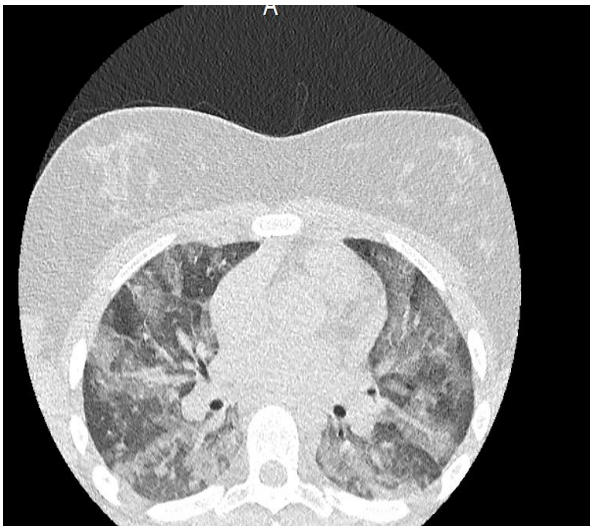
Clinical presentations of paediatric Covid19 have been similar to those in adult population. Paediatric patients with Covid19 present mild to moderate clinical symptoms, shorter course of disease, small number of complications and/or severe forms. Mostly, clinical findings in children with Covid19 are diverse, from fever or chills, malaise, painfull muscles and bones, sore throat, headache, nausea, vomiting, abdominal pain, diarrhea, loss of the sense of smell or taste to persistent dry cough, shortness of breath, difficult breathing, chest pain during breathing cycles. Evidently, these clinical findings overlap with many other clinical syndromes common in pediatric/adolescent ages, such as pneumonia, bronchiolitis, e-cigarette or vaping associated lung injury, acute intestinal infection. (8) . Although severe cases of Covid19 in children, including fatal cases, have been reported, most of children appear to have asymptomatic, mild, or moderate disease and recover within one to two weeks of disease onset (9 , 10) Why Covid19 appears to be less common and less severe in children than in adults is unclear. Various possibilitis are: that children have a less intense immune response to the virus than adults, that viral interference in the respiratory tract may lead to lower viral load, reduced cytokine release, different expression of the angiotensin converting enzyme 2 receptor. The speculation covers even more situations such as pre-existing cross-reactive antibodies, previously given live vaccines, healthier blood vessels or decreased exposure and decreased rates of testing of children (11,12, 13)

Laboratory findings

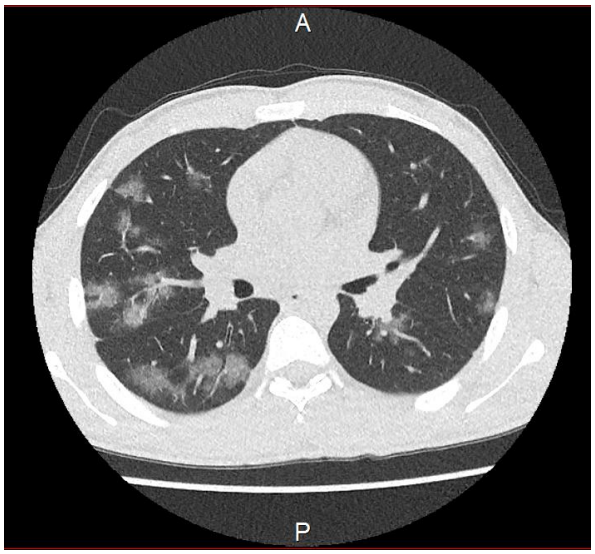
The complete blood count usually has been normal. Elevated lactate dehydrogenase (LDH) has been abnormal mostly (14). Approximately one-third had elevated C-reactive protein (CRP) above 5 mg/L and/or procalcitonin above 0.5 ng/mL. In observational studies, elevated inflammatory markers CRP, procalcitonin, interleukin 6, ferritin, D-dimer) at admission or during hospitalization, hypoxia at admission, and gastrointestinal symptoms at admission have been associated with severe disease in children (15.16.17).

Imaging in Covid19 paediatric patients

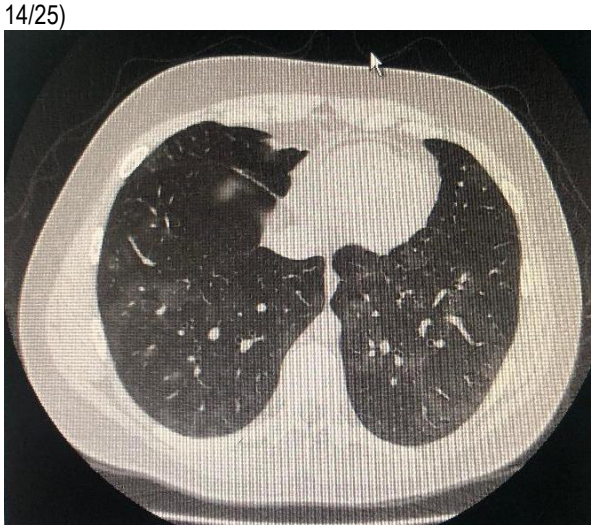
Chest X-ray has been the first choice. Chest X ray is recommended for children with confirmed diagnosis of Covid19 presenting with mild symptoms and pre-existing comorbidities, and for children with moderate to severe symptoms of lower respiratory involvement, risk factors for disease progression, complications, or worsening respiratory condition. Computerised tomography (CT scan) was indicated in children and adolescents developing clinical worsening, acute respiratory distress syndrome,progression or suspicion of pulmonary embolism, cardiac injury, kidney injury, liver disffunction (18.19).
In a separate meta-analysis of 1026 children with laboratory confirmed Covid19 who underwent CT scan imaging of the chest, 36 % had normal findings and 28 % had bilateral lesions (20). Ground glass opacities was found in 37% and consolidation or pneumonic infiltrates in 22 % of cases in this analyses. Findings typical for viral lower respiratory infections such as hyperinflation, peribronchial markings were not reported. In a small retrospective study from a single institution, 9 out of 11 children with MIS-C had pleural effusions compared with none of 16 children with Covid19 without MIS-C (21,22).
In our analyses CT scan abnormalities in children and adolescents were typical for Covid19 pneumonia, as it was observed in adults (CT severity score, CO-RADS clasification, Covid19 stadium). We present the most frequent and significant CT findings clearly visible on pictures 1,2,3,4.



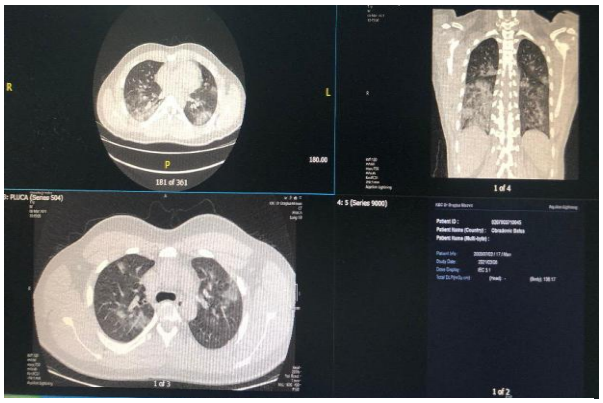
Picture 1. CT scan of 13 years old girl (CT scor 22/25)
Slika 1. CT nalaz kod 13 godina stare devojčice (CT skor 22/25)



Picture 2. CT scan of 18 years old male (CT scor 14/25)
Slika 2. CT nalaz kod 18 godina starog mladića (CT skor 14/25)



Picture 3. CT scan of 16 years old male (CT scor 17/25, in resolution)
Slika 3. CT nalaz kod 16 godina starog mladića (CT skor 17/25, promene u rezoluciji)



Picture 4. CT scan of 17 years old male with Sy Langdon Down(CT scor 14/25 in progression)
Slika 4. CT nalaz kod 17 godina starog mladićna sa sindromom Langdon Down (14/25, promene u progresiji)

Results

Medical Center „Dr Dragiša Mišović" has been appoinetd National Covid Center from March 2020. permanently and continously, and we still take care of Covid 19 paitents. Pediatric Department of Medical Center „Dr Dragiša Mišović" Children's Hospital for Lung Diseases and Tuberculosis was appointed National Pediatric Covid Center.

Children from the whole country were referred to our hospital for monitoring, diagnosis, treatment, from the early ages, the first days of life up to 18 years. During the Covid19 pandemic from March 16th 2020 until April 8th 2021., 734 children were admitted to a Hospital. At the same time 481 of accompanying persons were admitted too, and frequently they needed clinical monitoring, diagnosis and treatment. In the event of their worsening we transferred the adult Covid19 patients to adult departments of our Medical Center.Pediatric patients were confirmed SARS COV 2 positive (PCR or AG test) before admission. Very rarely, children with negative tests but highly suspected symptoms and positive epidemiological status were admitted. In summer 2020, nine children with negative SARS COV 2 test were presented with MISC.

Here, we will present a subgroup of our patients, hospitalized during autumn and winter season 2020/2021 due to Covid19 pneumonia, 67 of them, age range from 2 do 18 years, 41,2% of males and 58,8% females. (Table 1,2)

Table 1. Gender distribution
Tabela 1. Distribucija po polu

Gender(%)	Male	Female
	41.2	58.8

Table 2. Age distribution
Tabela 2. Distribucija po uzrastu

Years (%)	> 10 years	10 to 18 years
	7 (11,8)	60 (88,2)

According to worldwide experience and literature data the most prominent risk factor was obesity, in adults and children as well.
In our group, 47% were obese and rest of 53% were not. (Table 3)

Table 3. Distribution according to body weight
Tabela 3. Raspodela pacijenata prema telesnoj težini

Obesity (%)	Yes	No
	47	53

Half of our patients with Covid19 pneumonia presented with comorbidities, such as diabetes, asthma, food allergy, Down syndrome, renal disease, autoimmune hepatitis. (Table 4)

Table 4. Distribution according to comorbidites
Tabela 4. Raspodela prema komorbiditetima

Comorbidities (%)	Yes	No
	50	50

Complete laboratory and radiological investigations were ordered for patients during the hospital stay. However, here we will present some of these tests, chest X ray and CT scan findings as the most impressive and affirmative for diagnosis. Positive chest X ray for pneumonia in our group of children was found in 86,7% of cases. Chest radiography was not available in 7,3% because they were referred for CT scan directly and not for chest X ray.

Table 5. Chest X ray distribution
Tabela 5. Raspodela prema nalazu radiografije pluća

Chest X ray (%)	Not available	Negative for pneumonia	Positive for pneumonia
	7.3	6.00	86.7

Computerised tomography of the lungs remains the most valuable tool for viral pneumonia confirmation. In our group of patients CT scan was performed in 67,7% of cases, CT score was defined as for adult population, descriptive and numeric methods were used.For easier comparation we used numeric method, scale from 0 to 25 points. From 46 patients with CT of the lungs performed, 43,5% was defined with serious changes and high values of the CT score (Table 6,7)

Table 6. CT scan distributiopn
Tabela 6. Raspodela prema učinjenom CT pluća

CT (%)	Not performed	Performed
	32.3	67.7

Table 7. CT scor , mild to moderate and severe
Tabela 7. CT skor, blage promene i ozbiljne, teške promene

CT score (%)	0 to 10/25	11 to 25/25
46 patients	56,5	43,5

Parameters that contributed in the assessment of clinical condition of our patients were fever, duration of high fever,presence of respiratory and other symptoms, oxygen saturation and level of C reactive protein (CRP). The obtained results were recorded in tables 8,9,10,11,12,13.

Table 8. Fever in our patients.
Tabela 8. Temperatura kod naših pacijenata

Fever (%)	< 38,5 C	>38,5	No fever
	22	72	6

Table 9. Duration of fever before hospital admission.
Tabela 9. Dužina febrilnosti pre prijema u bolnicu

Duration of fever in days (%)	0 - 3	4 - 9	10 and more
	26.5	60.3	13.2

Table 10. Presence of respiratory symptoms (cough)
Tabela 10. Prisustvo respiratornih simptoma (kašalj)

Respiraty symptoms (%)	Present	Not present
	83.8	16.2

Table 11. Presence of other symptoms
Tabela 11. Prisustvo drugih simptoma

Other symptoms (%)	
Difficult breathing	13.2
Intestinal problems	29.4
Tiredness	55.9
Haedache	19.1
Loss of smell	8.9
Throat ache	19.1

Table 12. Level of CRP
Tabela 12. Vrednost CRP-a

CRP (%)	< 50	51 - 100	101 and more
	77.9	11.8	10.3

Table 13. Oxygen level (Hb saturation), pulse oxymetry
Tabela 13. Saturacija Hb kiseonikom, pulsna oksimetrija

Sa O_2 at room air (%)	< 90	91 – 94	95 and more
	6	19.1	74.9

The length of hospital stay was used as an assessment tool for severity of patients' condition. Evidently, more than 9 days was duration of hospital stay of 61,1% of patients, which respresents clearly the severity of infection and/or general condition.

Table 14. Length of hospitalization in days
Tabela 14. Dužina hospitalizacije u danima

Length of hospitalization in days (%)	< 4	5 - 8	9 and more
	4.5	34.4	61.1

Finally, we estimated the statistical difference between obese and non obese patients according to parameters such as CT score, length of hospitalization, duration of high fever, oxygen saturation and level of CRP.

Student's test was used for the analyses and significant difference was found for CT score and oxygen saturation.

The values of these parameters were abnormal in obese children while in non obese children these criteria were within normal range, so far, we conclude that high CT score and lower oxygen levels were critical for obese children with Covid19 pneumonia.

Table 14.Comparison between obese and non obese patients according to CT score, length of hospitalization, duration of high fever, Hb saturation and level of CRP
Tabela 14. Poređenje između gojazne i negojazne dece prema sledećim parametrima: CT skor, dužina hospitalizacije, trajanje visoke temperature, vrednosti pulsne oksimetrije, vrednost CRP-a

	Gojazni Mean ± SD	Negojazni Mean ± SD	T - test
CT score	10.78±5.04	7.19±6.10	t< 0.05
Length of hospitalization	35.17±44.01	29.71±45.66	t> 0.05
Duration of high fever	8.75±2.71	8.60±3.31	> 0.05
Hb Saturation	96.64±2.15	97.60±1.72	t< 0.05
CRP	5.24±2.50	5.51±3.53	> 0.05

Discussion

Children with underlying medical conditions such as obesity, diabetes, neurological conditions, congenital heart diseases, asthma or other chronic pulmonary diseases, immunosuppression or Down syndrome, have been at greater risk for developing severe disease. In a systematic review of 587 children (hospitalized children and outpatients) with laboratory confirmed Covid19 and joint comorbidities, 22% had an underlying condition. The most common underlying conditions were chronic pulmonary diseases, including asthma (45%), congenital heart diseases (23 %), immune suppression (12%), and hematologic or oncologic conditions (6%), obesity (27%), neurological and developmental conditions (22 %). Obesity was significantly associated with disease severity.
Our results are in accordance with literature data, particularly in terms of risk factors for serious pneumonia caused by Covid19. Some pediatric patients showed deterioration acompanied with dyspnea, cyanosis, progressive lymphocyte reduction, platelet decrease, transaminase or creatine kinase increase and the disease would develop progressively into acute respiratory distress syndrome, respiratory failure, septic shock, multiple organ dysfunction syndrome or coagulation disorders (23.24)
Currently, there are no drugs specifically approved by the U.S. Food and Drug Administration (FDA) for treatment of Covid19 in children. Treatment of Covid19 remains largely supportive and includes prevention and management of complications.

Conclusion

Having been involved in managing Covid19 paediatric patients from the very begining, we might have been able to observe significant rise in numbers of clinically and radiologically verified moderate to severe disease, particularly pnuemonia during autumn and winter 2020/2021. Frequently, but not necessarily these children and even more adolescents have at least one risk factor such as a comorbidity, especially obesity.

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Contributors.
ZZ developed the hypothesis, wrote the first draft of the majority of the manuscript with the exception of the radiological interpretation of the review. ZZ, VV compiled the references and prepared the final version of the manuscript. OO contributed to the development of the main hypothesis. IC,OS,AN,VA contributed in data analyses and prepared the data base, images.

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