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Features of COVID-19 in teenagers. Clinical cases

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Coronavirus infection in childhood is a common disease and has a number of features of the clinical course. There remain quite a lot of problems related to the variety of clinical symptoms, the severity of the course and treatment tactics in different age categories.

Purpose — to study the epidemiological and clinical features of the coronavirus disease COVID-19 in adolescents compared to the younger age group in order to predict the severity of the course and determine treatment tactics.

Materials and methods. A single-center retrospective open cohort study of 188 patients under the age of 18 hospitalized in the infectious disease department of the Chernivtsi Regional Children's Clinical Hospital with a confirmed respiratory infection caused by SARS-CoV-2 was conducted. This cohort of patients is divided into 2 clinical groups. The Group I consisted of children aged 12 to 18 years (43 children), the Group II included children aged 0 to 11 years (145 patients).

Results. Epidemiologically, extrafamilial sources of infection prevail in adolescence in the range of 44.2% (n=19), which is explained by greater social activity compared to children from birth to 11 years of age. For the 1st observation group, symptoms of damage to the lower respiratory tract are more characteristic, in particular, cough 81.4% (n=23), shortness of breath 51.1% (n=22), hypoxemia 14.2% (n=6) and symptoms of associated with intoxication syndrome (general weakness, asthenia 97.6% (n=42), decreased appetite, refusal to eat 74.4% (n=32), myalgia 11.6% (n=5), headache 14,2% (n=6)). The severity of the course of the coronavirus infection in adolescence is due to the dominance of lower respiratory tract lesions with the development of pneumonia in 58.2% (n=25) of cases, which required longer and more intensive treatment.

Conclusions. The share of adolescents hospitalized due to COVID-19 was 22.9% (n=43), among them with a severe degree of impairment of the general condition — 16.4% (n=7), which is due to the predominance of damage to the lower respiratory tract with the development of pneumonia in 58.2% (n=25) of cases. This cohort of patients is characterized by a longer intoxication syndrome, the epidemiological role of family contacts with regard to COVID-19 decreases, and the value of unidentified non-familial sources of infection increases — 44.2% (n=19).

The research was carried out in accordance with the principles of the Declaration of Helsinki. The research protocol was approved by the Local Ethics Committee of the institution mentioned in the work. Informed consent of parents or their guardians was obtained for conducting research.

No conflict of interests was declared by the authors.

Keywords: SARS-CoV-2, epidemiological, clinical features, adolescents, children.

Особливості перебігу COVID-19 у підлітків. Клінічні випадки

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Коронавірусна інфекція в дитячому віці є поширеним захворюванням і володіє рядом особливостей клінічного перебігу. Залишається доволі багато проблем, пов'язаних із різноманіттям клінічних симптомів, тяжкістю перебігу і лікувальною тактикою в різних вікових категоріях.

Мета — вивчити епідеміологічні та клінічні особливості COVID-19 у підлітків порівняно з молодшою віковою групою для прогнозування тяжкості перебігу та визначення тактики лікування.

Матеріали та методи. Проведено одноцентрове ретроспективне відкрите когортне дослідження 188 пацієнтів віком до 18 років, госпіталізованих до інфекційних відділень Чернівецької обласної дитячої клінічної лікарні з підтвердженою респіраторною інфекцією, зумовленою SARS-CoV-2. Цю когорту пацієнтів розподілено на дві клінічні групи. Групу I становили діти віком від 12 до 18 років (43 дитини), групу II — діти віком від 0 до 11 років (145 пацієнтів).

Результати. В епідеміологічному відношенні позародинні джерела інфікування переважають у підлітковому віці в межах 44,2% (n=19), що пояснюється більшою соціальною активністю порівняно з дітьми від народження до 11 років. Для групи I більш характерні симптоми ураження нижніх дихальних шляхів, зокрема, кашель — 81,4% (n=23), задишка — 51,1% (n=22), гіпоксемія — 14,2% (n=6), а також симптоми, пов'язані з інтоксикаційним синдромом (загальна слабкість, астенія — 97,6% (n=42), зниження апетиту, відмова від їжі — 74,4% (n=32), міалгії — 11,6% (n=5), головний біль — 14,2% (n=6)). Тяжкість перебігу коронавірусної інфекції в підлітковому віці обумовлена домінуванням ураження нижніх дихальних шляхів із розвитком пневмонії в 58,2% (n=25) випадків, що потребувало більш тривалого та інтенсивного лікування.

Висновки. Частка підлітків госпіталізованих із приводу COVID-19 становила 22,9% (n=43), серед них із тяжким ступенем порушення загального стану — 16,4% (n=7), що зумовлено домінуванням ураження нижніх дихальних шляхів із розвитком пневмонії у 58,2% (n=25) випадків. Для цієї когорти пацієнтів характерний більш тривалий інтоксикаційний синдром, зменшується епідеміологічна роль родинних контактів щодо COVID-19 і зростає значення невстановлених позародинних джерел інфекції — 44,2% (n=19).

Дослідження виконано відповідно до принципів Гельсінської декларації. Протокол дослідження ухвалено Локальним етичним комітетом зазначеної в роботі установи. На проведення досліджень отримано інформовану згоду дітей, батьків.

Автори заявляють про відсутність конфлікту інтересів.

Ключові слова: SARS-CoV-2, епідеміологічні, клінічні особливості, підлітки, діти.

According to official statistics, as of January 8, 2023, 167,639 cases of coronavirus disease caused by SARS-CoV-2 were registered in the Chernivtsi region, including 14388 in the children's population, starting from the date of the officially declared pandemic in Ukraine. During the specified period, 3,424 deaths were registered in the region as a result of the uncontrolled and/or complicated course of COVID-19, in particular, 5 children died. The largest number of confirmed cases of the disease among children was found in the age group of 11–17 years — 53%, in the second place — children aged 0–6 years — 26%, and this disease was most rarely registered in children aged 7–10 years — 21% [10]. At the same time, it should be noted that the current course of the disease in children has changed, and recent observations testify to the development of critical, life-threatening conditions in childhood in the range of 6–10% of children, and the severe course of the disease is more often observed in infants and children with accompanying chronic pathology [1,2]. Along with this, the data on the specifics of the course of the COVID-19 infection in adolescence turned out to be quite limited.

Today, it is known that the disease caused by SARS-CoV-2 in teenager patients is more often in a moderate and severe form compared to younger children [3–5]. Even in the absence of comorbidities, pneumonia with hypoxemia and hyperinflammation similar to that described in adults is much more common in adolescents. Nevertheless, there is evidence that the clinical course of COVID-19 pneumonia in adolescents is less severe, and the prognosis is better than in adults [7–9].

Interestingly, elevated levels of inflammatory markers at hospital admission, including C-reactive protein, D-dimer, and ferritin, were correlated with surrogate markers of severity, such as length of hospital stay and duration of respiratory support [6,11,12]. Hospitalization in the intensive care unit at admission were associated with lower levels of leukocytes and platelets and higher levels of C-reactive protein [13–14]. That is, these indicators allow early detection of adolescents with a high risk of severe forms of COVID-19.

The ***purpose*** of the work — to study the epidemiological and clinical features of the coronavirus disease COVID-19 in adolescents compared to the younger age group in order to predict the severity of the course and determine treatment tactics.

Materials and methods of the study

In accordance with the principles of bioethics, a single-center retrospective open cohort study was conducted, which included patients under the age of 18, hospitalized in the infectious diseases department of the Municipal non-profit enterprise «Chernivtsi Regional Children's Clinical Hospital» with a confirmed respiratory infection caused by SARS-CoV-2. By analyzing 188 cards of inpatients based on age differentiation, 2 observation groups were formed. The Group I consisted of children aged 12 to 18 years (43 children), the Group II included children aged 0 to 11 years (145 patients). Thus, among hospitalized patients, the share of teenagers reached 22.9%.

The COVID-19 was verified on the basis of positive results of a molecular genetic polymerase chain reaction (PCR) study with the detection of SARS-CoV-2 antigens in children. Material from nasopharyngeal and oropharyngeal swabs was used to determine SARS-CoV-2 antigens. A complex of clinical, laboratory and instrumental markers of the course of the infection caused by the COVID-19 was determined in hospitalized children.

The analysis of the research results was carried out using the computer package Statistica 6 StatSoft I Excell XP for Windows on a personal computer using parametric and non-parametric calculation methods. The diagnostic value of clinical and paraclinical results was studied based on their sensitivity (Se), specificity (Sp). The risk of event realization was studied taking into account attributive (AR), relative risks (RR) and the odds ratio (OR) of the event with determination of their 95% confidence intervals (95% CI).

The research was carried out in accordance with the principles of the Declaration of Helsinki. The research protocol was approved by the Local Ethics Committee of the institution mentioned in the work. Informed consent of children, their parents or their guardians was obtained for conducting research.

Results of the study and discussion

When studying the epidemiological features of coronavirus infection in children of the Chernivtsi region, it was established that positive epidemiological contact occurred in more than half of the cases with the prevalence of epidemiologically significant family contacts. There were no cases

Table 1

Features of the course of COVID-19 in children at the hospital stage (%)

Symptoms	Group I (n=43)	Group II (n=145)
General weakness, asthenia	**97.6**	86.7
Fever	79.1	**88.9**
Decreased appetite/refusal to eat	**77.4**	66.4
Pharyngitis	68.1	65.1
Nasal congestion	34.9	**46.8**
Rhinorrhea	13.9	**21.3**
Myalgia	**11.6**	5.8
Hypoxemia	**14.2**	3.6
Headache	**14.2**	3.5
Exanthema	2.3	2.8
Diarrhea	2.3	**5.8**

of infection in organized children's groups in this cohort, which is explained by the short period of possible visits due to restrictive quarantine measures. With the increase in the social activity of children and adolescents, the epidemiological role of family contacts decreases, and the significance of unidentified extrafamilial sources of infection increases. In particular, 19 adolescent children were identified as having an unknown source of infection, which was 44.2%.

Analysis of the clinical characteristics of the course of the coronavirus disease in children made it possible to distinguish certain age-related features that affected the frequency of certain symptoms in children of clinical age groups (Table 1). Thus, symptoms of damage to the lower respiratory tract prevailed in adolescence, in particular, cough (n=23), shortness of breath (n=22), and hypoxemia (n=6) were noted in the majority. In percentage terms, the frequency of registration of cough, shortness of breath, and hypoxemia in the I and II clinical groups was 81.4:48.4%, 51.1:21.8%, and 14.2:3.6%, respectively. Also, adolescents more often noted symptoms associated with intoxication syndrome (general weakness, asthenia 97.6% (n=42), decreased appetite, refusal to eat 74.4% (n=32), myalgia 11.6 (n=5), headache 14.2% (n=6), which is probably due to the verbal communication capabilities of children of this age category. On the other hand, in the comparison group, symptoms from the side of the upper respiratory tract dominated, in particular, nasal congestion 46.8% (n=68), rhinorrhea 21.3% (n=31) and fever 88.9% (n=129) and diarrhea 5.8% (n=8) were more frequently noted.

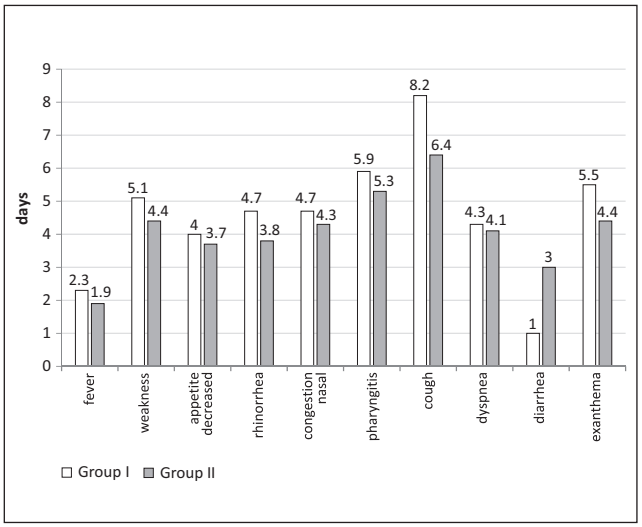

Fig. 1. Duration of clinical symptoms (days)

At the same time, in terms of duration, almost all symptoms of the disease were registered a little longer in children of the Group I, except for diarrhea, which, despite an insignificant share of representation in patients, was probably observed longer in children 0–11 years old, which can probably be caused by the subjectivity of the assessment by parents in children and groups and the possibility of self-assessment of their own condition by the majority of representatives of the comparison group. Thus, after the fifth day of treatment in the hospital, such clinical symptoms as general weakness, cough, phenomena of pharyngitis and exanthema persisted in adolescents, which were registered less often in this age group, but persisted for a longer time (Fig. 1).

The course of the COVID-19 in 16.4% (n=7) of the patients of the Group I was accompanied by a severe disturbance of the general condition, while in the patients of the Group II, a severe course of this disease was registered in only 6.9% (n=10). The predominance of the severity of the course in adolescence can be explained by the dominance in the majority of patients of this age group of lesions of the lower respiratory tract and the development of pneumonia in 58.2% (n=25) of cases in comparison with patients of the Group II, where the frequency of pneumonia did not exceed 23.9% (n=34). Clinical-epidemiological analysis showed that the severity of the course of the COVID-19 was associated in adolescents as follows: Se — 16.4% (95% CI: 9.68–25.21); SP — 93.1% (95%CI: 86.09–97.29); OR — 2.62 (95%CI: 0.9–7.4); RR — 2.4 (95% CI: 1.2–4.5), AR — 0.09. It is also worth noting that, compared to patients of the Group II, the Group I had an increased risk of damage to the lower respiratory tract as a result of a respiratory infection caused by SARS-COV-2: OR — 4.43 (95% CI: 2.4– 8.1); RR — 1.99 (95% CI: 1.36–2.9), AR — 0.35.

The relatively severe course of the COVID-19 in adolescent patients with a predominance of the tendency to involve the lower respiratory tract in the inflammatory process was also reflected in the average duration of inpatient treatment for patients of different ages. Thus, the average length of stay in an inpatient bed of children of the Group II was 8.6 days, compared to the Group I — 11.5 days.

The more severe course of the COVID-19 in teenagers was also reflected in the treatment tactics in this age group. In particular, adolescent patients probably received systemic glucocorticosteroids (GCS) 6.1±1.64 days for a longer period of time and required oxygen supplementation — 6.0±3.5 days, as well as more often received antibiotic therapy — 58.1% (n=25) and required infusion therapy (IT) — 37.2% (n=16) with glucose-saline solutions and the need to use direct-tacting anticoagulants — 13.9% (n=6). Features

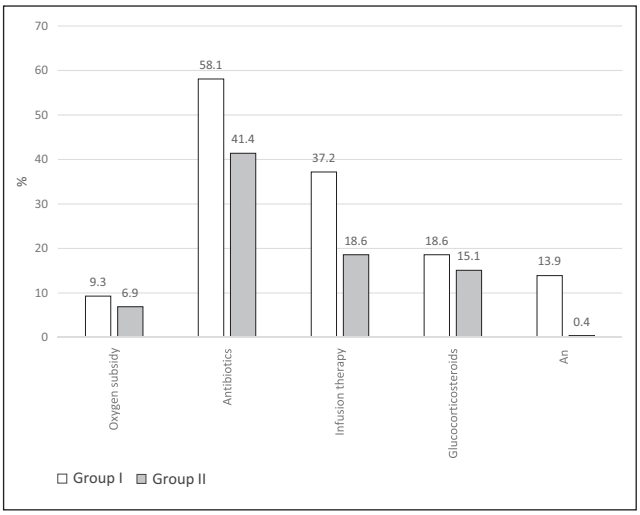

Fig. 2. Treatment for COVID-19 in children

and duration of treatment for COVID-19 at the inpatient stage in children of both comparison groups are shown in Table 2 and Fig. 2.

For a more visual demonstration of the clinical features of the course of COVID-19 in teenagers, we cite cases from practice.

Clinical case 1

Boy O., 16 years old, was hospitalized in the intensive care unit on the 5th day after the onset of the disease with complaints of an increase in body temperature to 39.5°C, cough, shortness of breath, skin rash. From the anamnesis: the 1st day — acute onset of the disease with an increase in body temperature to 39.5°C, cough; the 2–3rd days — increase in body temperature up to 39.5°C, cough, shortness of breath; the 4th day — a rash appeared all over the body, an increase in body temperature to 39.5°C, cough, shortness of breath; the day 5 — hospitalization in the intensive care unit of the Chernivtsi Regional Children's Clinical Hospital with suspicion of bilateral pneumonia, respiratory insufficiency of the I–II degree, hyperthermic syndrome. Suspected case of COVID-19? Epidemiological contact denies. During the objective examination at the time of hospitalization, SaO_2 — 94%, body temperature — 37.8°C; respiratory rate — 28/min. The general condition is severe, which is due to the

Table 2

Duration of treatment for COVID-19 in children (days)

Group	Oxygen subsidy	Antibiotics	Infusion therapy	Glucocorticosteroids
I	6.0±3.5	12.5±0.8	2.9±0.97	6.1±1.64
II	1.4±0.22	8.1±0.47	2.3±0.66	2.5±0.34

phenomena of broncho-obstruction of the II degree, hyperthermic, intoxication syndromes. The face is hyperemic, the whole body has an erythematous rash of various sizes. Chest retraction of the I–II degree. Auscultatory breathing over the lungs is weakened on both sides, wet fine-vesicular rales, more on the right. Diagnosis: Out-of-hospital viral-bacterial bilateral interstitial pneumonia, complicated II degree broncho-obstruction, I–II degree respiratory failure. COVID-19 confirmed by polymerase chain reaction (PLR). In the general blood analysis, a tendency to thrombocytosis (407×10^{10}), moderate neutrophilia (rod-nuclear — 31, segmentonuclear — 42) is observed. Among the results of additional research methods, attention is drawn to a three-fold increase in C-reactive protein (24 mg/ml) and D-dimer (1800 ng/ml), an increase in the level of procalcitonin (1.4 ng/ml). A positive result of the polymerase chain reaction of swabs from the throat/nose for SARS-CoV-2 was obtained on the 5th day from the onset of the disease, negative on the 16th day from the onset of the disease. X-ray examination revealed signs of bilateral polysegmental pneumonia. During the stay in the hospital, the patient had an increase in body temperature at the level of febrile values for 4 days. The patient underwent oxygen therapy — 3 days, antibacterial therapy (levoflox + meropenem) — 11 days, of which combined treatment — 9 days. Enoxiparin sodium, human immunoglobulin and dexamethasone were also used. On the 4th day of stay in the intensive care unit, the child's condition improved significantly, the child was transferred for further treatment to the department of airborne infections. On the 6th day, the rash disappeared. And already on the 15th day of treatment in the hospital after the negative results of the polymerase chain reaction smear, the child was discharged home in a satisfactory condition.

The peculiarity of this clinical case is the presence of bilateral interstitial pneumonia, probably of viral-bacterial origin in the absence of concomitant pathology, with signs of hypoxemia, which required treatment in the intensive care unit with oxygen supplementation; distinct signs of the inflammatory process with blood coagulation disorders. Thus, it can be argued that the disease progressed similarly to that of adults, but with a more favorable course.

Clinical case 2

Boy H., 10 years old, was hospitalized in the infectious department on the 4th day after the onset of the disease with complaints of an increase in body temperature to 38.2°C, a rash all over the body, itching. From the anamnesis: the 2nd day — increase in body temperature to 38.7°C; the 3rd day — increase in body temperature to 39°C, rash all over the body, itching. As prescribed by the doctor, he took Flemoxin, Cetrin, Nurofen; On the 4th day — they consulted a pediatrician, and he was hospitalized after being referred to the Chernivtsi Regional Children's Clinical Hospital. Diagnosis upon referral: Suspicion of COVID-19. Epidemiological contact denies. During an objective examination at the time of hospitalization, SaO_2 was 98%, body temperature was 37°C, and the respiratory rate was 24/min. General condition of medium severity due to hyperthermic, intoxication syndromes, catarrh of the upper respiratory tract. On the skin of the trunk, lower and upper limbs, a spotted-papular rash on a hyperemic background, prone to fusion, is noted. Diagnosis: acute viral infection of the upper respiratory tract of multiple localization, medium-severe course. COVID-19-Acute respiratory disease. In the general blood analysis, leukocytosis with neutrophilia, a tendency to thrombocytosis is noted. Among the results of additional research methods, attention is drawn to a three-fold increase in C-reactive protein (24 mg/ml) and D-dimer (1400 mg/ml), the level of procalcitonin within the normal range (0.18 ng/ml). A positive result of the polymerase chain reaction of swabs from the throat/nose for SARS-CoV-2 was obtained twice (on the 3rd and the 8th day from the onset of the disease). During the ultrasound examination of the organs of the abdominal cavity, an increase in the size of the spleen was revealed. During the stay in the hospital, the body temperature was kept within normal limits. The patient was treated with ceftriaxone antibacterial therapy for 10 days, anticoagulants and antiaggregants, glucocorticosteroids were administered. On the 8th day from the moment of illness, the rash disappeared. On the 10th day, the child was discharged home in satisfactory condition.

Thus, this clinical case is distinguished by the presence of a polymorphic rash in a child, areas of confluent nature with hemorrhagic elements, probably due to vasculitis against the background of elevated body temperature and minimal signs of catarrh of the upper respiratory tract, but with a high level of indicators of inflammatory markers and signs of hypercoagulation.

Conclusions

Among pediatric patients hospitalized for COVID-19, the share of adolescents was 22.9% (n=43).

In adolescence, the epidemiological role of family contacts with regard to COVID-19 decreases, and the value of unidentified non-familial sources of infection increases — 44.2% (n=19).

The clinical course of the coronavirus disease in adolescent patients is characterized by a longer intoxication syndrome and symptoms of damage to the lower respiratory tract.

The severity and duration of treatment for COVID-19 is higher in children of the Group I 16.4% (n=7) compared to the Group II (6.9% (n=10), which is due to the predominance of lower respiratory tract lesions with the development of pneumonia in 58.2% (n=25) of cases. Adolescent age as a prognostic factor for a more severe course of COVID-19 had the following value: Se — 16.4% (95% CI: 9.68–25.21); SP — 93.1% (95%CI: 86.09–97.29); OR — 2.62 (95%CI: 0.9–7.4); RR — 2.4 (95% CI: 1.2–4.5), AR — 0.09.

No conflict of interests was declared by the authors.

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