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COVID-19 IN NEWBORNS: OWN
EXPERIENCE ON THE EXAMPLE
OF CLINICAL CASES

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Summary.

Introduction. Currently, there is controversial information regarding the epidemiologic characteristics and severity of COVID-19 in pregnant women and newborns. Most researchers report the same severity of disease in pregnant and non-pregnant women, and a milder course of disease in the neonatal period, with the possibility of critical illness in some infants. Ideas about the possibility of transmission of SARS-CoV-2 to a newborn have changed. Since intrauterine transmission of the novel coronavirus is currently considered rare, COVID-19 in newborns is usually associated with postnatal transmission of the virus.

The aim of the work was to analyze the epidemiologic and clinical features of the COVID-19 in newborns based on the analysis of clinical cases.

Material and methods. On 2020, at the beginning of the COVID-19 pandemic, 11 newborns were admitted to the infectious diseases departments of Chernivtsi Regional Children's Clinical Hospital, 9 children were referred from home by a family physician, and 2 children were transferred from maternity care facilities. Diagnosis was confirmed by PCR-RT detection of SARS-CoV-2 RNA in nasal/oropharyngeal swabs.

The research was conducted in accordance with the principles of bioethics, the conclusion of the Commission on Biomedical Ethics of the Bukovinian State Medical University on the observance of moral and legal rules for conducting medical-scientific research, Protocol No. 6 dated March 16, 2023.

The research was carried out within the framework of scientific and research activity of the Department of Pediatrics and Infectious Diseases of Children of the Bukovinian State Medical University "Modern epidemiological, clinical-paraclinical and diagnostic features of the most common inflammatory infectious and non-infectious diseases in children", state registration number: 0122U002208.

Results. The analysis of the epidemiologic data allowed to identify an intrafamilial source of infection in all identified cases (in one case the source of infection could not be identified), in most cases it was the mother, in one case the source of infection was the father and the grandmother. In most families there are older siblings who could serve as a potential additional source of infection, but respiratory symptoms in siblings were identified in one third of the families.

In the late neonatal period, cases of horizontal virus transmission were characterized by mild symptoms of upper respiratory tract infection as acute nasopharyngitis, one case - as a mixture with secretory diarrhea. COVID-19 in another child was accompanied by acute gastroenteritis and moderate dehydration. The clinical picture of coronavirus infection in the remaining third of cases was characterized by lower respiratory tract infection as acute tracheobronchitis, acute obstructive bronchitis and bronchiolitis.

Two infants were transferred from the maternity hospital after delivery because of COVID-19 maternal symptoms and SARS-CoV-2 RNA detection in the infants' nasal/oropharyngeal swabs on the first day of life. These children were asymptomatic with no clinical or laboratory evidence of an infectious-inflammatory process during observation.

Conclusions. The presence of an exclusively family source of infection can be considered an epidemiological feature of COVID-19 in the neonatal period. In the case of horizontal transmission of the SARS-CoV-2 virus in newborns, the disease COVID-19 in most cases proceeds as mild upper respiratory tract infection, less often – as lower respiratory tract infection and/or secretory diarrhea. In the case of maternal COVID-19 disease before childbirth the vertical and/or antenatal infection mode and the subsequent asymptomatic neonatal COVID-19 cannot be denied.

Keywords: Newborns; COVID-19; Peculiarities of Epidemiology; Clinics.

Introduction

Compared to the adults COVID-19 in children is characterized by a predominance of mild and asymptomatic cases. Peculiarities of the disease in the pediatric population include a shorter incubation period and a relatively better prognosis with faster recovery. At the same time, children can be potential, asymptomatic virus carriers with a long period of its release. During COVID-19 pandemic, pregnant women and neonates are considered vulnerable populations. Cardiopulmonary adaptation

mechanisms of pregnant women (eg, increased heart rate and stroke volume, as well as decreased residual lung capacity) may increase the risk of hypoxemia. In this aspect, pregnant women can be considered as a high-risk group in the management strategy of the condition and the possibility of prevention of diseases associated with lung lesions, such as COVID-19. [1, 2].

To date, there is no convincing evidence that pregnant women have greater risk of contracting COVID-19 [3, 4], however, it has been established

that pregnancy increases the risk of severe disease caused by other types of coronaviruses, as well as other viral respiratory infections such as influenza [5]. At the same time, temporary immunosuppression of pregnant women can increase the risk of infection, including by the SARS-CoV-2 [6, 7]. Despite the available data on the asymptomatic COVID-19 in a third examined pregnant women [8], as well as despite the absence of a probable difference in clinical symptoms and disease severity in pregnant and non-pregnant women [9], infection during the third pregnancy trimester is accompanied by the risk of hospitalization in the intensive care unit (about 1%), with the probability of invasive mechanical ventilation about 0,3%. Concomitant diseases and conditions of the pregnant woman, in particular, age over 40 years, obesity, anemia, arterial hypertension and diabetes, are additional risk factors for the severity of the disease in this group [10-12]. Thus, some studies indicate the possibility of a severe disease in pregnant women in 10% of cases [13, 14]. In addition, the cytokine storm triggered during pregnancy by COVID-19 can cause severe damage to the fetus, with subsequent autism spectrum disorders and brain development abnormalities in newborns [15].

One of the main problems related to COVID-19 is the potential negative impact of the severity of the pregnant woman's condition on the fetus, the probability of vertical transmission of SARS-CoV-2, as well as the consequences of neonatal COVID-19 for the child's body in the future [1, 16].

Until recently, although the possibility of intrauterine transmission of SARS-CoV-2 was not denied, it was not confirmed, in particular, due to the limited number of observations, while the objective criteria for transmission confirming in the fetus and newborn remained debatable [17]. The fact of placental infection with SARS-CoV-2 during pregnancy has been established, at the same time, whether placental infection leads to neonatal infection remains unclear [18]. Taking into account the accumulation of research results that note the presence of SARS-CoV-2 RNA in the biological fluids of the fetus and newborn, as well as the positive results of serological tests (specific IgM in the newborn), intrauterine transmission of COVID-19 has a high probability, at the same time, the probability of vertical transmission of infection. Maternal exposure to COVID-19 in the third trimester is generally low (approximately 3,2%) without significant consequences for newborns [19]. There remains a paucity of observations and insufficient data on vertical transmission of the SARS-CoV-2 virus in the first two trimesters of pregnancy.

Newborns, like their own mothers, are a group at high risk of COVID-19 due to limited age peculiarities of immune protection [1]. Because intrauterine transmission of SARS-CoV-2 is currently considered rare, the COVID-19 in newborns is usually associated with postnatal infection. Transmission of respiratory viruses, including SARS-CoV-2, from the mother to the newborn, occurs through the airborne route, mainly through close household contact, as well as a result of in-hospital infection and contact with infection sources in public places [20, 21].

The disease in newborns usually is mild, although

some infants have a severe COVID-19 [13]. In the presence of COVID-19 symptoms in the mother during childbirth, most of the infected newborns remained asymptomatic or had mild symptoms with rapid resolution during follow-up [22, 23]. Clinical manifestations of COVID-19 in newborns differ from those in older children and adults, with gastrointestinal symptoms and loss of appetite being the most common. Other symptoms include fever, cough and other respiratory symptoms, lethargy, diarrhea, vomiting. Symptoms in newborns are less pronounced than in adults, the disease in adults is usually accompanied by fever, myalgia, fatigue, cough, shortness of breath and respiratory failure, while gastrointestinal symptoms are rare [21, 23]. Despite the milder symptoms, the neonatal and infant age can be a factor in prolonging the release of the SARS-CoV-2 virus [24].

Taking into account the controversy and lack of information about the peculiarities of the COVID-19 clinical symptoms in newborns [25], in this paper, using the example of our own observation of clinical cases of hospitalized children, we expand the knowledge of doctors about the features of the COVID-19 in the neonatal age.

The aim of the work was to analyze the epidemiological and clinical peculiarities of COVID-19 infection in newborns based on the analysis of clinical cases.

Material and methods

On 2020 at the beginning of the COVID-19 pandemics in the infectious departments of the Chernivtsi Regional Children's Clinical Hospital, we monitored 11 hospitalized newborns. Patients were selected by the method of simple sampling according to the chronology of hospitalization. In particular, 9 children were referred by a primary care physician from home, and 2 newborns were transferred from maternity care institutions. By sex, the distribution was as follows: 8 girls and 3 boys.

Examination and treatment of patients was carried out in compliance with the bioethics rules, according to current national guidelines and local clinical medical protocols. Verification of the diagnosis was carried out on the basis of the detection of RNA of the SARS-CoV-2 virus in a naso-/oropharyngeal swab by the PCR method, performed in the virological laboratory of the Chernivtsi Regional Center for Disease Control and Prevention of the Public Health Ministry of Ukraine. Neonatal age of children and detection of SARS-CoV-2 RNA in a naso-/oropharyngeal swabs by PCR were considered criteria for inclusion in the cohort. The results were analyzed by basic descriptive statistics.

The research was conducted in accordance with the principles of bioethics, the conclusion of the commission on biomedical ethics of the Bukovinian State Medical University regarding the observance of moral and legal rules for conducting medical scientific research, protocol No. 6 dated March 16, 2023.

Results and discussion

According to the results of clinical cases analysis (1-9) of neonatal COVID-19 with a horizontal

transmission, it is shown that the children were hospitalized in the late neonatal period, the average age was 17,8±1,8 days, two thirds (66,7%) were female newborns (Table 1). Most of the babies (88,9%) were born at term through birth canals (77,8%), and the rest of the babies were born by caesarean section according to obstetric indications, one baby was born prematurely.

The bigger part of children (88,9%) were hospitalized on the 1st-2nd day of the disease, which was probably due to the vigilance of parents and primary care doctors in this age period. In most families (77,8%), newborns had older brothers and

sisters, which could recognize as a potential additional source of infection, in particular, respiratory symptoms in sibs were verified in 33,3% of cases. The intra-familial source of SARS-CoV-2 virus was established in 88,9% of cases, sick mothers were in most cases (66,7%), the father and the grandmother were sources of infection in two separate cases. In all cases, the sources of infection were confirmed by SARS-CoV-2 virus RNA detection in the naso-/oropharyngeal swab by PCR. In one case, the source of infection could not be established. Table 2 shows the clinical peculiarities of COVID-19 in newborns with a horizontal transmission.

Table 1

General and epidemiological characteristics of hospitalized newborns with the horizontal SARS-CoV-2 transmission

| Patient | Age, days | Sex | Pregnancy parity | Full preterm | Childbirth type | Confirmed source of infection |
|---------|-----------|-----|------------------|---------------|-------------------|-------------------------------|
| 1. | 19 | m | III | full-term | vaginal | not confirmed |
| 2. | 21 | m | III | full-term | vaginal | father |
| 3. | 24 | f | II | full-term | vaginal | both parents |
| 4. | 15 | f | II | full-term | vaginal | mother |
| 5. | 19 | f | I | full-term | vaginal | grandmother |
| 6. | 16 | f | II | full-term | vaginal | mother |
| 7. | 13 | f | I | full-term | caesarean section | mother |
| 8. | 10 | f | II | preterm | caesarean section | mother |
| 9. | 24 | m | II | full-term | vaginal | mother |

Thus, the main clinical peculiarities of COVID-19 in newborns were respiratory and gastrointestinal lesions, accompanied by an increase in body temperature. Most of the cases (55,5%) were characterized by mild upper respiratory tract infection as acute rhinitis and pharyngitis, one of the case demonstrated mix with the phenomena of secretory diarrhea. COVID-19 in another child

was accompanied by an isolated picture of acute gastroenteritis and moderate dehydration. The clinical picture of coronavirus infection in the remaining 33,3% cases was characterized by lower respiratory tract infections as acute tracheobronchitis, acute obstructive bronchitis, and bronchiolitis; in the last two cases, respiratory symptoms were accompanied by mild respiratory failure.

Table 2

Clinical characteristics of hospitalized newborns with horizontal SARS-CoV-2 transmission

| Patient | Day of hospitalisation | Feeding type | Fever, °C | Clinical peculiarities | Disease severity | Co-morbidities | Days in-hospital treatment |
|---------|------------------------|---------------|-----------|----------------------------------|------------------|--|----------------------------|
| 1. | I | breastfeeding | TILL 38,8 | rhinitis, pharyngitis | moderate | jaundice, urinary tract infection | 10 |
| 2. | III | breastfeeding | TILL 37,8 | bronchiolitis | severe | - | 7 |
| 3. | II | breastfeeding | TILL 37,6 | rhinitis, pharyngitis | mild | hypoxic encephalopathy | 8 |
| 4. | I | mixed | TILL 38,0 | enteritis | moderate | - | 11 |
| 5. | II | formula | ABSENT | rhinitis, pharyngitis | moderate | hypoxic encephalopathy, nitrate hemoglobinopathy | 7 |
| 6. | II | breastfeeding | TILL 38,5 | bronchitis | moderate | hypoxic encephalopathy, jaundice | 9 |
| 7. | I | breastfeeding | TILL 38,8 | rhinitis, pharyngitis, enteritis | mild | - | 13 |
| 8. | I | formula | до 38,5 | rhinitis, pharyngitis | moderate | congenital heart defect | 7 |
| 9. | II | formula | до 37,8 | bronchoobstruction | moderate | acute otitis media | 11 |

Most of the children (55,5%) had a high grade fever, the increase in body temperature in a third of the patients did not exceed low grade fever, and in one child neurological symptoms due to nitrate methemoglobinopathy were predominance.

Among the clinical cases, the most severe COVID-19 occurred in a child suffered from bronchiolitis because of requirement of respiratory protection as oxygen therapy and compensation of respiratory fluid losses as slow infusion of glucose-salt solutions. Two newborns received antibacterial therapy with III-generation cephalosporins because of verified the urinary tract infections and otitis media. At the same time, the condition of some children was aggravated by some neonatal conditions as hypoxic encephalopathy, neonatal jaundice, and one child had a heart defect.

Two girls were born by SARS-CoV-2 verified mothers and transferred from maternity care institutions. These two cases of COVID-19 in children, confirmed by for SARS-CoV-2 RNA detection by PCR test performed on the 1st day of life immediately after birth. Both children were full-term, born through birth canals. In one case of observation hypoxic encephalopathy was verified, in the other girl, only the processes of physiological adaptation of the newborn were noted. Both girls did not have any clinical or laboratory signs of an infectious-inflammatory process during their in-patient observation. In a week of observation, the babies were discharged with a negative result of the PCR test for SARS-CoV-2 RNA.

According to analysis of clinical cases, it is possible to state the differences between the clinical picture of COVID-19 in the early and late neonatal period. Verified COVID-19 cases immediately after birth were asymptomatic, which can probably be explained by the possibility of transplacental transmission and the protective role of specific maternal virus-neutralizing IgG.

Because of nasopharynx and oropharynx swabs collection was carried out immediately after birth with the minimization of the time of postnatal contact between the mother and the child before the collection of the swabs, as well as the difference in the clinical picture, we can assume the impossibility

of horizontal transmission of SARS-CoV-2 in these asymptomatic cases. At the same time, no other biological fluids were used to confirm the fact of vertical transmission of the new coronavirus SARS-CoV-2. The difficulties of confirmation the SARS-CoV-2 transmission type in our cases is also related to the limited number of observations. Thus, in our opinion, SARS-CoV-2 vertical transmission in these asymptomatic confirmed cases seems quite likely.

Conclusions

1. An epidemiological peculiarity of COVID-19 in the neonatal period can be considered the presence of family source of infection, mostly among parents and older siblings.

2. In the case of horizontal transmission of the SARS-CoV-2 virus in newborns, the disease of COVID-19 in most cases occurred as mild upper respiratory tract infection, less often as a lesion of the lower respiratory tract and gastrointestinal tract.

3. In the case of maternal disease few days before delivery and the presence of clinical picture of SARS-CoV-2 infection during childbirth, the vertical and/or antenatal route of virus transmission with the subsequent asymptomatic COVID-19 with virus secretion from the first day of extrauterine life cannot be refuted.

Prospects for further research

They consist in the accumulation of experience in the management of newborns infected with the SARS-CoV-2 virus, with different routes of virus transmission and different severity of COVID-19.

The research was carried out within the framework of the scientific and research activity of the Department of Pediatrics and Children's Infectious Diseases of the Bukovinian State Medical University «Modern epidemiological, clinical-paraclinical and diagnostic features of the most common inflammatory infectious and non-infectious diseases in children», state registration number: 0122U002208.

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COVID-19 У НОВОНАРОДЖЕНИХ: ВЛАСНИЙ ДОСВІД НА ПРИКЛАДІ КЛІНІЧНИХ ВИПАДКІВ

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Резюме.

Вступ. Наразі існує контрверсійна інформація щодо епідеміологічних характеристик та тяжкості перебігу COVID-19 як у когорті вагітних, так і новонароджених. Більшість дослідників повідомляють про однакову тяжкість захворювання у вагітних і невагітних жінок та легший перебіг захворювання у неонатальному періоді з можливістю розвитку критичних станів в окремих немовлят. Зазнали трансформацій уявлення щодо можливостей трансмісії SARS-CoV-2 новонародженій дитині. Оскільки внутрішньоутробна передача нового коронавірусу вважається наразі рідкісною, реалізація COVID-19 у новонароджених, зазвичай, пов'язана з постнатальною передачею вірусу.

Метою роботи було проаналізувати епідеміологічні та клінічні особливості інфекції COVID-19 у новонароджених на основі аналізу клінічних випадків.

Матеріал і методи дослідження.

В інфекційних відділеннях ОКНП «Чернівецька обласна дитяча клінічна лікарня» під спостереженням знаходилися 11 новонароджених, ушпиталених упродовж 2020 року на початку пандемії, спричиненої інфекцією COVID-19, зокрема 9 дітей скерованих лікарем первинної ланки з дому, та 2 – переведених з пологодомічних закладів. Верифікація діагнозу проводилася на підставі виявлення РНК вірусу SARS-CoV-2 у назо-/орофарингеальному мазку методом ПЛР.

Дослідження проводилися згідно з принципами біоетики, висновок комісії з питань біомедичної етики Буковинського державного медичного університету щодо дотримання морально-правових правил проведення медичних наукових досліджень, протокол № 6 від 16.03.2023 р.

Дослідження виконано в рамках НДР кафедри педіатрії та дитячих інфекційних хвороб Буковинського державного медичного університету «Сучасні епідеміологічні, клініко-параклінічні та діагностичні особливості найбільш поширених запальних захворювань інфекційної та неінфекційної природи у дітей», № держреєстрації: 0122U002208.

Результати дослідження. Аналіз епідеміологічних даних дозволив установити внутрішньосімейне джерело інфікування у всіх встановлених випадках (в одному випадку джерело інфекції встановити не вдалося), у більшості випадків – це матері, по одному випадку джерелом інфікування були батько та бабуся. У більшості сімей новонаро-

джених дітей є старші брати і сестри, що могло послугувати потенційним додатковим джерелом інфікування, респіраторні симптоми у сибсів верифіковано у третини сімей.

У пізньому неонатальному періоді з горизонтальною трансмісією вірусу більшість випадків характеризується нетяжким ураженням верхніх дихальних шляхів у вигляді гострого ринофарингіту, в одному із спостережень – у поєднанні із явищами секреторної діареї. Перебіг COVID-19 ще в однієї дитини супроводжувався ізольованою клінікою гострого гастроентериту з явищами дегідратації середньої тяжкості. Клінічна картина коронавірусної інфекції у решти третини випадків характеризувалася ураженням нижніх дихальних шляхів у вигляді гострого трахеобронхіту, гострого обструктивного бронхіту та бронхіоліту.

У двох дітей, що були народжені від матерів, в яких COVID-19 діагностовано перед початком пологів, що були переведені з полопомічних закладів у зв'язку із позитивним результатом ПЛР тесту на визначення РНК вірусу SARS-CoV-2 у дитини, проведеним на I добу життя одразу після народження, відмічався безсимптомний перебіг без жодних клінічних чи лабораторних ознак інфекційно-запального процесу упродовж спостереження.

Висновки. Епідеміологічною особливістю COVID-19 у неонатальному періоді можна вважати наявність виключно родинного джерела інфекції. У випадку горизонтальної трансмісії вірусу SARS-CoV-2 у новонароджених захворювання COVID-19 у більшості випадків перебігає у вигляді нетяжкого ураження верхніх дихальних шляхів, рідше – з ураженням нижніх дихальних шляхів та гастроінтестинального тракту. В разі захворювання матері перед пологами та наявності клініки COVID-19 під час пологів, не можна спростувати вертикальний та/або антенатальний шлях інфікування з наступним безсимптомним перебігом захворювання.

Ключові слова: новонароджені; COVID-19; особливості епідеміології; клініка.

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