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Review

COVID-19 Management in Newborn Babies in the Light of Recent Data: Breastfeeding, Rooming-in and Clinical Symptoms

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Abstract

COVID-19 infection proceeds to spread rapidly, it has affected approximately 22 million people and resulted in 770.000 deaths worldwide so far (18 August 2020). The effect of COVID-19 infection on newborn babies still remains unclear. There is limited data regarding the effect of the virus in fetal life and among neonates after birth. Due to insufficient data, an ideal management method or treatment and follow-up guideline for disease in newborn babies cannot be established. In the recent three studies with the highest number of cases, it is reported that mothers who had COVID-19 infection in the last trimester, can breastfeed their babies if they comply with the appropriate hygiene and transmission prevention rules. It is also reported that pregnant women who got infected during pregnancy, have higher rates of maternal mortality, preterm birth frequency and cesarean delivery. Moreover it is asserted that vertical transmisson of the virus is possible and the babies who have community-acquired COVID-19 infection after birth often have symptoms of fever, hypoxemia, cough, tachypnea, less frequently feeding difficulty, retraction, ral, nasal congestion and exanthema. Topics as; its transmission via vaginal secretions during vaginal delivery, presence of the virus in breast milk and whether it has a teratogenic effect in intrauterine period, have not been fully explained. In this study, it is aimed to review the studies on newborn babies with COVID-19 infection and to compile the epidemic data, clinical findings, diagnosis and current information recommended for treatment. Although there is a limited number of published data on babies of mothers who had COVID-19 infection in the last period of pregnancy and babies who had infection in the neonatal period, the effects of the virus on the fetus in the early period of pregnancy and the long-term problems of newborn babies remain unknown.

Keywords: Breastfeeding; clinical symptoms; COVID-19; management; newborn.

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All over the world, the new type of corona virus disease (COVID-19) continues to spread invasively in all age groups, especially in older ages. According to the data of the World Health Organization, while 22.492.312 people were infected with the virus all over the world as of August 21, 2020, 788.503 people died.[1] When the age distribution of positive individuals was examined, it was reported that 1% of the cases in China were under 10 years old and 1% were between the ages of 10-19, in the USA, 0.5% was under 4 years of age and 1.3% in the 5-17 age range.[2, 3] Al-

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though its incidence is low in the childhood age group, it is observed that the mortality rate in the period under 1 year is higher than adults and other childhood age groups.[4, 5] In studies in China, while severe and critical illness develops at a rate of 8.2% under the age of 1 year, this rate decreases with increasing age and it has been reported that it is 0.6% in the 6-10 age group and 1.1% in the 11-15 age range.[6]

In the last decade, RSV (Respiratory Syncytial Virus) and Influenza viruses (especially H1N1 subgroup) are seen as factors in lower respiratory tract infections in the childhood age group. While the prevalence of these viruses in childhood age groups is higher than in adults, the frequency of mortality and serious disease development due to these viruses is lower than adults. Severe respiratory failure picture, developed by the effects of Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV-1) and Middle East Respiratory Syndrome Corona virus (MERS-CoV) and lower mortality rates in childhood age groups than adults, SARS-CoV-1 and MERS CoV being under the age of 19 as 7.9% and 3.4% are reported.[7, 8] From December 2019; beginning of the COVID-19 epidemic; until today, very few studies have reported that pregnant women and newborn babies have been affected by the disease.

In the first published studies, it was reported that the COVID-19 infection which is detected in 31 pregnant women in Iran[9] and 9 and 16 pregnant women in two different studies in China,[10, 11] was overcome without a serious problem in both the mother and the baby, and the virus did not pass vertically from mothers to babies. However, the fact that the virus was detected in a small number of babies in the early period in recent studies,indicates that vertical transmission is possible even in low cases.[12]

It is declared that COVID-19 infection in Turkey has been identified in 1% of the individuals in the pediatric age (1 day to 17 years), and that rarely 3 cases are in the newborn period.[5] When the status of the child cases in Turkey are examined, it is detected that 50.4% has mild symptoms, that 0.8% had severe disease development, that the requirement of intensive care is 4.27% and it has been found that 80% of pediatric cases in need of intensive care are under 1 year of age.[5] COVID-19 rapidly increases. It is declared that diagnosis is made on 254.520 people in total on 21 August 2020, in Turkey,and 6058 people lost their lives, and the mortality rate is 2.63% in all included age groups based on COVID-19 infection according to the data of Ministry of Health.[5, 13]

New type of corona virus infection continues to contain many unknowns for newborn babies. The effects of infection on the fetus in the first two trimesters of pregnancy and the effects of SARS CoV-2 on newborn babies in the long term after birth are unknown. Is it contagious to the baby's family and healthcare professionals? How should protection be? What should the baby's feeding method be? Are the antibodies of the mother who had the infection during pregnancy protective for the baby? Unfortunately, it does not seem possible to give the exact answers to these questions nowadays. The most important deficiency ahead is the limited data available on newborn babies with COVID-19 infection.

In this review, it is aimed to evaluate the results of the babies of pregnant women with COVID-19 infection and the babies with COVID-19 infection in newborn period in company with today's latest information and to evaluate the management of the disease. It is recommended that readers follow up-to-date information and follow the guidelines of national and international associations, as the disease progresses rapidly as well as rapid data flow.

Virus properties:

The new corona virus infection was detected in China for the first time in December 2019 and gradually spread all over the world. While the World Health Organization named the disease as Coronavirus Disease 19 (COVID-19) on February 11, 2020, the International Committee on Taxonomy of Viruses determined the name of the virus as SARS-CoV-2.[14, 15] The coronavirus family is single-stranded, it has RNA virus characteristics, and is widely found in humans and other creatures (cat, dog, bat, cattle, camel, bird, chicken). While it causes respiratory, gastrointestinal and neurological system symptoms in humans, it causes cold symptoms most commonly. As a classification, Corona virus - Orthocoronavirus-betacoronavirus family; Subgroup B- includes SARS CoV-1 and SARS CoV-2, while subgroup C includes MERS-CoV.

SARS CoV-2

SARS CoV-2 is a single-stranded, 29.903 bp long, spike-containing envelope structure, and is characterized by an RNA virus with a radius of approximately 60-140 nm.[16] Among the SARS-like corona viruses found in bats, it has 88% genetic similarity with bat-SL-Co0VZC45 and batSL-CoVZC21, similar to SARSCoV1 in the rate of 79% and similar to MERS-CoV in the rate of 50%.[17] SARS CoV-2 is a low resistant virus; it is inactivated with disinfectant containing 75% ethanol, chlorine or peracetic acid for 30 minutes at 56 ºC.[16]

Pathophysiology

At the cellular level, SARS CoV-2 in mucosal epithelium (nose, mouth, nasopharynx) alveolar epithelium, vascular endothelium (heart, renal tubules) and enterocytes (ileum and colon) in the apical membrane of the cell wall with S

protein and angiotensin converting enzyme 2 (ACE-2) receptor acts by binding and entering the cell with endocytosis.[18] After viral replication, the endothelial-epithelial barrier is disrupted, and edema develops with wall thickening in the alveoli and increased monocytes and lymphocytes in the interstitial area. This situation is thought to cause the ground-glass appearance seen on computed tomography.[19] It is thought that the virus down-regulates the ACE-2 receptor, causing an increase in angiotensin 2 swing and causing an increase in angiotensin 2 levels leading to pulmonary edema and respiratory failure.

Transmission

It is most commonly transmitted by droplets. A high risk of transmission is considered if the face-to-face meeting with an infected person is closer than 6 feet (180-200 cm) long and the duration is more than 15 minutes. Contagion can be much faster with speech, cough, sneezing. It is known that contagion infects as a result of contact with an infected surface, it has been reported that contamination from infected surfaces has been in hospital rooms.[20]

Vertical transmission: Although it has been reported in many studies that there is no transplacental transmission from mother to baby during pregnancy, there is not enough data to reach a complete conclusion on the subject. In studies conducted on pregnant women who had COVID-19 infection in the last trimester of pregnancy, no vertical transmission of the virus to the baby was found in the umbilical cord blood, placenta and amniotic fluid.[10] In a review including 222 newborn babies born from pregnant women with COVID-19 positive; it has been reported that samples taken from their babies within 36 hours-17 days after birth were collected, and all samples taken after birth were found as negative, therefore it has been reported that vertical transmission could not be demonstrated.[21] However, there is no study on the effect of the infection on the baby in the first 2 trimesters of pregnancy. It is known that intrauterine vertical transmission is not detected in SARS and MERS infections developed with other similar viruses.[16] In the literature, it has been reported that the virus was detected in the amniotic fluid and placental tissue in the children of two pregnant women with COVID-19 infection and in the swab culture taken from the nasopharynx in the first 48 hours of life.[22, 23] Therefore, it is still not fully known whether the virus will pass through a vertical route and cause a congenital infection in the fetus. It is observed that in none of the nasopharynx samples taken in 12-24 hours, 5-7th day and 14th day from newborn babies of 116 pregnant women infected with COVID-19 in New York, in USA, did not pass the virus to the baby.[24] Finally,widest series of studies relating COVID-19 infections in pregnancy is published inTurkey. According to the study involving 125 infants, virus in tracheal aspirate culture have been detected in the first day of life of a baby,suggested that vertical transmission might be possible.[12]

Fecal-oral transmission: It is known that SARS CoV-2 nucleic acid is detected in fecal sampling of individuals with the disease.[16] For this reason, it should not be forgotten that fecal wastes of individuals with the disease can be contagious.

It has been reported that in adults the incubation period is between 1 and 14 days after the contact with the virus, that symptoms begin within an average of 5 days after the development of viremia, and that symptoms are seen within 10-12 days in 97.5% of the cases.[19, 25] The main factor in the spread of the virus is the high contagiousness of the virus in the presymptomatic period. It is reported that contagiousness develops in the presymptomatic period with a rate of 44-62%.[26]

Why is COVID-19 less severe in children?

It has been suggested that ACE-2 (Angiotensin Converting Enzyme) activity in children is higher compared to adults may be protective against severe respiratory failure caused by COVID-19.[4] It is known that the lymphocyte count, which is the indicator of the natural defense system, is generally normal in children with COVID-19.[27] Less cytokine release due to lymphocyte in children is thought to contribute to the milder clinical picture in children. When acquired immunity is evaluated; it has been suggested that mortality and morbidity due to COVID-19 are lower in populations with BCG (Bacillus Calmette-Guérin) vaccine.[28] It has been shown that BCG vaccine causes epigenetic changes in monocytes, decreases viremia, BCG vaccine reduces acute upper respiratory tract infections in adults and reduces related mortality rates in children.[29, 30] It is being suggested that routine live vaccines (Mumps, Measles, Rubella and Influenza) and previous viral infections can modulate the immune system in children and gain protective properties against COVID-19 infection.[4] In addition, the higher regeneration capacity in children compared to adults may contribute to the faster recovery process.

The course of the disease can be summarized in three stages.

1. Initial phase: The initial phase of flu-like symptoms with high viral load.
2. Critical phase: It is the period in which the inflammatory response is at the forefront, viral titration decreases but inflammatory cytokines (interleukin 2, 6, 7, 10 and Tumor Necrosis Factor alpha) increase. It is known that the rate of cytokine increase in adults positively correlates with the development of morbidity and morbidity.

3. Recovery period: It is a period which viral titration decreases, the amount of cytokine decreases, anti-SARS CoV-2 Ig G and Ig M develops in serum, usually 7-10 days after the onset of symptoms.

Diagnosis

The most commonly used method nowadays for the diagnosis of COVID-19 is to show the nucleic acid of the virus with reverse transcription polymerase chain reaction (RT-PCR). The most common sampling sites are the nasopharynx and oral cavity, sputum, lower respiratory tract sampling-tracheal aspirate material, blood and feces areas. The positivity rate of the test is around 60% and the positivity rate increases in repeated sampling. Although the highest rate of positivity is detected in the bronchoalveolar lavage sample, the difficulty and not being comfortable of taking the sample, reduces the applicability of this sampling method.[31]

Fetal period

The effects of the virus in the fetal period are unknown. The data on the contact status of the pregnant with the virus during fetal life is quite limited. Although the reported data are not sufficient, it is thought that the vertical transmission of the virus is low in probability.[32] It is not fully known whether the virus has the potential to cause congenital malformation, stillbirth, premature birth, and intrauterine growth retardation.[32] Does having an infection in early pregnancy provide protection for the baby? Does the infection have the potential to cause congenital anomalies in the early period? For the answers to these questions, studies on pregnant women and their babies with COVID-19 infection during the first two trimesters of pregnancy are needed.

Mode of delivery

In China, where the disease first spread, it has been reported that the mode of delivery in pregnant women with COVID-19 was predominantly done by cesarean section.[10] Since the effect of delivery method on viral transmission is not known exactly, normal delivery may not be preferred to reduce the risk of transmission to the baby. The longer delivery period in vaginal deliveries increases the contact time between healthcare workers and the mother and may increase contagiousness under unsuitable conditions. However, there is no proven data on vaginal secretions and transmission to the baby. The World Health Organization recommends that cesarean delivery in COVID-19 pregnant women should be performed according to the week of gestation, the severity of the mother's disease and fetal viability, as well as providing medical necessity.[33] In recent studies, it has been reported that the rate of cesarean delivery in pregnant women with COVID-19 infection is between 71.2% and 83%.[12, 24] There are some dangers in the delivery room about the postnatal cord clamping time, skin-skin sensual contact and the first breastfeeding. Turkish Neonatal Society does not recommend delaying cord clamping post-partum.[34]

Delivery room management

In the presence of detection of COVID-19 infection or suspicion of infection, it is recommended to deliver in the negative pressure isolation room.[32] It is necessary to have as few healthcare workers as possible in the delivery room. It is recommended that babies should be cleaned or washed as soon as possible after birth because it will remove body secretions that are potentially contaminated with the mother.[34] For postnatal care and interventions to be applied to the baby after birth, the baby should be placed in an incubator instead of a radiant heater.[35] All healthcare professionals in the delivery room must be present with droplet path and aerosol with preventing equipment (N95 mask, visor, goggles, apron, cap, gloves).[36] It is recommended to take only one person authorized to apply neonatal resuscitation program recommendations to the delivery room, in pregnant women at risk or in situations where intervention may be required, to reduce the risk of contact with the possible virus and its spread.[32, 36] The neonatal team should be ready outside the room where the birth is made, and if necessary, the baby should be taken to a different area outside the room and care should be provided. It is reported that if the general condition of the pregnant woman is good and there is no need for intubation or positive pressure ventilation, which seriously increases the spread of the virus, delivery can be performed in normal pressure isolation rooms with all the anti-contamination equipment of the healthcare personnel.[32] Before and after the birth, the room and allequipmentin the delivery room should be properly cleaned.

Should the mother and baby be followed in separate rooms whose mother is COVID-19 positive? Should the baby be separated from the mother? Can a baby be breastfed with breast milk after birthwhose mother is COVID-19 positive?

Some publications in China, where the first cases on the subject were seen, have been reported that the mother and the baby should be followed separately.[35] It is clear that this situation will cause anxiety and worry in the family, especially in the mother, and will cause maternal deprivation and a decrease in sucking success in the baby. After developments, some institutions do not recommend the

separation of mother and baby routinely.[21] The decision whether the mother and the baby should be separated is a decision made together with the clinical team and the family. In this decision, each case should be evaluated separately, and the decision should be made considering the mother's health status and possible transmission risks.

Can a mother with COVID-19 breastfeed her baby?

There is still not enough scientific evidence to answer this question in the last 6 months experienced all over the world. Breast milk is a unique nutritional material that strengthens the baby's defense system with all its components. However, is it possible to pass on the baby due to the presence of COVID-19 virus in breast milk? The presence of SARS CoV2 in breast milk has not been demonstrated to date. The World Health Organization and Centers for Disease Control and Prevention (CDC) report that the mother can breastfeed the baby when appropriate conditions are provided to prevent transmission.[37, 38] Close contact of the baby with the mother will create a serious risk for the baby when the conditions preventing the transmission are not provided. Although transmission from breast milk is not known, it is well known that it can be transmitted through the respiratory tract from an infected mother during breastfeeding. Turkish Neonatal Society recommends to evaluate breast-feeding foreach baby and mother individually and to let to make decision relating breast-feeding by the mother and family.[34] The World Health Organization stated that standard nutritional guidelines should be followed by taking all necessary infection control measures.[39]

CDC reported that the mother should express her milk with a milk pump after proper hand hygiene is provided and that the milk can be given to the baby with a feeding bottle by a healthy healthcare worker, when the baby is temporarily separated from the mother after birth to reduce contagiousness. The mother should strictly pay attention for hand hygiene before, during and after milking, and the milk pump should be disinfected before and after each milking. If the mother and baby should be cared in the same room, the baby should be at least 2 meters (6 feet) away, the mother should wear a surgical mask if she wants to breastfeed, and should ensure proper hygiene of her hands, body surface (breast) and objects that will touch the baby before each breastfeeding.[37] If the mother is symptomatically infected with COVID-19 and wants to breastfeed her baby; however, breastfeeding should be allowed if the mother does not have fever in the last 72 hours that would require antipyretic and if major respiratory symptoms regress.[32] It should not be forgotten that all breast milk carriers (baby bottles) or containers used in the newborn unit during COVID-19 may be the carrier vector of the virus, considering the presence of asymptomatic mothers.All bottles used in the unit should be wiped with disinfectant and placed in plastic disposable bags. The most recently published observational study on postpartum breastfeeding of pregnant women with COVID-19 infection yielded different results. In the study conducted in the United States of America, 116 pregnant women with COVID-19 infection were monitored in the New York region. 82 babies were followed up together in the same room with their mothers.The mothers of 64 babies breastfed their babies by wearing masks and following hygiene rules (hand hygiene, wiping the breast).Babies are monitored in the incubator except breastfeeding and nursing period.No virus has been detected in any of these babies.Therefore,it is suggested that mothers who have had COVID-19 can breastfeed their babies when appropriate conditions are provided.[24] In a multicenter study involving 125 infants in Turkey,it has been reported that 56.8% of infants fed with formula and 36% were fed with expressed breast milk.[12] In the study conducted on 37 newborns whom mothers did not have COVID-19 infection during pregnancy and later had a social-acquired COVID-19 infection; it was found that the feeding method of babies was 22% breastfed, 52% breast milk and 26% formula fed.[40] It is thought that the inability to fully clarify the transmission of the virus to the baby by breastfeeding, the close contact of the mother and the baby by breastfeeding, and the fear of families and healthcare professionals about the possible transmission of the virus to the baby reduce the frequency of breastfeeding.

Babies with positive COVID-19 in the postnatal period and all babies who are suspected to be hospitalized for different reasons after birth, should be hospitalized in a single, negative pressure isolation room if possible. In units with a high number of patients, babies can be hospitalized in intensive care rooms where more than one baby can be bedded by cohorting.[34]

Baby visit

Visiting newborns with COVID-19 should not be allowed. [16] If the mother is positive for COVID-19; visits to the Neonatal Intensive Care Unit (NICU) should not be allowed. If the mother does not have fever or has not taken antipyretic in the last 72 hours and respiratory symptoms have completely improved and if two RT PCR tests examined at 24-hour intervals and after it is confirmed to be negative, visits can be allowed.[32] A restriction should also be made on visiting other infants in the NICU. Visits of these babies hospitalized for other health reasons should be limited to two people a day, and these two people should not to be at the bedside of the baby at the same time.[32]

Baby transport

If a baby born from a pregnant woman diagnosed with COVID-19 is to be transported, it is recommended to intend a transport incubator and transport with this incubator only for these patients. In-hospital and out-of-hospital transport team should take all protective measures, and all equipment (transport incubator, monitor and equipment) before and after transport should be disinfected.[34] When leaving the delivery room, apron, cap, glove should be changed, the mask should not be changed unless it is soiled or moist.[32]

NICU management

It is ideally recommended to place newborns whom mothers diagnosed with COVID-19 or newborns who are suspected/diagnosed with COVID-19 in single rooms and, if possible, in rooms with a negative aspiration system.Isolation rooms in units without substructure, or intensive care rooms can be used by cohorting. In this case, the entrances and exits of the rooms should be under control, and no entry and exit should be made unless necessary. In order to minimize the risk of contamination, it is recommended that only one healthcare worker enter the room with all protective equipment. In order to minimize the risk of contamination, it is recommended that only one healthcare worker suitable with all protective equipment enter the room. It should be ensured that the door of the patient monitoring room is constantly closed. Measures should be increased in the presence of patients receiving respiratory support. It is very important to take precautions during aerosolization methods (nebulization, intubation-extubation, open aspiration, non-invasive ventilation, nasogastric-orogastric tube placement) on these patients asit is very important for healthcare personnel to be minimally affected by exposure.[33, 41] Non-invasive respiratory support is provided by the usage of breathing apparatus via the methods as nasal intermittent positive pressure ventilation (N-IPPV), nasal continuous positive airway pressure (nCPAP), high flow nasal cannula, etc. Since these ventilation modes are open methods, they carry a high risk of airway and droplet transmission. For this reason, watching the patient with the lowest possible pressure and with a mask covering the patient's mouth and nose will minimize the risk of contamination.[42] When invasive respiratory support is needed, rapid intubation should be performed by clamping the appropriate intubation tube, and if mask ventilation is required, a HEPA filter should be placed between the mask and the oxygen source. If the vocal cords are difficult to see due to personal protective equipment, intubation with a video laryngoscope can be applied. It is appropriate to prefer closed suction systems during aspiration, and while providing invasive respiratory support, HEPA filters at the expiratory outlet of mechanical ventilators should be placed as it will significantly reduce the risk of aerosolization contamination.[43] Fortunately, there are very few declarations of newborns who need advanced respiratory support for definite or suspected COVID-19, and it has been observed that these babies have concomitant comorbidities such as prematurity, asphyxia, or non-COVID-19 sepsis.[40] In addition, all disposable materials used in the patient care room and the patient's wastes such as diapers should be disposed of as medical waste in double waste bags.

Clinical symptoms in newborns

Babies with COVID-19 do not have a specific clinical finding. It is frequently associated with intrauterine growth retardation and preterm delivery in the perinatal period. However, the cause and effect relationship between intrauterine growth retardation and preterm birth cannot be explained directly as COVID-19 infection, and coincidental coexistence situation dominates. In a review in which 222 newborns were evaluated, it was reported that while the most common clinical findings were increased preterm delivery rate, intrauterine fetal distress, respiratory failure findings (RDS and TTN), pneumonia, low birth weight, chorioamnioitis, meconium-stained amnion were reported as case reports.[21] In a study fulfilled to evaluate 125 infants in Turkey, it was reported that the rate of preterm births was 26.4% and rate of birth with low birth weight was 12.8%.[12]

The relationship between postnatal tachypnea, feeding intolerance, mechanical ventilation requirement and abnormal laboratory results and COVID infection is not fully known. Fever, respiratory distress, dyspnea, cyanosis, tachycardia, feeding intolerance, vomiting and lethargy are common symptoms in newborn babies with COVID-19 infection.[34] According to the study fulfilled on 37 babies whom mothers did not have COVID-19 infection during pregnancy and had community-based COVID-19 infection after then, fever in the frequency of 49%,hypoxemiain the frequency of 41%, cough in the frequency of 27% and detection of the symptoms of tachypnea as 24% are detected. Other symptoms detected less frequently are feeding difficulty, retraction, ral, diarrhea, nasal congestion and runny nose and exanthema.[44] In the study involving the babies of mothers who had COVID-19 infection in the last period of pregnancy, 4 babies who were found to be positive for SARS CoV-2 after birth and 121 babies who were found to be negative for SARS CoV-2 were compared; it has been reported that the 5-minute Apgar score and neutrophil count are low, the need for mechanical ventilation and continuous positive airway pressure (CPAP) are high, and the hospital stay is longer in babies with positive SARS CoV-2.[12]

Laboratory and Imaging Analysis

In the pediatric age group with COVID-19 infection, it is seen that lymphopenia can be seen while blood count values are generally normal, that C-Competitive Protein (CRP) value is normal or increased, that procalcitonin level is <0.5 ng/ml. In cases of severe disease in pediatric patients, an increase in interleukin-6, ALT, AST, CK, CK-MB and myoglobin levels can be detected.[5] In pediatric cases with confirmed diagnosis of COVID-19, it has been reported that there is no finding in lung computed tomography (CT) at a rate of 40%, and among the findings detected, bilateral ground-glass opacity, unilateral or bilateral local patch-like shadowing and rarely interstitial abnormalities are found in the order of frequency.[27] There is not enough data regarding laboratory analyzes in babies with COVID-19 detected in the newborn period. The Turkish Neonatal Society recommends to detect the complete blood count, liver function tests, creatine phosphokinase, lactate dehydrogenase in babies with suspected COVID-19, and to investigate RT-PCR examination from the upper/lower respiratory tract, blood or stool for definitive diagnosis.[34] Chest radiography, ultrasound, and lung CT may be useful in evaluating neonatal pneumonia. In babies with COVID infection, it was observed that 36% had positive findings in AC X-ray and 80% in lung CT.[44] It has been reported that the need for respiratory support is high in the presence of symptomatic COVID-19 infection in newborn babies, and the CRP value and Prothrombin Time (PT) can be used as a precursor to determine the severity of the disease.[44]

The American Academy of Pediatrics (AAP) recommends to perform the nasopharynx RT-PCR virus test within 24 hours from the babies of all pregnant women with COVID-19 and to take a second sample within 48 hours.[36] In some centers, the test is taken within the first 24 hours after birth, and if the general condition of the baby is good, the second test is taken before discharge and at least 24 hours after the first test. It was reported that the second test was taken on the 5th day in babies in cases which the duration of hospitalization in the newborn intensive care unit is predicted long.[32]

Treatment

For the treatment of newborn babies, neonatologists, pediatric infectious diseases specialists, radiologists, newborn nurses and assistant healthcare personnel should work in harmony as a team. When the diagnosis of COVID-19 is confirmed in an adult and pediatric patient, if the patient's symptoms are mild, isolation at home is recommended.[5] However, this recommendation for newborn babies with low defense system is not appropriate to be accepted due to insufficient data available. It is recommended that all newborns diagnosed with COVID-19 must be followed by hospitalizing.

There is no specific treatment model for newborn babies with COVID-19. Standard general support care (calorie support with appropriate fluid and electrolyte support) should be provided orally as much as much as possible. Non-invasive nCPAP support should be given in cases with respiratory failure, and it should be known that this method increases the risk of transmission by aerosol. In case of severe respiratory failure, the baby should be intubated and respiration should be supported with an individualized lung protective mechanical ventilation strategy. Surfactant, inhaled nitric oxide, and high frequency oscillatory ventilation (HFOV) can be used in severe cases with respiratory failure.[34] The use of broad-spectrum antibiotics is not recommended in case of COVID-19 infection. Antibiotic use should be applied in secondary bacterial infections seen after viral infections.There is no proven anti-viral drug for COVID-19 in the neonatal period. Studies on the use of Remdesivir, Lopinavir-ritonavir, hydroxychloroquine, azithromycin + hydroxychloroquine, interferon alfa-2b, favipiravir, glucocorticoid and tocilizumab in adults with COVID-19 have been reported, and there is not sufficient evidence regarding the use, efficacy and safety of these drugs in the pediatric age group and newborn infants.[5]

In the treatment of 37 newborn babies whose COVID-19 infection was proven by RT-PCR, antibiotics were administered at a rate of 54%, azithromycin at a rate of 38%, oseltamivir at a rate of 32%, corticosteroids at a rate of 11%, and hydroxychloroquine at a rate of 5%; it has been reported that no side effects such as prolonged QTc or necrotizing enterocolitis due to drugs were observed in infants, and additionally surfactant was administered to one patient and IVIG therapy was administered to one patient.[44] When all the limited data are evaluated, it is seen that there is no drug that can be used successfully in a specific treatment in a newborn baby with COVID-19 infection and only symptomatic support can be given to babies.

Discharge

If the baby is asymptomatic, it can be discharged when the RT-PCR test taken every 2 days is negative. In case of discharge, the mother should also have a negative RT-PCR test and there should be no positive cases at home. Babies with COVID-19 should be monitored under quarantine for 14 days after discharge.[34] In cases where quarantine cannot be applied, the discharge of the baby should be postponed and should not be discharged until the appropriate conditions are provided by individualizing.

The mother or anyone who will provide home care should

not be infected. However, if there is a compulsory situation and the baby will be discharged; care can be provided by home care providers (close relatives or caregivers). It is necessary to maintain a distance of at least 6 feet (2 meters) between the infected person and the baby, and take contamination precautions (mask, gloves, hand hygiene). All discharged newborn babies should be followed up regularly by home care services or relevant health institutions.

COVID-19 Management in our Unit

In the neonatal clinic of our hospital, a total of 4 babies have been followed up due to the presence of proven COVID-19 infection in their mothers, since March, when the cases were first seen in our country. 3 of the pregnant women performed cesarean delivery and 1 performed normal spontaneous vaginal delivery. Deliveries took place in neutral pressure rooms, as there are no negative pressure delivery rooms in our hospital.A separate baby intervention room was created for COVID infection in the delivery room. Only an experienced neonatal nurse, who had received neonatal resuscitation program training, entered the birth from the neonatal team. A neonatologist and a neonatal nurse were present in the intervention room. The baby was taken to the intervention room without waiting after birth. Our healthcare staff, who completely dressed personal protective equipment for COVID-19 (N95 mask, visor, goggles, bonnet and gloves), brought newborn babies to our neonatal intensive care unit with the transport incubator used only for this situation.

Babies were monitored in isolated neutral pressure rooms and closed incubators and were cared by the same nurse and doctor throughout the day. The instructions of the hospital infection committee for putting on and taking off the equipment, hung in the isolation rooms, were strictly followed. None of the babies had respiratory distress or pathological symptoms or signs related to other systems, so no additional treatment was given.

The first nasopharyngeal swab sample was taken from the babies within the first 24 hours and the second nasopharyngeal swab sample was taken 24 hours after the first sample. COVID-19 RT-PCR result was negative in all samples taken from babies. However, complete blood count, liver and kidney function tests and signs of infection were found within normal limits. There were no findings in the chest radiographs that would suggest COVID-19 or other respiratory problems of the newborn.

Our hospital has the title of a baby-friendly hospital since 2004 and supports breast milk as the first step in nutrition. Detailed information was given to families about COVID infection and feeding of babies, data on current breastfeeding and breast milk were shared. As a result of all these conversations, babies were fed with formula because mothers did not want to give their own milk.

The families of all four babies refused to be feed by breast milk or expressed breast milk. No virus and RT PCR were detected in the breast milk of three mothers on the first day. The babies were followed in separate rooms until the two consecutive nasopharyngeal swab tests of the mothers were negative. When mothers were found to be negative, they started breastfeeding their babies.

All babies were fed exclusively breast milk at 1-month follow-up. Intensive care visits were restricted for all infants hospitalized at NICU throughout the process. The interviews about the situation of the babies were made daily by phone.

Disclosures

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