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Coronavirus disease (COVID-19) and neonate: What neonatologist need to know

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Abstract:

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) cause china epidemics with high morbidity and mortality,the infection has been transmitted to other countries. About 3 neonates and more than 230 children cases are reported. The disease condition of mainly children was mild.There is currently no evidence that SARS-CoV-2can be transmitted transplacentally from mother to the newborn. The treatment strategy for children with Coronavirus disease (COVID-19) is based on adult experience. Thus far, no deaths have been reported in the paediatric age group. This review describes the current understanding of COVID-19 infection in newborns and children.

Since December 2019, patients with fever, dry cough, normal or decreased white blood cell counts who were initially diagnosed as " Fever of Unknown Origin with pneumonia " have been continuously increasing in Wuhan[1]. The causative agent of this unexplained infected pneumonia was identified as Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) which not only has a strong human-to-human transmission,but also causes severe pneumonia to death[2]. SARS-CoV-2 is so aggressive that the infection has been transmitted to other countries and is seriously imperilling human life. WHO has declared this disease to constitute a Public Health Emergency of International Concern on 30 January 2020 [3]. A total of

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26359 suspected cases and 31225 confirmed cases with 639 deaths linked to this pathogen on February 7, 2020[4].Different age group are generally susceptible to SARS-CoV-2. At present, neonates have been diagnosed with Coronavirus disease (COVID-19). Neonatologist should be vigilant assessing newborn baby delivered by infected mather or brought up by infected housemaid and improve the knowledge of prevention and treatment of COVID-19.

Etiology of COVID-19.

SARS-CoV-2 is single stranded RNA viruses, belongs to subgenus Sarbecovirus of the genus Betacoronavirus[5]. SARS-CoV-2 particles contain spike and envelope, virions are spherical,oval, or pleomorphic with diameters of approximately 60-140 nm.Culture times were 4 days on human airway epithelials cell lines and 6 days on Vero E6 / Huh-7 cell lines. The SsRNA was 29,903 bp in length. The organization of the SARS-CoV-2 genome is 5′-leader-UTR-replicase-S (Spike)－E (Envelope)-M (Membrane)-N (Nucleocapsid)-3′UTR-poly (A) tail with unknown open reading frames[6].Its reference sequence (NC_045512.2) is with 80.26% sequence identity (and query coverage above 98%) to the human Severe acute respiratory syndrome (SARS) coronavirus genome (NC_004718.3) [7],however Middle East respiratory syndrome (MER）coronavirus is lower related to SARS-CoV-2 which is a group 2c β-coronavirus. SARS-CoV-2 exhibits very high sequence similarity to the Guangdong pangolin coronaviruses in the receptor-binding domain which indicates pangolins may be an intermediate host of the virus before dissemination to humans [8]. SARS-CoV-2 has weak resistance ,56 ℃ for 30 min, 75% ethanol, chlorine containing disinfectant and peracetic aci can inactivated SARS-CoV-2 [9]. SARS-CoV-2-S uses the SARS-coronavirus receptor, angiotensin-converting enzyme 2 (ACE2) for entry host cells. ACE2 is a surface molecule highly expressed in AT2 cells of lung, along with esophageal upper epithelial cells and absorptive enterocytes from ileum and colon which indicated digestive system along with respiratory systems is a potential routes for SARS-CoV-2 [10,11]. The expression level of ACE-2 in Asian populations is significantly higher than that in European and American populations, and ACE-2 on male cells are higher than on female cells,

which can partially explain the incidence rate of novel coronavirus pneumonia are higher in male and Asia [12,13].

Transmission

The symptomatic patients with Coronavirus disease are the main disseminators, but the asymptomatic patients should not be underestimated. The current data shows major transmission routes are droplets transmission,contact transmission, and aerosol transmission. fecal-oral transmission cannot be ignored,because the nuclear acid of the SARS-CoV-2 is detected in the fecal samples of patients in the United States and China[14]. Maternal-infant vertical transmission is doubtful-there have been no documented neonates of intrauterine vertical transmission occurring with SARS and MERS[15, 16].According to existing complete data, amniotic fluid, cord blood, neonatal throat swab, and breastmilk samples from six newborn babies delivered by infected mathers were tested for SARS-CoV-2, and all samples tested negative for the virus. [17].

Clinical presentation of COVID-19

The incubation periodes of COVID-19 were 1–14 days, and the mean has been estimated to be 5.2 days (95% confidence interval 4.4 to 6.0) and 97.5% of those who develop symptoms will do so within 10.5 days (95% CI: 7.3 to15.3) of infection [18]. From the first confirmed child case who was reported in Shenzhen on 20th January 2020 to 6

February 2020, at least 230 COVID-19 cases in children (⩽18 years)

have been reported in china. The SARS-CoV-2 rapid spread in children suggests it has a strong transmission capacity in special population(neonate, children). SARS-CoV-2 infection can range from asymptomatic infection to severe respiratory distress in neonate and children. However, Respiratory distress occur in children with underlying conditions. One patient had severe malnutrition and survived surgery for congenital heart disease, the other had bilateral hydronephrosis and left-kidneycalculi.The clinical course of COVID-19 was generally milder in children than adults.The most common clinical symptoms of COVID-19 included fever, fatigue and dry cough. A few patients showed upper respiratory symptoms such as nasal obstruction, nasal discharge and sore throat. Gastrointestinal symptoms such as abdominal discomfort, vomiting, abdominal pain and diarrhea may also occuerd.C-reactive protein was normal or temporary upregulation, ALT levels and myocardial enzyme were not

obviously abnormal changes. Chest imaging normalities were present in asymptomatic infectioned patients. SARS-CoV-2 can be mixed to different pathogen including mycoplasma pneumonia, influenza A,influenza B,RSV and EB virus. The clearance time of SARS-CoV-2 nucleic acid from nasopharyngeal swab were recorded in 3 children, nine days in two patients, 12 days in one patient[19]. Thus far, no deaths have been reported in the children which is similar to SARS [19.20]. Three newborns have been diagnosed up todate who mainly belonged to family cluster cases.One 17 days old neonate diagnosed as COVID-19 infection had fever, cough and vomiting milk.In his family,the housemaid was the earliest case,subsequently, the mother was infected[21]. The second newborn appeard fever on 5 days after birth whose mather also confirmed infected. The third one who was born by the infected mother was silent and diagnosed on 30h after birth by the viral nucleic acid test.Short breath,vomiting milk, cough and fever were present in neonates. The vital signs of those neonates were stable, the disease condition ware slightly, there is no severe emergency case until now[19, 21 ,22,23].

Diagnosis

Diagnosis of COVID-19 is based on a comprehensive contact and travel history and precise laboratory tests. Current diagnostic tools were the nucleic acid or virus gene tests. Samples included nasopharyngeal swab, sputum, secretion of lower respiratory tract, blood and feces. Nasopharyngeal swab is the most common specimens,however, its detection positive rate is less than 50%. Repeated detection is necessary to improving the positive rate. The positive rate of bronchoalveolar lavage fluid was high,but it is not suitable for most of patients due to increased risk of cross-infection[24,25]

Infection control and Treatment

Neonatologist must wear protective equipment (including hats,goggles, protective suits, gloves, N95 masks, etc.) to resuscitate neonates delivered by confirmed and/or suspected COVID-19 puerperant. If the puerperant is positive for SARS-CoV-2, the neonate must be isolated, then detected SARS-CoV-2 [26].

Early identification and early isolation are imperative for COVID-19 control. COVID-19 neonates should be placed in negative pressure rooms or in rooms in which room exhaust is filtered through high-efficiency particulate air (HEPA) filters with reference to MERS

management[16]. No visiting are allowed for neonates of COVID-19. Treatment mainly depends on adult patients clinical experience due to few cases in children. There is no specific drug treatment for SARS-CoV-2 just like MERS-CoV and SARS-CoV[19.26], Symptomatic and supportive treatment are the mainstay of therapy for patients of SARS-CoV-2 infection including the supply of oxygen, the maintenance of water electrolyte and acid-base balance.The supplement of water and electrolyte should be appropriate, so as to avoid aggravating the pulmonary edema and reduced oxygenation[27]. For newborns with severe acute respiratory distress syndrome, high-dose pulmonary surfactant (PS), inhaled nitric oxide (iNO), high-frequency oscillatory ventilation (HFOV) and extracorporeal membrane lung (ECMO) may be useful.In the United States, A patients' conditions were improved apparently after treatment with nucleoside analogue-remdesivir, but there was just one case,the efficacy needs further verification[28]. Interferon-α2b nebulization were be applied in MERS-CoV and SARS-CoV,so it could be considered to use in SARS-CoV-2 infection[29,30]. In addition,three potential drug combinations (sirolimus plus dactinomycin, mercaptopurine plus melatonin, and toremifene plus emodin) are candidate repurposable drugs[31]. Moreover, convalescent sera from SARS-CoV-2-recovered patients may be useful for SARS-CoV-2 infection, because of a significant reduction in the mortality following convalescent sera from SARS-recovered patients treatment [32].

Conclusions

COVID-19 can result in asymptomatic to severe illness, Fortunately children without underlying diseases appeared to have mild disease. The disease condition of the neonates were also slightly. Though this new virus come out without specific antiviral drugs treatment, neonatologist need to more virological,epidemiological and clinical data to treat and manage COVID-19.

Conflicts of Interest:

The authors declare that they have no conflict of interest.

Authors' Contributions

Qi Lu and Yuan Shi conceived this review. Qi Lu wrote the manuscript, Yuan Shi revised the manuscript.

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