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Liver involvement in SARS-CoV-2 vertically infected newborn

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The novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which causes the disease termed coronavirus disease 2019 (COVID-19), was declared a pandemic on March 2020 (1). The main clinical manifestations of COVID-19 involve the upper and lower respiratory system; however, it was demonstrated that other organs and systems might be implicated, including the liver and the gastrointestinal (GI) tract (2). Recent studies suggest that children are less likely to become infected with the virus compared to adults (3, 4). In addition, newborns and infants have clinical symptoms and laboratory and radiologic abnormalities less specific and less evident compared to older individuals (5). Therefore, many cases might remain subclinical or unrecognized in early life, due to neonatal stronger innate immune response and lower propensity to proinflammatory cytokine response (6). Hepatic injury in COVID-19 adults and children has been reported (2, 6–9). Liver injury was characterized by slight increases in hepatocyte-related enzymes, including alanine aminotransferase (ALT) and aspartate aminotransferase (AST). In children with COVID-19, hepatitis has been reported to be associated with a severe presentation of the disease named multisystem inflammatory syndrome in children (MIS-C) (7). To our knowledge, hepatic involvement in SARS-CoV-2- infected term-born newborns has never been described. A recent report of the World Health Organization (WHO) defines the modality of mother-to-child transmission of SARS-CoV-2 (10). It mainly occurs horizontally in the early postnatal period, i.e., via droplets, respiratory secretions, saliva and direct contact, but oro-fecal transmission is also described. Vertical transmission, i.e., in utero or intrapartum, is also possible. The consequences of the vertical transmission on the fetus and newborn are still poorly defined.

We report liver involvement in a case of neonatal SARS-CoV-2 infection vertically acquired. The detection of the virus by RT-PCR in nasopharyngeal swab at age < 24 h defines the possibility of vertical transmission of SARS-CoV-2 (10). In addition, the neonate was born by C-section with intact amniotic membranes, thus suggesting a transplacental transfer of the virus (10). Compared to other viruses, SARS-CoV-2 is less placentotropic but can infect and cross the placenta due to the binding to angiotensin converting enzyme- 2 (ACE2) receptors expressed in different feto-placental tissues. Neonates infected by SARS-CoV-2 can alternatively be asymptomatic (45%) or develop symptomatic COVID-19 infection (55%); in this latter case, the most common symptoms include fever, GI, respiratory and neurological manifestations (16). Liver injury was reported in COVID-19 adult and pediatric patients and can be attributed to different factors, including hypoxic–ischemic damage viral or drug-induced hepatocyte injury. In this case, liver injury was probably caused by a direct coronavirus-mediated mechanism, whose mechanistic details, albeit linked to ACE2 receptor expression in cholangiocytes and hepatocytes (59.7 and 2.6%, respectively), remain presently unknown. Alternative explanations for neonatal liver involvement were likely excluded by the evidences that the neonate had a normal acid–base status and did not receive any medication before the first blood test examination. Maternal tests were negative for major congenital infections and neonatal blood cultures were negative; also, the Expanded Newborn Screening performed according to the Italian National Institute of Health neonatal screening program excluded inherited metabolic disorders. Unsurprisingly, we found the persistence of the virus in the feces until the last sample analyzed at 7 DOL. Emerging data suggest the prolonged presence of SARS-CoV-2 RNA in stool samples or rectal swabs even after the patients' respiratory specimens become negative and much attention has been paid to the possibility of viral shedding from the GI tract and fecal–oral transmission. Recent literature suggested that liver involvement, in case of SARS-CoV-2 infection, is possible, but to our knowledge, there are no reports that clearly described this association. A report by Kalamdani et al. described the case of 12 newborns positive for SARS-CoV-2. Nine out of 12 newborns were tested for liver enzymes (AST and ALT) and reported a slight increase of median values of AST and ALT, lower compared to our case report and in the range of normality considering the vast majority of cases. Moreover,

authors reported just one value and it is not specified in which day of life the blood drown was performed. Sisman et al. described a case report of a preterm infant with intrauterine transmission of SARS-CoV-2 infection with slightly elevated AST (64 U/l range 10–35) and normal ALT; however, the trend of liver enzyme elevation was not described. Zeng et al. described a case series of 33 neonates born to mothers with COVID-19. Among them, three newborns tested positive for SARS-CoV-2. One had elevated AST (63 U/L) and ALT (88 U/L) and was born preterm (31 weeks GA). Moreover, his clinical course was complicated by respiratory distress syndrome, pneumonia and suspected sepsis; thus, other causes of elevated transaminases were plausible. We presented a case of a well-documented neonatal infection, describing AST and ALT trend over time and exclusion of other causes of hepatic involvement. This clinical case suggests that possible liver damage should be sought in all newborns born to COVID-19-positive mothers, regardless of the clinical condition. However, further studies are needed to confirm our observations. Longer follow-up and prospective studies are needed to determine the real impact of SARS-CoV-2 virus in the liver.

Recent Publications

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Speaker Biography

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