

## Case Report

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# Neonatal hepatitis in a term newborn: sequelae to in utero COVID-19 infection

Pushwinder Kaur\*

Department of Pediatrics, PIMS, Jalandhar, Punjab, India

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**\*Correspondence:**

Dr. Pushwinder Kaur,

E-mail: pushwinder566@gmail.com

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## ABSTRACT

Neonatal hepatitis is a common disease entity seen among newborns. It is known as inflammation of liver parenchyma in newborns, specifically in first month of life. Most common cause of neonatal hepatitis is viral infection which infects liver in utero or in postnatal period. Newborns carrying neonatal hepatitis mostly present with jaundice, failure to gain weight and hepatosplenomegaly. Neonatal hepatitis due to in utero COVID infection is diagnosed by conjugated hyperbilirubinemia, raised SGOT and SGPT levels and raised COVID antibody levels. Treatment includes addition of fat-soluble vitamins, phenobarbitone and supportive care. Here author is reporting a rare case of 11 days old newborn with neonatal hepatitis, who presented with severe jaundice (TSB/DB- 44/22) hepatosplenomegaly and hypoxemia with mild respiratory distress. Maternal history revealed high grade fever with low cell count during 5th month of gestation, though COVID RAT was negative and RT-PCR was not done. Baby was managed in NICU with IV antibiotics, IV fluids, oxygen by prongs, oral fat-soluble vitamin supplementation, adequate calorie intake and phenobarbitone. Baby responded very well to the treatment and discharged in healthy condition after 7 days. Paucity of data documenting in utero COVID-19 infection as cause of neonatal hepatitis led us to report this rare case.

**Keywords:** Neonatal hepatitis, Jaundice, Hepatosplenomegaly, Phenobarbitone

## INTRODUCTION

Neonatal hepatitis is defined as inflammation of the liver parenchyma in neonatal period.<sup>1</sup> Viral infections like CMV, rubella, hepatitis A, B or C are the well-known causes of neonatal hepatitis.<sup>2</sup> Coronavirus is transmitted from mother to baby by vertical transmission.

Clinical manifestations of neonatal hepatitis include failure to gain weight, conjugated jaundice, dark coloured urine and enlarged liver and spleen. Diagnosis is based on conjugated hyperbilirubinemia, deranged LFT, ultrasound abdomen depicting increased hepatic echogenicity, positive neonatal COVID RT-PCR and/or positive COVID antibodies, positive maternal COVID RTPCR/Anatibodies. Treatment mainly focus on supportive care including fluid supplementation along with continuation of breastfeeding, fat soluble vitamin supplementation and phenobarbitone.

Fat malabsorption leads to deficiency of fat-soluble vitamins, which are supplemented in high amounts. Phenobarbitone (antiepileptic drug) increase hepatic glucuronyl transferase activity and enhances conjugation of bilirubin. Various case reports conducted till date has documented that maternal coronavirus infection during pregnancy can infect the fetus in utero or during labour and most of the babies born to the infected mothers were asymptomatic with few, who had fever, pneumonitis and sepsis. Herein author reported a rare case of neonatal hepatitis with pneumonitis in a term neonate born to COVID infected mother.

## CASE REPORT

A term/AGA (2.5 kg) female baby born to G4P3L3A0 mother by normal vaginal delivery at private nursing home, cry immediate was admitted at day 11 of life with jaundice. Baby was immediately handed over to mother

after delivery and breast feeding was started as per protocol. Baby remained stable till 9 days of life, when mother noticed yellow discolouration of eyes and dark coloured urine. On examination, baby had yellow discolouration of eyes, vitals normal, liver palpable 3 cm below the right costal margin and spleen tip palpable. Initially possibility of unconjugated hyperbilirubinemia was kept and iv fluids, iv antibiotics and phototherapy started. But surprisingly reports revealed conjugated hyperbilirubinemia (TSB/DB- 44/22, SGOT/SGPT- 368/278, ALP- 136, GGT- 67). Further work up for neonatal hepatitis was done and hepatitis B, hepatitis C, TORCH was ruled out. Reticulocyte count and G6PD levels came out to be normal, hence haemolysis as a cause of jaundice was precluded. Thyroid profile was also normal.

As the cause of neonatal hepatitis was not clear yet, maternal history was reviewed and history of high-grade fever with low cell count during 5<sup>th</sup> month of gestation outburst. As per mother's knowledge COVID RAT was done and it was negative. COVID RT-PCR was not done. Keeping possibility of in utero COVID infection as cause of neonatal hepatitis, babies COVID RT-PCR and antibodies were ordered and unexpectedly antibodies came out to be positive. Ultrasound abdomen showed increased echogenicity of liver which was again suggestive of neonatal hepatitis.

Baby was managed conservatively with IV fluids, breast feeding, fat soluble vitamin supplementation, phenobarbitone and IV antibiotics. Also, baby had mild respiratory distress with saturation upto 87% without oxygen on admission and CXR revealed bilateral infiltrates. Gradually general condition of the baby improved, jaundice decreased (TSB/DB- 16.1/9.7, SGOT/SGPT- 293/225, ALP- 213, GGT- 74), respiratory distress settled and discharged in healthy status. Baby remained in regular follow up in paediatrics OPD and found healthy and gaining weight with regular fall in bilirubin levels during OPD visits. Liver function tests took almost one month to completely normalise.



**Figure 1: Neonatal hepatitis.**

## DISCUSSION

Neonatal hepatitis is a liver dysfunction that affects neonates.<sup>1</sup> It is most commonly caused by viruses and rarely by metabolic disorders.<sup>2</sup> Differential diagnosis of neonatal hepatitis is vast and a step wise approach based on the history and physical examination is helpful to quickly discern the primary cause. Viruses that have been identified include rubella virus, cytomegalovirus, hepatitis A and B virus, Herpes simplex virus, coxsackie virus, echo virus and paramyxovirus.<sup>3</sup> Corona virus like other viruses can infect the liver and leads to inflammation, though data documenting such manifestation is missing. Metabolic disorders like galactosemia, cystic fibrosis, alpha 1 antitrypsin deficiency can also cause neonatal hepatitis. Biliary atresia also presents as conjugated hyperbilirubinemia, which needs to be investigated and surgically treated.

Neonates with neonatal hepatitis most commonly present with jaundice, high coloured urine and enlarged spleen and liver. Clinically this can be differentiated from the physiologic jaundice with dark coloured urine. Those infected with TORCH group of pathogens also have petechiae, chorioretinitis and microcephaly.

Neonatal hepatitis is diagnosed by series of investigations like deranged liver function test, TORCH test, blood culture, urine culture, newborn screen for galactosemia, thyroid profile, alpha 1 antitrypsin level, immunoreactive trypsinogen levels, ultrasound abdomen and liver biopsy. US abdomen is done to rule out any biliary atresia and choledochal cyst.

US abdomen shows increased hepatic echogenicity in neonatal hepatitis. Liver biopsy is an important diagnostic modality and various causes of neonatal hepatitis can be differentiated based on liver biopsy results like viral infection (CMV or HSV inclusions), idiopathic neonatal hepatitis (multinuclear giant cells, extramedullary hematopoiesis, hepatocellular cholestasis) and metabolic liver disease (steatosis and pseudoacinar formation of hepatocytes).<sup>4</sup>

Management of neonatal hepatitis is mainly focussed on early identification and treatment of cause like bacterial and viral infections should be treated with antibacterial and antiviral agents respectively. As growth failure due to defective fat absorption, defective protein and carbohydrate metabolism and increased metabolic demand is the most common complication of neonatal hepatitis, therefore adequate nutritional therapy is of greatest importance.<sup>5,6</sup> Adequate calorie intake, protein intake and fat-soluble vitamins is must to overcome growth faltering.

## CONCLUSION

Neonatal hepatitis presents as conjugated hyperbilirubinemia with dark coloured urine. Viral infections are the most common cause of neonatal

hepatitis. In utero exposure to corona virus can also infect fetal liver and lead to Neonatal Hepatitis. Hence any newborn who presents with neonatal hepatitis should also be investigated for coronavirus in the coming years. Early diagnosis and intervention can prevent growth faltering in neonates.

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