NICU TIMES
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MOTHER & CHILD CENTRE

An interesting case of cyanosis in a newborn

- Cyanosis in cardiac diseases may be associated with minimal respiratory distress, normal PaCO2 levels and may not respond to oxygen therapy
- Double outlet right ventricle (DORV) is a cono-truncal abnormality which may be associated with cyanosis in a newborn
- Treatment of doubly committed DORV may involve staged multiple cardiac surgeries • Routine pulse oximetry screening can improve early diagnosis of critical congenital heart disease

Case report:

Baby of Mrs S, was born to a 25 year old G3A1L1 mother who conceived naturally with normal antenatal scans. A single, live, term (38 weeks), male baby delivered by vaginal delivery with birth weight 2600 grams. The baby cried immediately after birth and did not require any resuscitation. The baby was referred to our centre in view of respiratory distress and mild cyanosis at 16 days of postnatal life. On examination, baby had a HR-146/min, RR 72/min (Tachypnoea), BP 72/56 (58) mmHg, SpO2 88-90% in room air. All pulses were well felt, CFT was 2 seconds.

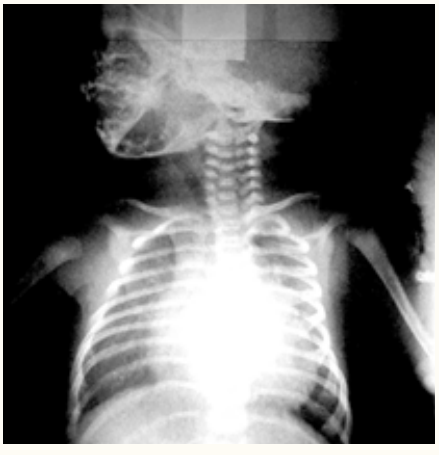
AF - at level. S1,S2 were distinguishable with continuous systolic murmur in all areas, Sub-coastal and supra sternal retractions present with bilateral air entry. Abdomen was soft with liver 1 cm below the right coastal margin. Cry tone and activity were normal, Bilateral femoral pulsations were well felt and no other obvious external congenital anomalies present.

Anthropometry:

Weight at birth: 2600 grams, weight at admission-2800 grams, Head Circumference : 35 cms, Length: 49 cms which suggested appropriate weight gain.

Investigations showed normal counts, blood gas with pH 7.33, CO2 38 mmHg, HCO3 18 mEq/L, Chest x ray showed cardiomegaly (Fig. 1).

Fig. 1: Chest X-ray of the neonate showing cardiomegaly



Pediatric cardiologist, was consulted – echo cardiography showed Double outlet right ventricle (DORV) with large ventricular septal defect (VSD), pulmonary arterial hypertension (PAH) , no RVOT

Hence in view of congestive cardiac failure which manifested in the form of subcostal retractions and tachypnoea with cardiomegaly, baby was started on oxygen support at 0.5 litres/minute and Inj. Furosemide. Dobutamine infusion was started to increase cardiac inotropy and oral digoxin was started. Gradually, as the respiratory distress settled down, baby was weaned off to room air after 24 hours of admission. Dobutamine infusion was tapered and stopped after 12 hours. Oral aldactone was also added at discharge. Electrolytes were checked to rule out adverse effects of lasix and spirionolactone which were normal.

Nutritional requirements of baby were Initially met by OG feeds at admission and gradually as the respiratory distress settled down, breast feeds/oral feeds were started after 26 hours of admission. which baby accepted and tolerated oral well. The surgical intervention planned was PA banding followed by DORV repair with/ without single ventricle correction later (parents were counselled about the need).

Description:

Double outlet right ventricle (DORV) accounts for about 2-3% of all congenital heart defects, with a birth prevalence rate of 1/ 10,000V. DORV is a rare cono-truncal anomaly in which both the aorta and pulmonary artery originate, either entirely or predominantly, from the morphologic right ventricle. No arteries are connected to the left ventricle .

DORV results from a failure in the fetal development of the cono-truncus, which is the primary outlet of the heart during embryonic development. The cono-truncal anomalies result in neural crest and second heart field dysfunction. DORV is associated with chromosomal anomalies such as 22q11.2 deletion syndrome, trisomy 13, trisomy 18 and CHARGE syndrome and others. Ventricular septal defect (VSD) always occurs with DORV, while other possible defects are Endocardial cushion defects, Coarctation of the aorta ,Mitral valve problems, Pulmonary atresia, Pulmonary valve stenosis, Right-sided aortic arch, Transposition of the great arteries.

With biventricular repair, patients have, on average, a normal life expectancy, with possible risk or re-operation. All patients that have received surgery for a DORV require life-long surveillance by a cardiologist. Univentricular palliation requires a very close follow up.

Conclusion of the index case:

Hence baby was discharged with oral digoxin, Lasix, aldactone till surgery in hemodynamically stable condition with spontaneous respiration at room air, with saturations above 90%.

Frequently Asked Questions

1. What is the relevant history to be elicited in a neonate with cyanosis?

Ask for onset of bluish discoloration, severity, location (upper and lower limbs, mucosal membranes), progression and occurrence of cyanotic spells. Cyanosis since birth may be a manifestation of critical pulmonary duct dependent lesions, admixture lesions and parallel circuits. Cyanosis disproportionate to respiratory distress is a manifestation of congenital cyanotic heart disease with decreased pulmonary blood flow. Cyanosis on crying is classical of heart disease while cyanosis relieved on crying is suggestive of choanal atresia.

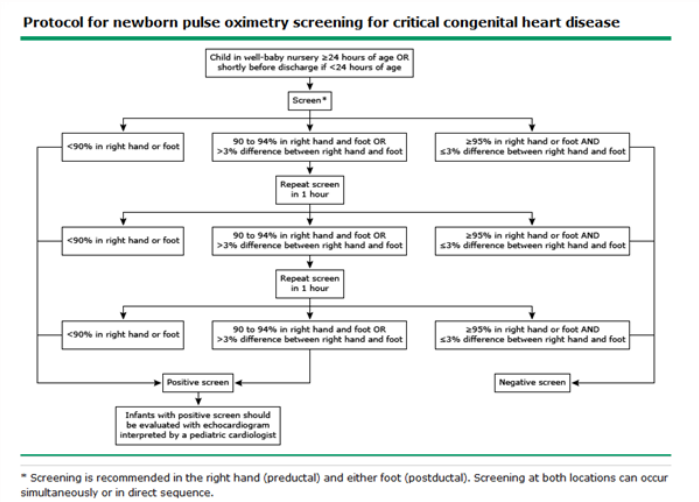
2. What are the key points in examination in a neonate with cyanosis?

Note the general well-being, activity, posture, symmetry in all limbs, location or extent of cyanosis (over gums, tongue, buccal mucosa, palms and soles), differential cyanosis, head size and jaundice. Look for other congenital malformations. Jaundice with murmur (pulmonary stenosis) can be seen in Alagille's syndrome. Examine the anterior fontanelle for any cranial bruit and abdomen for hepatic bruit seen in Vein of Galen malformation and hepatic AV malformation respectively.

Facial dysmorphism may be noted in neonates with trisomies 21 or 18, DiGeorge syndrome, Turner's syndrome and VACTERL association which are known to be associated with congenital heart disease.

3. How does pulse oximetry help in detecting congenital heart disease?

Pulse oximetry screening for critical congenital heart disease is performed as follows



4. What is the role of clinical examination in determining the etiology in a neonate with suspected heart disease?

Specific clinical findings, when present help in narrowing down the type of congenital cardiac disease

Clinical findings	Conditions
Wide pulse pressure	PDA, AV malformations , Aortic regurgitation
Bounding pulses	Anemia, PDA, Vein of Galen malformation, Truncus arteriosus, Aorto-pulmonary window, Aortic regurgitation
Feeble pulses	In all 4 limbs- myocardial dysfunction/ shock, weak femoral pulses- coarctation of aorta (palpable femoral pulses may not rule out coarctation)
Hyperdynamic precordium	Left to right shunts (PDA) or severe mitral / aortic regurgitation
Palpable P2	Severe Pulmonary arterial hypertension (PAH)
S3	Ventricular dysfunction, heart failure
Continuous murmur	PDA, Hepatic AV malformation, Vein of Galen malformation
Wide and Fixed split S2	Atrial septal defects (although murmur of ASD is rarely audible until 2 years)

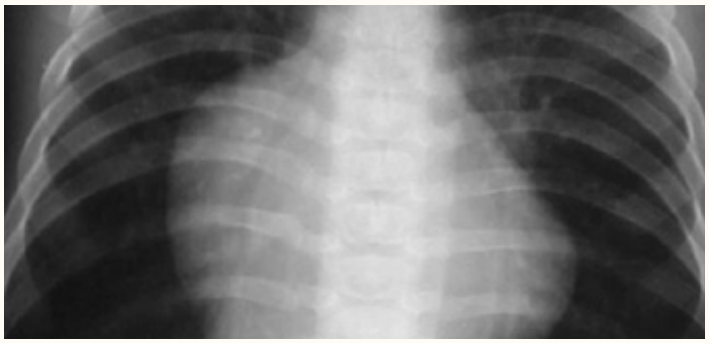
5. How does blood gas help us in a case of cyanosis?

Response to oxygen with hyperoxia test although seldom used now with the advent of echocardiography, is an useful tool for the diagnosis of cyanotic congenital heart disease. A PaO2 of more than 160 mm Hg upon inhalation of 100% oxygen by oxygen hood for 10 minutes makes the cardiac cause of cyanosis unlikely, a value of >250 mm Hg (passed hyperoxia test) completely excludes it. An arterial PaO2 of < 100 mm Hg (failed hyperoxia test), and/ or the rise is not more than 10 to 30 mm Hg in the absence of clear cut lung pathology is most likely due to intracardiac right-to-left shunting and is virtually diagnostic of cyanotic CHD.

Frequently Asked Questions

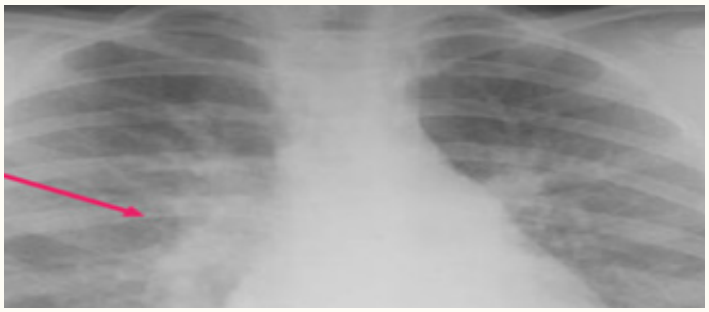
6. How does Chest X-ray help in diagnosis of a neonate with cyanotic CHD?

Chest x-ray suggestive of 1) dark Lung Fields, 2) Thin peripheral vessels and 3) small Hila usually suggest decreased pulmonary blood flow. This may be suggestive of Tetralogy of Fallot (VSD + PS) physiology - seen in (a) TOF (VSD/ PS) (b) DORV/ VSD/ PS (c) AVSD/ PS (d) TGA/ VSD/ PS (e) Single ventricle/ PS and (f) Tricuspid atresia with restrictive VSD and/ or PS



On the other hand, a chest x-ray s/o dilated right descending pulmonary artery (figure below), prominent Hilar pulmonary arteraies, PA traced till lateral 3rd of lung field and end on vessels >4 in one lung field may imply presence of pulmonary plethora. This is suggestive of the group of conditions - Transposition physiology - Complete TGA or DORV/ subpulmonic VSD (Taussig Bing). It may be also seen in admixture lesions

1) At systemic or right atrial level: TAPVR, Mitral/ Aortic atresia with IVS 2) At left atrial level: Tricuspid atresia 3) At ventricle/ great artery level: Single ventricle, Complete AVSD with straddling AV valve, DORV/ subaortic or inlet VSD, Persistent truncus arteriosus



7. What is unique about the index case?

DORV with non-committed VSD is present in 12% to 17% of patients which makes the present case rare.

8. What are the other modalities of diagnosis for congenital heart diseases?

The present case is diagnosed by 2D-ECHO CARDIOGRAPHY but other advanced Diagnostic modalities based on 3D echocardiography showing both great arteries arising from the right ventricle can be used for precision. In complex forms, cardiac catheterization-angiography, magnetic resonance imaging (MRI) and /or computed tomography (CT) scan are required. Recently, 3D printed models have been very useful to plan the surgery.

DORV can be diagnosed by fetal echocardiography with a good degree of accuracy when the two vessels arise entirely from the right ventricle.

9. How is DORV managed?

In the presence of two viable ventricles, biventricular repair is the optimal treatment for DORV and it is quite safely achieved in the simple forms (DORV-VSD type, DORV-Fallot type and DORV-TGA type). In the complex forms (DORV with non-committed VSD, DORV-atrioventricular septal defect-pulmonary stenosis-heterotaxy), univentricular repair (Fontan operation) is often preferred. In this case, due to increased pulmonary blood flow, PA banding followed by ventricular repair is chosen.

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Neonatal Cholestasis - An Approach

- Neonatal cholestasis represents elevation of conjugated bilirubin to > 20% total
- A systematic approach must be followed to rule out underlying galactosemia, extra hepatic biliary atresia, hypothyroidism and urosepsis
- Niemann Pick disease is one of the causes of massive spleno hepatomegaly with cholestasis

Our index case presented on day 26 of life, a product of 3rd degree consanguineous marriage, second born of twins, male, born at term gestation to a primigravida mother by LSCS with birth weight of 2500 grams. The newborn cried immediately after birth, and did not require any resuscitation. Baby was admitted in NICU for symptomatic polycythemia and partial exchange transfusion was done at 2 hours age. Post this baby was well and was discharged. Baby presented to our unit on day 26 of life with h/o persistent jaundice since birth. Abdominal distension was noted since 2 days prior to admission. H/o depigmented stools and high coloured urine was present. No h/o fever, seizures, decreased activity. No history of liver disease in family.

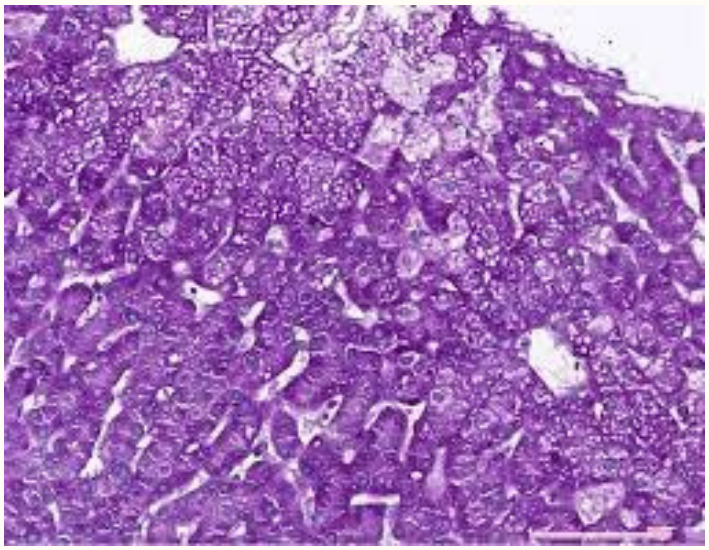
On examination baby was having yellow sclera, activity good, vitals were stable, CVS - systolic murmur was present. The newborn had massive splenohepatomegaly, liver 5-6cms below RCM, spleen 6-7 cms below LCM, Bilateral hydrocele was present.

On evaluation, serum bilirubin total was 16.4mg/dl, direct fraction 4.3mg/dl. SGOT and SGPT were mildly elevated at 100-200 IU/L, GGT-56 UL(Normal); This suggested direct hyperbilirubinemia with mild transaminitis. Blood counts showed mild thrombocytopenia - CBP- Hb-10.3gm%,WBC-6900/cumm,Platelets-82000/cu.mm. 2D Echo showed 4 mm ASD (L-R shunt), mild dilated RA and RV. TSH was normal. Liver functions were essentially preserved with total protein-3.4gm/dl, PT-12.4sec, APTT-46.6sec, INR-1.12. Renal evaluation was normal - Serum creatinine 0.6 mg/dL, CUE –Normal.

At admission, initial work up was done and baby was started on fat soluble vitamins A,D, E and K supplementation, oral urso-deoxy cholic acid (UDCA) and continued on oral feeds.

Suspecting intrauterine infections and storage disorders in view of massive splenohepatomegaly, CMV DNA PCR was done which was negative, HbsAg was negative, USG abdomen confirmed splenohepatomegaly and picked up mild ascites. Gall bladder was well delineated and there was no e/o triangular cord sign. HIDA scan was done after priming which showed evidence of good hepatocyte function with non visualisation of intestinal activity till 24 hrs and was suggestive of biliary outflow obstruction (? biliary atresia). Hence, liver biopsy was done, which showed canalicular proliferation with no ductular proliferation which was suggestive of PFIC (progressive familial intrahepatic cholestasis) [Fig.1]. However genetic studies which came up in 45 days confirmed a mutation of NPC1 gene suggestive of Niemann Pick disease type C. Niemann Pick disease type C is characterised by a rare genetic defect with inability to metabolise cholesterol withy massive spleno hepatomegaly.

Fig. 1 : Histopathology of liver sample – s/o Niemann Pick type C



LIKELY PATHOGENIC VARIANT CAUSATIVE OF THE REPORTED PHENOTYPE WAS DETECTED

Gene (Transcript) ‡	Location	Variant	Zygosity	Disease (OMIM)	Inheritance	Classification
NPC1 (-) (ENST00000269228.10)	Exon 3	c.275A>G **(p.Gln92Arg)**	Homozygous	Niemann-Pick disease type C1; Niemann-Pick disease type D	Autosomal recessive	Likely Pathogenic

The diagnostic criteria for PFIC included: (i) a history of chronic unremitting cholestasis, hepatomegaly/ hepatosplenomegaly+pruritus and biochemical findings characteristic of the disease (ii) exclusion of other causes by various investigations. Serum GGT was used to differentiate PFIC III from I and II patients. Type I and II are characterized by a low GGT level whereas type III is associated with high GGT levels. The management involved medical ± surgical treatment along with nutritional rehabilitation, multivitamin supplementation and treatment of coexisting rickets. Prior to 1990s, LT was the only effective therapy for PFIC. In recent years, alternative surgical options [partial external biliary diversion (PEBD), partial internal biliary diversion (PIBD)] which divert bile salts from the enterohepatic.

recirculation have shown therapeutic promise in low serum gammaglutamyltransferase (GGT) PFIC. LT is curative in PFIC at an advanced stage with established cirrhosis. In a series of 13 patients undergoing LT for PFIC, authors have reported a 2 year survival of 85%.

Frequently Asked Questions

1. What is the most acceptable definition of direct hyperbilirubinemia?

Although there are discrepancies among various laboratories and techniques, a practical definition of the cholestatic infant is one where direct bilirubin is greater than 1.0 mg/dL if the total bilirubin is less than 5 mg/dL, or a value of direct bilirubin that represents more than 20% of the total bilirubin if the total bilirubin is greater than 5 mg/dL..[1]

2. When should prolonged jaundice alert the physician?

The Cholestasis Guideline Committee of the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN) recommends that any infant noted to be jaundiced at 2 weeks of age be evaluated for cholestasis with measurement of total and direct serum bilirubin. However, breast-fed infants who can be reliably monitored and who have an otherwise normal history (no dark urine or light stools) and physical examination may be asked to return at 3 weeks of age and, if jaundice persists, have measurement of total and direct serum bilirubin at that time.[1]

3. Does the method of bilirubin testing have any impact on detection of cholestasis?

The most commonly used laboratory determination (the diazo or van den Bergh method) does not specifically measure conjugated bilirubin but reports “direct bilirubin”, which tends to overestimate conjugated bilirubin. For methodological reasons, the higher the total bilirubin (even if it is all unconjugated), the higher the reported direct bilirubin. A specific measurement of conjugated bilirubin, such as that obtained with the Ektachem system, is optimal.[1]

4. What are the common causes of neonatal cholestasis (NCS)?

The most common causes of cholestatic jaundice in the first months of life are biliary atresia and neonatal hepatitis, which account for most cases (Table 1). Neonatal hepatitis has referred to a histologic appearance of widespread giant cell transformation.

In a large Indian series, hepatocellular causes were seen in 53%, obstructive causes in 38%, ductal paucity in 3% and other 6% cases were idiopathic.

Infants with cholestatic jaundice caused by bacterial sepsis, galactosemia, hypopituitarism, or gallstones often appear acutely ill. These disorders require early diagnosis and urgent treatment.

5. What are the important causes of cholestasis where early diagnosis can make a significant difference to outcomes?

Substantial observational evidence suggests that earlier diagnosis and surgical repair of extrahepatic biliary atresia (EHBA) lead to better outcomes. The Kasai porto-enterostomy appears to have the greatest likelihood of re-establishment of bile flow and the longest term survival of the infant’s native liver when performed before the age of 45 to 60 days.1

Conditions such as sepsis, galactosemia, hypothyroidism and panhypopituitarism must be recognised early to prevent progression.

6. What is the practical utility of pale, clay coloured stools to detect possible biliary obstruction?

The sensitivity, specificity and positive predictive value of pale stools for the detection of biliary atresia (BA) before 60 days as determined by a color-coded stool chart was noted to be 89.7%, 99.9% and 28.6%, respectively. So, pale stools is more specific than sensitive as a marker of obstruction.[4]

7. What are the useful laboratory tests in a neonate with direct hyperbilirubinemia?

The investigatory approach should take into consideration the clinical condition and presentation of the child (Fig. 2).

The evaluation of cholestatic jaundice in infants between two and eight weeks of age should be undertaken in a staged approach. In a sick baby with cholestatic jaundice possibilities of galactosemia, toxoplasmosis, herpes, tyrosinemia, sepsis, malaria, etc. should be considered and ruled out. The next step is to distinguish biliary atresia from other causes of neonatal cholestasis, because early surgical intervention for biliary atresia results in improved outcome.

The further tests should be individualised rationally based on the results of above tests. If the level of serum alpha-1 antitrypsin is found to be low, Pi typing is indicated. If an obvious extrinsic obstruction (such as choledochal cyst) is present, referral for surgery is warranted.[1]

8. What is the usefulness of imaging in a neonate with cholestasis?

Ultrasonography - It is most helpful in the diagnosis of choledochal cysts but can also suggest the diagnosis of biliary atresia; suggestive findings for the latter are the inability to visualize the gallbladder and the presence of the “triangular cord sign” (triangular or band like periportal echogenic density >3 mm in thickness). The latter is more specific than sensitive for the diagnosis of EHBA.[5]

Scintigraphy - Hepatobiliary scintigraphy with technetium-labeled iminodiacetic acid analogues may provide some more information in distinguishing biliary atresia from neonatal hepatitis. Infants with biliary atresia usually have normal uptake of the isotope but absent excretion into the intestine, whereas those with neonatal hepatitis typically

have delayed uptake but appropriate excretion. However, nonvisualization of the gallbladder or lack of excretion can occur in patients without biliary atresia. Pretreatment for five days with phenobarbital (5 mg/kg per day) increases the accuracy of this test by enhancing isotope excretion.[5]

Additional tests such as MRCP (Magnetic Resonance Cholangiopancreatography) and ERCP (Endoscopic retrograde cholangiopancreatography) are not routinely recommended in view of limited data in neonates and young infants.[1]

9. What does percutaneous liver biopsy add to the evaluation of a neonate with cholestasis?

The NASPGHAN guideline recommends that a percutaneous liver biopsy be performed in most infants with undiagnosed cholestasis, especially when obstruction cannot be reliably ruled out.[1,5] Findings supportive of biliary atresia in the liver biopsy are - expanded and edematous portal tracts, bile duct proliferation, bile duct damage, and intraductular bile plugs. Liver biopsy specimens obtained early in the course of biliary atresia may be indistinguishable from hepatitis. Other diagnostic findings from a biopsy include PAS-positive granules in alpha-1 antitrypsin deficiency, ductal paucity in Alagille syndrome, necro-inflammatory duct lesions in sclerosing cholangitis, and other findings that are relatively specific for metabolic and storage diseases.

Brough and Bernstein demonstrated the diagnostic usefulness of the percutaneous liver biopsy and established the diagnostic criteria that are in current use.[6]

10. What are the principles of management of a neonate with cholestasis?

Management of NCS is multi-pronged and includes management of nutrition, concurrent infections and complications.

Nutritional management[2,4]

1. In breastfed infants, breastfeeding should be encouraged and medium-chain triglyceride (MCT) oil should be administered in a dose of 1-2 mL/kg/d in 2-4 divided doses in expressed breast milk. Older children should be offered a diet rich in calories (125% of recommended dietary allowance [RDA]), rich in medium chain triglycerides (MCT), vegetable protein (2-3 g/kg/day), vitamins, trace elements and minerals. Almost 2-3% calories should come from essential fatty acids. This may be possible by providing milk-cereal-mix fortified with MCT.

2. Infants with cholestasis require supplementation with fat-soluble vitamins administered orally as water-soluble preparations. Suggested daily vitamin and mineral supplementation are given in Panel I.

Pruritus

Depending on its severity, it can be treated in the following order: Ursodeoxycholic acid (UDCA) (20 mg/kg/day), rifampicin (5-10 mg/kg/day), and phenobarbitone (5–10 mg/kg/day).[5]

Associated Problems

Portal hypertension- Variceal bleeding may need require with endoscopic sclerotherapy. Ascites requires bed rest, salt restriction (restrict added salt to 1 mEq/kg/day-0.5 to 1 g salt), avoidance of diet containing extra salt and diuretics like spironolactone and frusemide. Intractable and tense ascites may require paracentesis. Hepatic encephalopathy should be managed with oral lactulose, oral amoxycillin or metronidazole, colonic washes, restricted proteins, evacuation of blood from GIT, correction of hypoglycemia, electrolyte imbalance and blood loss.[4]

Specific treatment

Special infant formula and diets are recommended for children with specific diagnosis (galactosemia, fructosemia and tyrosinemia). Treatment with nitisinone (1 mg/kg/d) in addition to dietary restriction leads to rapid reduction of toxic metabolites in tyrosinemia. Specific therapy is recommended for patients with CMV (if associated neurological involvement), herpes and toxoplasmosis related cholestasis. There is no role for steroids in idiopathic neonatal hepatitis.[4]

Kasai's porto-enterostomy (PE) consists of removal of the atretic extrahepatic tissue and a Roux-en-Y jejunal loop anastomosis to the hepatic hilum. PE may be considered successful if serum bilirubin normalizes after surgery.5 Liver transplantation may remain the only option for infants with EHBA with decompensated liver disease (ascites and/or encephalopathy) or failed portoenterostomy.[2]

Conclusions

Neonatal cholestasis constitutes almost one-third of children with chronic liver disease in major hospitals in India. EHBA, neonatal hepatitis and metabolic causes are the most important causes in India. Early identification of the cause is essential for a favorable outcome. This requires specific biochemical tests, imaging studies and interpretation of histopathology by experienced personnel. To ensure early referral, there is an urgent need to sensitize pediatricians, obstetricians and other primary-care physicians on the need for early evaluation.

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Table 1: List of common causes of neonatal cholestasis

Obstructive cholestasis

Extrahepatic biliary atresia*
Choledochal cyst
Spontaneous perforation of bile ducts
Biliary stenosis
Gallstones or biliary sludge
Inspissated bile

Hepatocellular cholestasis

Idiopathic neonatal hepatitis*
Infectious hepatitis*

Viral infection

- Cytomegalovirus
- HIV
- Rarer- Adenovirus, Enterovirus, Parvovirus, Herpes

Bacterial infection

- Urinary tract infection
- Sepsis
- Syphilis

Toxoplasmosis

Genetic/metabolic disorders

- Alpha 1-antitrypsin deficiency*
- Tyrosinemia
- Galactosemia
- Progressive familial intrahepatic cholestasis (PFIC)* types 1-4
- Cystic fibrosis
- Neonatal hemochromatosis

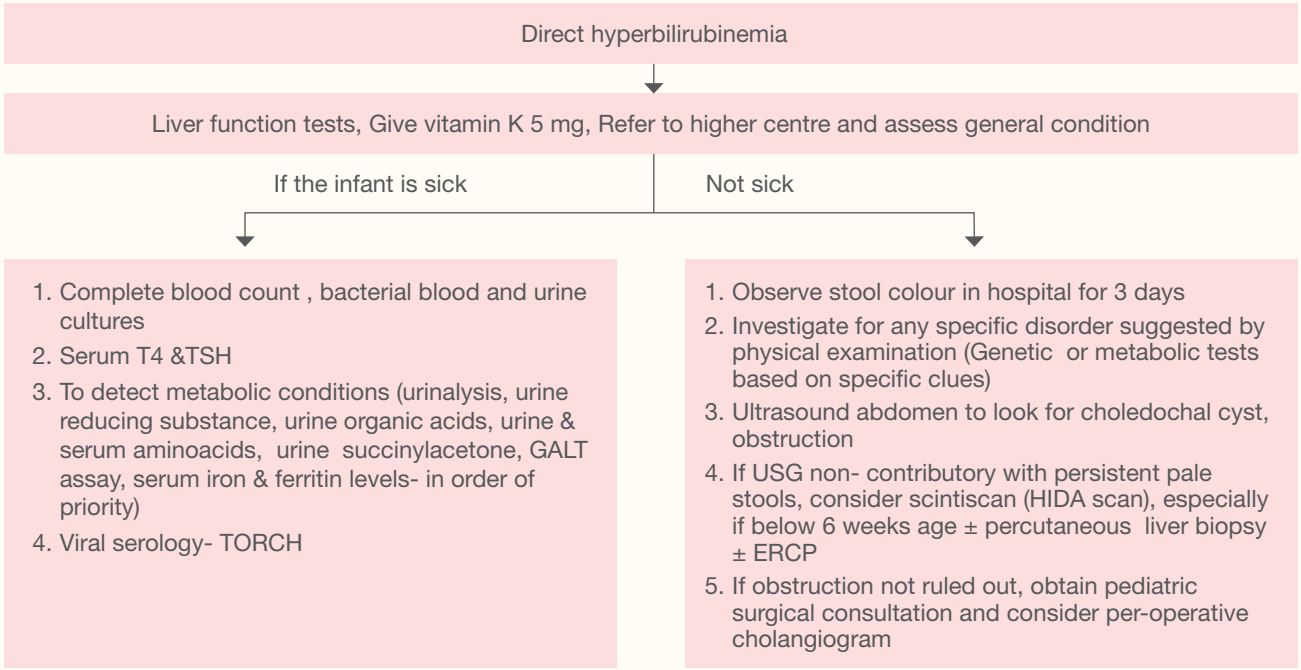
Syndromic paucity of interlobular bile ducts or Alagille syndrome*
Endocrine

- Panhypopituitarism
- Hypothyroidism

Toxic/secondary to shock/ intestinal obstruction
Parenteral nutrition-associated cholestasis*

*The highlighted ones are the most common causes in the list

Fig. 2: Approach to investigating a neonate with cholestasis1,2



Panel I: Suggested Daily Vitamin And Mineral Requirements In Infants With Cholestasis[5]

- Vitamin A –5000-25,000 IU/day orally
- Vitamin D –400-1200 IU/day orally; 1,25 dihydroxy Vitamin D3 (0.05-0.2 ug/kg/day) is recommended in the presence of significant bone changes or patients having severe cholestasis
- Vitamin E - 50-400 IU/day or 15-25 IU/ kg/day orally (1 mL of Evion drops contains 50 mg of tocopherol acetate or 75 IU vitamin E)
- Vitamin K - 2-5 mg IM, SC or IV 4 weekly; If the INR is markedly prolonged, intramuscular injections should be avoided. Vitamin supplementation should be continued till 3 months after resolution of jaundice
- Water soluble vitamins -1-2 times the RDA orally
- Minerals- Calcium 20-100 mg/kg/day and phosphorous 25-50 mg/kg/day along with zinc 1 mg/kg/day

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Baby was born preterm at 28 weeks of pregnancy

- Day eighth, the baby's oxygen levels were falling and the baby was facing increasing breathing difficulty that required ventilation
- Parents - We are overwhelmed to bring our baby back home

KIMS Cuddles is happy to share the success story of one of the youngest COVID-19 survivors going home. The baby was born preterm on April 17th 2021 — at 28 weeks of pregnancy — due to severe COVID-19 in the mother needing mechanical ventilatory support. Born with a birth weight of just 1000 grams and treated initially for prematurity related respiratory distress, the baby's first COVID-19 screening swab came out negative. On day eighth of birth, the baby's oxygen levels were falling and the baby was facing increasing breathing difficulty that required ventilation. A repeat PCR test culminated that the neonate was SARS-COV2 positive. The baby, who then weighed only 920 grams, was then put on ventilator and shifted to COVID isolation ICU by the team of doctors at KIMS Cuddles for further management.

The newborn was nursed by our team of doctors and nurses in personal protective equipment in a specialized isolation neonatal ICU and provided ventilatory support, intravenous antibiotics, and nutrition. The neonate was monitored with multi para monitors showing a real time display of its vitals such as blood pressure, oxygen saturations etc. The ventilator support was weaned to nasal ventilation and later to CPAP (continuous positive airway pressure). The newborn was managed with a combination of supportive care and steroids.

During this phase, the family including father Mr. Rahul, a medical coder by profession and mother Ms. Bala Mounika, residents of Kukatpally, were constantly updated about the newborn's clinical condition using video calls. Efforts were undertaken to motivate the mother to send expressed breast milk due to the numerous advantages of the same. After clinical recovery and another PCR test, the neonate was shifted out of isolation after recovering from COVID-19. The baby was nursed in radiant warm room and given appropriate developmentally supportive care with mother's milk, kangaroo care, micronutrient supplementation and thermal support. The baby had consistent weight gain of nearly 15-20 grams/day and was transitioned from tube feeds to oral feeding. After nearly 30 days of meticulous medical attention in the hospital, the baby was discharged in good health on breast feeding with a weight of 1500 grams on May 17th 2021.

Doctors team, at KIMS Cuddles, has been working tirelessly for high risk mothers and high risk preterm newborns including those affected with COVID-19 to provide world class services with compassion and human touch.

Baby's father Mr. Rahul said, "We are overwhelmed to bring our baby back home from KIMS Cuddles. We had been really worried when we came to know that our baby was COVID-19 positive. Dr Aparna promised us that she would give our baby safely. We were constantly updated about the newborn's clinical condition through video calls KIMS Cuddles team made our dreams come true by sending our baby back home safely after a month of baby's birth. We are happy to learn that our baby is one of the youngest COVID-19 survivors in Hyderabad."

Our team at KIMS Cuddles has delivered 35 mothers with COVID-19 of which only 2 newborns tested positive - both tested positive in the second week suggestive of postnatal transmission. All babies survived with nearly 20% requiring NICU admission.

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Device closure of PDA in an extremely preterm neonate

- The baby, born extremely preterm with birth weight of 1138 grams
- Early CPAP started PEEP 6 cms, FiO2 30%
- The neonate underwent PDA device closure on day 28 of life using Piccolo Amplatzer device under fluoroscopy guidance after elective ventilation

Case report:

Baby of Mrs. A , was born at 28 weeks' gestation to a 32 year old primigravida mother who conceived naturally with antenatal scans showing left dysplastic kidney with hydroureter. The baby, born extremely preterm with birth weight of 1138 grams delivered by vaginal delivery with birth weight 1138 grams. The baby did not cry immediately after birth. The baby was given 1 cycle of PPV for 1 min, Apgars were 4 and 8 at 1 and 5 minutes respectively. On examination, baby had HR - 158/min, RR -52/min, BP - 70/40mmHg, All pulses were well felt. S1 S2 heard normally, there was no murmur, bilateral air entry heard, no added sounds appreciated, Silverman Anderson's score was 4-5/10, abdomen was soft with no organomegaly; cry, activity appropriate, hypotonia+, No obvious congenital anomalies.

Immediately after birth baby was shifted to NICU. Early CPAP started PEEP 6 cms, FiO2 30%. Surfactant given via INSURE technique – in view of radiological e/o RDS (Fig. 1) with FiO2 requirement 30% and continued on CPAP. CPAP settings were adjusted as per baby's requirement and weaned off CPAP on day 16. Due to worsening distress with increased retractions, baby was restarted on CPAP on day 20 of life.

Baby was hemodynamically stable at birth. Early screening ECHO done on day 2 showed a large (2.8 mm) hemodynamically significant PDA with moderate to large ventricular septal defect (VSD) with e/o left atrial dilatation, started on paracetamol, given for 72 hours. Repeat 2D ECHO on day 5 – large PDA and VSD, restarted on 2nd course of paracetamol and diuretic was added due to cardiomegaly and hepatomegaly. Nutritional requirements were initially met by enteral feeds and TPN. At 12 hours, trophic feeds started, along with TPN. Baby reached full feeds on day 8, crossed birth weight on day 20 of life. On day 20 of life, due to worsening distress, with hyper dynamic precordial activity, bounding pulses and harsh systolic murmur, x-ray showed cardiomegaly (Fig. 2 and 3); repeat ECHO was done which showed Large hS PDA with duct measuring 3.2 mm, moderate sized peri membranous VSD with L-R shunt and dilated left heart . Baby was started on oral Ibuprofen (third) course, but there was no improvement. Due to failure of medical management of PDA, we planned surgical / intervention based closure of the hsPDA. On the advice of the pediatric cardiology team, the neonate underwent PDA device closure on day 28 of life using Piccolo Amplatzer device under fluoroscopy guidance after elective ventilation. After procedure, baby was extubated to nasal CPAP within 24 hours and weaned to room air on day 32 following a course of postnatal steroids for bronchopulmonary dysplasia. The baby has been discharged at 34 weeks' post-conceptional age with a weight of 1700 grams on fortified mother's milk.

Investigations showed normal counts, blood gas with pH 7.143, CO2 51.9 mmHg, HCO3 14 mEq/L

Fig. 1 - Chest x ray showed RDS on day 1
Fig. 2 – X-ray chest on day 18 showing evolving BPD and cardiac enlargement
Fig. 3 – Chest X-ray on day 20 with cardiomegaly

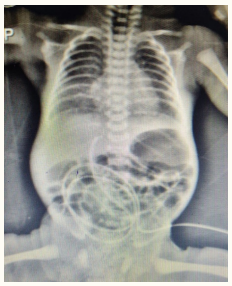

Fig. 1

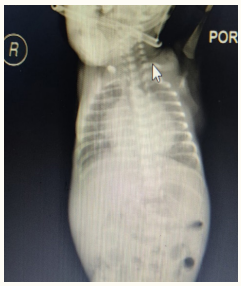

Fig. 2

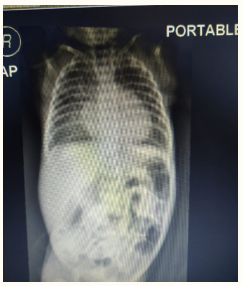

Fig. 3

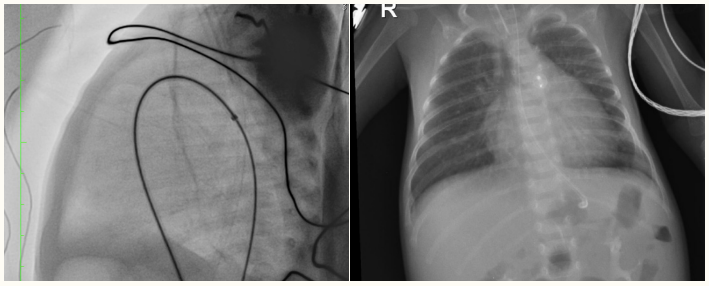

Fig 4 – Wire from LFV (Left femoral vein)
Fig 5 – X-ray showing Device in situ

Frequently Asked Questions

1. How do you identify PDA in Newborn?

PDA is identified on the basis of clinical signs such as hyper dynamic precordial activity (visible precordial pulsations in more than 2 rib spaces), bounding pulses, wide pulse pressures, persistent tachycardia (>180 beats/min) and the presence of a pan systolic murmur or continuous murmur over the precordium. The most common finding a PDA in preterm neonates may be worsening requirement for mean airway pressure (MAP) or oxygen (FiO2) in a neonate recovering from RDS.

2. What are the indications of closure of PDA?

Opinions have varied on whether PDA can be considered a silent bystander versus whether it may be considered as a source of worsening cardio respiratory status in preterm neonates.

Various staging systems based on clinical as well as echocardiographic criteria have been proposed to decide whether a PDA requires treatment.

The following table summarises the role of echocardiographic variables in determining the hemodynamic significance of PDA.

Table : Classification of PDA based on echocardiographic markers

Parameter	No PDA	Mild	Moderate	Large
Features of ductus arteriosus				
Transductal diameter (mm)	0	<1.5	1.5-3	>3
Ductal velocity Vmax (cm/s)	0	>2	1.5-2	<1.5
Antegrade PA diastolic flow (cm/s)	0	>30	30-50	>50
Pulmonary overcirculation				
Left atrial/ aortic ratio	1.13 ± 0.23	<1.4	1.4-1.6	>1.6
Left ventricular/ Aortic ratio	1.86± 0.29	-	2.15±0.39	2.27±0.27
Mitral E wave/ A wave ratio	<1	<1	1-1.5	>1.5
IVRT (ms)	<55	46-54	36-45	<35
Systemic hypoperfusion				
Retrograde diastolic flow (%)	10	<30	30-50	>50
Aortic stroke volume (ml/kg)	≤2.25			≥2.34
Left ventricular output (LVO) (ml/kg/min)	190-310	-	-	>314
LVO/ SVC ratio	2.4±0.3	-	-	4.5±0.6

SVC- Superior vena cava, IVRT – Isovolumic relaxation time, PA – Pulmonary artery, Empty boxes- data unavailable.

Two courses of medical treatment are generally attempted before deeming it to have failed.

3. What are the advantages of using device closure over surgical closure of PDA?

Advantages are:

- Median time to return to baseline respiratory status is significantly shorter than the surgical closure.
- Lesser respiratory and hemodynamic compromise
- No risk of pneumothorax, chylothorax, vocal cord palsy, infection

4. What are the adverse effects of device closure?

Embolisation and risk of left pulmonary and aortic obstruction are the important adverse effects, particularly in extremely preterm neonates.

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