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June 2022

[1] Upadhyay P, Lal BB, Sood V, Khanna R, Gupta E, Rastogi A, Alam S. Incidence and predictors of relapse after stopping antiviral therapy in Pediatric chronic hepatitis B. Pediatr Infect Dis J. 2022 Sep 1; 41(9):714–719. doi: 10.1097/INF. 000,000 000,0003602. Epub 2022 Jun 7. PMID: 357,03278.

In this study, the authors have sought to evaluate the incidence of relapse after stopping antiviral therapy in pediatric chronic hepatitis B (CHB) and to identify its predictors. A total of 31 HBsAg-positive children who had been on antivirals for at least 2 years with undetectable hepatitis B virus-deoxyribonucleic acid (HBV-DNA) and normal alanine aminotransferase (ALT) on three consecutive occasions over the last 12 months and antivirals were stopped if liver biopsy showed histological activity index <5 and fibrosis (Ishak) <3. Virological [elevation of HBV-DNA (> 2000 IU/mL)] and biochemical (a rise in ALT levels to >2 times the upper limit of normal) relapse was seen in 12 (38.7%) and five (16.1%) children within 12 months of stopping antiviral treatment. They have noted that discontinuation of antiviral treatment in children with CHB resulted in a relapse in one-third of the patients and concluded that relapse was frequent in those who were HBeAg-positive at the time of stopping therapy [hazard ratio (HR): 6.208] and in those who required longer therapy for HBV-DNA to become undetectable (HR: 1.027).

[2] Gopan A, Sen Sarma M, Har B, Singh RK, Agrawal V, Yachha SK. An unusual cause of obstructive jaundice in childhood: Intra-choledochal malignant neuroendocrine tumour. J Paediatr Child Health. 2022 Jun 18. doi: 10.1111/jpc. 16,060. Epub ahead of print. PMID: 357,16114.

In this case report, the authors have described an intracholedochal malignant neuroendocrine tumor (NET) in a 13-year-old child who presented with cholestatic symptoms of jaundice and pruritus with soft hepatomegaly and mild ascites who underwent en bloc resection of the extrahepatic biliary apparatus with no recurrence at 24 months of follow-up. The authors have highlighted that the extrahepatic biliary apparatus is a rare site for NET.

July 2022

[3] Jain S, Kumar K, Malhotra S, Sibal A. Rare case of primary carnitine deficiency presenting as acute liver failure. BMJ Case Rep. 2022 Jul 19; 15(7):E 247,225. doi: 10.1136/bcr–2021– 247,225. PMID: 358,53679; PMCID: PMC 930,1812.

Through this illustrative case report, the authors have highlighted the clinical presentation of systemic primary carnitine deficiency (due to mutations in the *SLC22A5* gene which leads to defective fatty acid oxidation) with acute liver failure in children and demonstrated that early identification and treatment using L-carnitine could be lifesaving.

[4] Mehra A, Semwal P, Bhat NK, Bolia R. A prospective observational study of hepatic dysfunction in children on antitubercular drugs. Indian J Pediatr. 2022 Jul 22. doi: 10.1007/s 12,098-022- 04,317-7. Epub ahead of print. PMID: 358,67272.

In this prospective observational study spanning over 18 months, the authors have aimed to assess the frequency, risk factors, and prognosis of antitubercular drug-induced liver injury (TB–DILI) in children <18 years put on antitubercular therapy (ATT) for pulmonary or extrapulmonary tuberculosis. Out of the 81 patients enrolled, 10 (12.3%) developed TB–DILI at a median of 8.5 (3–18) d of starting ATT. All patients were symptomatic with the most common symptoms being anorexia and nausea (80%). Authors have concluded that a higher baseline ALT was independently associated with DILI with an adjusted odds ratio (OR) of 2.1 [95% confidence interval (CI) 1.3–3.4], $p = 0.01$, and eight patients tolerated reintroduction of ATT in a sequential manner, 9–24 d after discontinuation.

[5] Ojha S, Bharadia L, Chaturvedi A. Refractory congenital chylous ascites: First report of fibrin glue and mesh application by laparoscopy. J Minim Access Surg. 2022 Jul–Sep; 18(3):469–471.

Laparoscopy has been used for diagnosis but not for glue and mesh application in congenital chylous ascites (CA) where the lymphatic leak is unidentified. Authors have presented the first experience of laparoscopic fibrin glue and mesh application in a 7-month-old infant with refractory congenital CA with successful outcomes and a long postoperative follow-up of 36 months.

August 2022

[6] Kanungo S, Chatterjee P, Bavdekar A, Murhekar M, Babji S, Garg R, Samanta S, Nandy RK, Kawade A, Boopathi K, Kanagasabai K, Kamal VK, Kumar VS, Gupta N, Dutta S. Safety and immunogenicity of the Rotavac and Rotasiil rotavirus vaccines administered in an interchangeable dosing schedule among healthy Indian infants: A multicentre, open–label, randomised, controlled, phase 4, non–inferiority trial. Lancet Infect Dis. 2022 Aug; 22(8):1191–1199.

In this multicenter, open-label, randomized, controlled, phase IV, noninferiority trial authors have aimed to compare the safety and seroresponse of recipients of a mixed regimen vs a single regimen (Rotavac or Rotasiil) against rotavirus in 1979 infants from two sites in India. Eligible infants were randomly allocated to six groups in

equal numbers to receive either the single vaccine regimen [i.e., Rotavac–Rotavac–Rotavac (group I) or Rotasiil–Rotasiil–Rotasiil (group II)] or the mixed vaccine regimen [i.e., Rotavac–Rotasiil–Rotavac (group III), Rotasiil–Rotavac–Rotasiil (group IV), Rotavac–Rotasiil–Rotasiil (group V), or Rotasiil–Rotavac–Rotavac (group VI)]. They observed that seroresponse rate in the mixed vaccine regimen group [33·5% (95% CI 30·9–36·2)] was noninferior compared with the single vaccine regimen group [29·6% (26·1–33·4)]; the seroresponse rate difference was 3·9% (95% CI 0·7–8·3). The proportion of participants with any type of solicited adverse events was 90·9% (95% CI 88·4–93·0) in the single vaccine regimen group and 91·1% (89·5–92·6) in the mixed vaccine regimen group. No vaccine-related serious adverse events or intussusception were reported during the study. They have concluded that Rotavac and Rotasiil can be safely used in an interchangeable manner for routine immunization since the seroresponse was noninferior in the mixed vaccine regimen compared with the single vaccine regimen allowing flexibility in administering the vaccines, helping to overcome vaccine shortages and supply chain issues, and targeting migrant populations easily.

[7] Menon J, Shanmugam N, Rammohan A, Hakeem A, Reddy MS, Rela M. Neurological complications in pediatric liver transplant recipients. Pediatr Transplant. 2022 Aug 12:E 14,376. doi: 10.1111/petr. 14,376. Epub ahead of print. PMID: 359,59774.

In this single-center study, a retrospective review of neurological complications (NC) and their risk factors in consecutive pediatric recipients (age less than 18 years) who underwent liver transplantation (LT) between October 2018 and November 2019 was performed. Among 71 children enrolled, 15 (21.1%) had NC. NC included cerebrovascular accident (n = 1), seizures (n = 5; 4 generalized, 1 focal), central pontine myelolysis (CPM) (n = 1), diaphragmatic palsy (n = 2), peripheral neuropathy (n = 1), extrapyramidal movements (n = 3), and encephalopathy beyond 96 hours (n = 2). On univariate analysis, preexisting hepatic encephalopathy (HE), high PELD/MELD score, pre-LT ventilation, pre-LT infection, higher day 1 postoperative bilirubin (all $p < 0.05$), and higher tacrolimus were found to predict postoperative NC whereas on multivariate analysis, pre-LT HE was the only predictive factor. Authors have concluded that pretransplant HE was the single most significant predisposing factor for post-LT neurological complications.

[8] Menon J, Rammohan A, Vij M, Shanmugam N, Rela M. Current perspectives on the role of liver transplantation for Langerhans cell histiocytosis: A narrative review. *World J Gastroenterol* 2022; 28(30): 4044–4052

In this minireview, the authors have summarized the current evidence and discussed the practical aspects of the role of liver transplantation (LT) in the management of Langerhans cell histiocytosis (LCH) given the lack of clarity with regards to indication, timing, and post-LT management, including immunosuppression and adjuvant therapy. LT is usually offered to LCH patients in remission with decompensated liver disease. Authors have reiterated the paucity of currently available literature, and the undefined role of LT in LCH, and emphasized the need for large collaborative, multicentre studies to provide recommendations on the management algorithm for LCH.

[9] Maria A, Lal BB, Khanna R, Sood V, Mukund A, Bajpai M, Alam S. Rotational thromboelastometry-guided blood component use in cirrhotic children undergoing invasive procedures: Randomized controlled trial. Liver Int. 2022 Aug 17. doi: 10.1111/liv. 15,398. Epub ahead of print. PMID: 359,77053.

In this single-center randomized controlled trial authors have aimed to evaluate the efficacy and safety of using rotational thromboelastometry (ROTEM)—based transfusion strategy in cirrhotic children undergoing invasive procedures. Enrolled cirrhotic children were randomized to the ROTEM (n = 30) and conventional groups (n = 30) received blood component transfusion using predefined criteria. They have observed that only 46.7% of children in the ROTEM group received a blood component compared to 100% in the conventional group ($p < 0.001$). The requirement of FFP (ROTEM: 43.3%, Conventional: 83.3%, $p = 0.001$) was significantly lower in the patients receiving ROTEM-guided transfusions. There was no difference in procedure-related bleeding and transfusion-related complications between the two groups. ROTEM was cost-effective (p = 0.002) despite the additional cost of the test. Authors have concluded that ROTEM-based transfusion strategies result in lower blood component transfusion in cirrhotic children undergoing invasive procedures without an increase in the risk of procedure-related bleeding and are cost-effective.

[10] Gopan A, Srivastava A, Mathias A, Yachha SK, Jain SK, Mishra P, Sarma MS, Poddar U. Efficacy and predictors of pain response to combined antioxidants in children with chronic pancreatitis. Dig Dis Sci. 2022 Aug 28. doi: 10.1007/s 10,620-022- 07,676-5. Epub ahead of print. PMID: 360,30482.

In this single-center study, authors have aimed to evaluate markers of oxidative stress (OS), and efficacy and predictors of response to antioxidants (AO) in improving pain in children with chronic pancreatitis (CP). Antioxidants were given to 48 CP children for 6 months. About 38/48 cases completed 6 months of therapy. CP cases had higher OS [thiobarbituric acid reactive substances (TBARS) (7.8 vs 5.2 nmol/mL; $p < 0.001$)] and lower antioxidant levels [ferric reducing ability of plasma (FRAP) (231 vs 381.3 µmol/L; p = 0.003), vitamin C (0.646 vs 0.780 mg/dL; $p < 0.001$)] than controls. Significant reduction in TBARS and S-SOD and increase in FRAP, vitamin C, and selenium occurred after 6 months. Around 10.5% of cases had minor side effects. About 26 (68%) cases had a good response, with 9 (24%) becoming pain-free. Subjects with severe ductal changes had lower median BMI (-0.73 vs 0.10; p = 0.04) and responded less often than those with mild changes (17/29 vs 9/9; p = 0.036). Authors have concluded that antioxidant therapy is safe. Pain response is seen in 68% of cases, less often in patients with severe ductal changes.

[11] Vandriel SM, Li LT, She H, Wang JS, Gilbert MA, Jankowska I, Czubkowski P, Gliwicz-Miedzińska D, Gonzales EM, Jacquemin E, Bouligand J, Spinner NB, Loomes KM, Piccoli DA, D'Antiga L, Nicastro E, Sokal É, Demaret T, Ebel NH, Feinstein JA, Fawaz R, Nastasio S, Lacaille F, Debray D, Arnell H, Fischler B, Siew S, Stormon M, Karpen SJ, Romero R, Kim KM, Baek WY, Hardikar W, Shankar S, Roberts AJ, Evans HM, Jensen MK, Kavan M, Sundaram SS, Chaidez A, Karthikeyan P, Sanchez MC, Cavalieri ML, Verkade HJ, Lee WS, Squires JE, Hajinicolaou C, LertudomphonwanitC, Fischer RT, Larson-Nath C, Mozer-Glassberg Y, Arikan C, Lin HC, Quintero Bernabeu J, Alam S, Kelly D, Carvalho E, Ferreira CT, Indolfi G, Quiros-Tejeira RE, Bulut P, Calvo PL, Önal Z, ValentinoPL, Desai DM, Eshun J, Rogalidou M, Dezsőfi A, Wiecek S, Nebbia G, Borges Pinto R, Wolters VM, Tamara ML, Zizzo AN, Garcia J, Schwarz K, Beretta M, Sandahl TD, Jimenez-Rivera C, Kerkar N, Brecelj J, Mujawar Q, Rock N, Busoms CM, Karnsakul W, Lurz E, Santos-Silva E, Blondet N, Bujanda L, Shah U, Thompson RJ, Hansen BE, Kamath BM. Global ALagille Alliance (GALA) Study Group. Natural history of liver disease in a large international

cohort of children with alagille syndrome: Results from The GALA Study. Hepatology. 2022 Aug 29. doi: 10.1002/hep. 32,761. Epub ahead of print. PMID: 360,36223.

In this international multicenter (67 centers in 29 countries) retrospective study, a contemporary cohort of 1,433 children (born between January 1997 to August 2019) with clinically and/or genetically confirmed diagnoses of Alagille syndrome (ALGS) were enrolled, and native liver survival (NLS) and event-free survival rates were assessed and early biochemical predictors of clinically evident portal hypertension (CEPH) and native liver survival (NLS) were identified. Children (>6 and ≤12 months) with median total bilirubin (TB) levels between ≥5.0 and <10.0 mg/dL had a 4.1-fold (95% CI 1.6–10.8) and those ≥10.0 mg/dL had an 8.0-fold (95% CI 3.4–18.4) increased risk of developing CEPH compared with those <5.0 mg/dL. Median TB levels between ≥5.0 and <10.0 mg/dL and >10.0 mg/dL were associated with a 4.8 (95% CI 2.4–9.7) and 15.6 (95% CI 8.7–28.2) increased risk of transplantation relative to <5.0 mg/dL. Median TB < 5.0 mg/dL were associated with higher NLS rates relative to ≥5.0 mg/dL, with 79% reaching adulthood with native liver ($p < 0.001$). It was concluded from this large international cohort of ALGS that only 40.3% of children reach adulthood with their native liver and a TB <5.0 mg/dL between 6 and 2 months of age was associated with better hepatic outcomes.

Missed Inadvertently in Previous Issues

2022

[1] Tripathy TP, Patidar Y, Chandel K, Varadarajan A, Sood V, Laroia ST. Embryonal rhabdomyosarcoma of the biliary tree as a differential in a paediatric patient presenting with biliary dilatation: Not always a choledochal cyst. Acta Med Litu. 2022; 29(1):112–117. doi: 10. 15,388/Amed.2021.29.1.2. Epub 2022 Jan 24. PMID: 360,61928; PMCID: PMC 942,8640.

Rhabdomyosarcoma (RMS) is a soft tissue malignant musculoskeletal tumor and is the most prevalent soft-tissue sarcoma in the pediatric population. Although, embryonal RMS of the biliary tree is a rare entity, however, it is the most common cause of pediatric malignant obstructive jaundice. Through this illustrative case report of a 4-year-old with cholestatic jaundice, authors have highlighted that embryonal RMS of the biliary tract mimics the appearance of a choledochal cyst and emphasizes the necessity of keeping embryonal RMS as a differential in pediatric cases of obstructive jaundice.

[2] Bolia R, Goel AD, Sharma V, Srivastava A. Biliary diversion in progressive familial intrahepatic cholestasis: A systematic review and meta–analysis. Expert Rev Gastroenterol Hepatol. 2022Feb; 16(2):163–172. doi: 10.1080/ 174,74124.2022. 203,2660. Epub 2022 Feb 15. PMID: 350,51344.

In this meta-analysis, the authors have aimed to compare the three biliary diversions (BD) procedures in progressive familial intrahepatic cholestasis (PFIC) with refractory pruritus partial external biliary drainage (PEBD), partial internal biliary drainage (PIBD), and ileal exclusion (IE) in terms of improvement in pruritus, serum bile acid (BA), and need for liver transplantation (LT). A total of 25 studies [424 children (PEBD-301, PIBD-93, IE-30)] were included. Pruritus resolved in 59.5% (PIBD: 72%, PEBD: 57% and IE: 48 %) cases. The absolute decrease in BA and bilirubin discriminated responders and non-responders. Eventually, 27% required LT: PIBD 10.7%, PEBD32%, and IE 27%. The postoperative BA and bilirubin determined the need for LT. Complications were commoner in PEBD than PIBD (38% vs 21.8%: $p = 0.02$). Authors have concluded that 59.5% of children have pruritus relief after BD and 27% need LT. PIBD has lower complications and LT requirements than PEBD depending on PFIC type and follow-up duration.

[3] Mathur P, Gupta PK, Udawat P, Mittal P, Nunia V. Hepatobiliary malformations: Proposed updation of classification system, clinicopathological profile and a report of largest pediatric giant choledochal cyst. HPB (Oxford). 2022 Mar; 24(3):422–432.

In this study, the authors have aimed to update the classification of hepatobiliary malformations and study the clinicopathological profile of pediatric choledochal cyst (CDC) and pediatric giant choledochal cyst (GCC) (cyst size greater than 10 cm) patients who have undergone surgery. This retrospective study was performed on 57 pediatric patients ($n = 52$ CDC, $n = 5$ GCC) who were treated at tertiary care teaching hospitals over a period of 4 years (2016–2020). The average age was 4.615 years and female to male was a ratio of 3.7:1. The classical triad was known to be more common and seen in 60% GCCs as opposed to 14.5% in CDCs. Values of serum bilirubin, SGOT, SGPT, and PT/INR were elevated in the CDC series and normal in GCC patients. They have also reported one of the largest GCC measuring $23 \times 10 \times 9$ cm in size. Authors have proposed a revised classification of hepatobiliary malformations and these were divided into 2 broad headings, choledochal [CBD dilatation present] (congenital and acquired) and extracholedochal (CBD dilatation) absent spectrum. Choledochal spectrum was again divided into congenital and acquired, and congenital and further subdivided into major and minor on the basis of their occurrence. Major cysts were divided into three types cystic, fusiform and extrahepatic with intrahepatic dilatation. Minor was divided into focal segmental, CDC with diverticula, CDC with cystic duct dilatation, and multiple extrahepatic biliary tract dilatations. Acquired CDC was classified on the basis of the presence or absence of abnormal biliopancreatic junction (ABPJ).

[4] Acharyya, Bhaswati C.; Roy, Mandira; Chakraborty, Hema. Unifocal gastric Langerhans cell histiocytosis in a child—A unique case to remember. JPGN Reports: May 2022 - Volume 3 - Issue 2 - p e192. doi: 10.1097/PG9. 000,000 000,0000192

In this case report, authors have described a rare unifocal gastric Langerhans cell histiocytosis (LCH) diagnosed in a 4-year-old boy who presented with insidious onset abdominal pain lasting for a month. Authors have illustrated that gastrointestinal LCH Pediatric acute viral hepatitis may be a rare differential in a child where gastrointestinal symptoms are not explainable by usual clinical or investigational findings, where a timely endoscopy with an expert histopathological analysis could clinch the diagnosis.

[5] Sarma MS, Ravindranath A. Pediatric acute viral hepatitis with atypical variants: Clinical dilemmas and natural history. World J Hepatol. 2022 May 27; 14(5):944–955. doi: 10.4254/wjh.v14. i5.944. PMID: 357,21282; PMCID: PMC 915,7701.

In this minireview authors have described the dilemmas in the understanding and management of atypical features of acute viral hepatitis (AVH) which occur in about a quarter of children. These include prolonged cholestasis, relapsing hepatitis, an ascitic form of AVH, late-onset hepatic failure (LOHF), intravascular hemolysis, and provoking an autoimmune trigger leading to autoimmune hepatitis. The authors have incorporated illustrative diagrams depicting the natural history of these atypical manifestations which are comprehensive and

informative. The most common entities, such as prolonged cholestasis and relapsing hepatitis, cause liver dysfunction and are often confused with chronic liver diseases (CLDs). Similarly, an ascitic form of AVH and late-onset hepatic failure are close differential diagnoses of acute-on-chronic liver failure and decompensated CLD. Authors conclude that a combination of a thorough history, clinical findings, basic investigations, and outcome on follow-up allow focused workup and management in atypical AVH.

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