Publications by ISPGHAN members in Pubmed Indexed Juornals (December 2019 – June 2020)

December 2019

1.)Nagendra Kumar, Anshu Srivastava, Niraj Kumari, Somit Mittal, Surender K. Yachha,Zafar Nayez, Ujjal Poddar. Prevalence, nature, and predictors of colonic changes in children with extrahepatic portal vein obstruction. Gastrointestinal Endoscopy.2019.December 06. doi.org/10.1016/ j.gie.2019.11.042*[Epub ahead of print]*

Medical literature on colonic changes in children with extrahepatic portal venous obstruction (EHPVO) is limited.

Authors evaluated children with EHPVO to determine (1) prevalence, distribution, and nature of changes in the colon, (2) relation of colonic mucosal changes with disease duration,extent of thrombosis of spleno portal axis (SPA), presence of portal hypertensive gastropathy (PHG), and status of esophageal varices (EV) , and (3) histological changes in colonic mucosa and its correlation with endoscopic findings. Subjects were evaluated by colonoscopy with ileoscopy and biopsy, clinicolaboratory profile and SPA imaging. Colonic changes were classified as varices (rectal/ colonic) and portal hypertensive colopathy (PHC, colitis-like, or vascular lesions).Morphometric analysis of colonic biopsies was performed. 54 Children (<18 years) with EHPVO were prospectively enrolled either at diagnosis or during follow-up. Children who were on beta blockers, had previous surgery for portal hypertension (portosystemic shunt, splenectomy, or devascularization), had coexisting chronic liver disease or who refused to participate were excluded. Rectal and colonic varices were seen in 51(94%) and 2 (3.7%) cases. 75% cases had PHC,and colitis-like lesions were more common than vascular lesions.Colopathy changes were pancolonic in 52.5%, left-sided in 42.5%, and right-sided in 5% cases. Sixteen percent (8/49) cases had ileal changes. Children with PHC had PHG more often, more endotherapy sessions and large EVs less often than those without colopathy. Extent of SPA thrombosis was similar in patients with and without PHC. Number of capillaries per crypt was higher in EHPVO than in controls. Morphometric changes had no correlation with endoscopy. Authors have concluded that majority of EHPVO children had colonic changes and 16% had ileopathy. "Colitis-like" changes and left-side involvement were more common. Patients with PHG and eradicated EVs had a higher risk of PHC

2.) Aditi Kumar, Sadhna B. Lal, Anmol Bhatia and Ashim Das. ***Role of noninvasive tools for prediction of clinically evident portal hypertension in children*****. European Journal of Gastroenterology & Hepatology 2019. December 20. DOI: 10.1097/ MEG.0000000000001716.** [Epub ahead of print]

In this study, authors aimed to evaluate the utility of splenic stiffness measurement (SSM) and liver stiffness measurement (LSM) by sonoelastography based on principles of point shear wave elastrography (pSWE), as well as blood-based non-invasive tools (NITs), for predicting varices in children with portal hypertension (PHTN) of different etiologies, considering endoscopy as the reference standard. 85 consecutive, treatment-naïve children with PHTN and 97 controls were enrolled study from July 2017 to November 2018. Each case was evaluated by esophagogastroduodenoscopy (EGD) and various NITs. SSM and LSM, at cutoffs of 3.8 and 3.2 kPa, respectively, discriminated PHTN cases from controls with an area under the curve (AUROC) of 0.67 (0.59–0.74). Both SSM and LSM predicted varices in CLD, but in EHPVO, only SSM predicted varices. SSM of 5.2 and 12.8 kPa, in CLD and EHPVO subgroups, respectively, had AUROC of 0.73 and 0.94 for variceal prediction. Blood-based NITs performed better than elastography in the CLD subgroup. Authors have concluded Blood-based NITs outperform elastography for prediction of PHTN/varices in children with CLD. SSM by pSWE is a better predictor of varices than LSM, especially in the EHPVO subgroup.

January 2020

1.)Moinak Sen Sarma and Aathira Ravindranath. Portal Cavernoma Cholangiopathy in Children and the Management Dilemmas. Journal of Clinical and Translational Hepatology 2020.January 1. DOI: 10.14218/JCTH.2019.00041 *[Epub ahead of print]*

In this review, authors aimed to collate all existing literature on portal cavernoma cholangiopathy(PCC) in childhood and also compare with adult studies.They conclude that PCC is an important complication of EHPVO that affects the long-term prognosis.Optimum modality of imaging and management of asymptomatic PCC in children still has many unanswered questions. Large scale studies are needed to discern the natural history of PCC in children and the effect of different types of portosystemic shunt surgeries on PCC .

2.)Zaheer Nabi, Rupjyoti Talukdar,Ravikanth Venkata,Mohsin Aslam,Upender Shava and D. Nageshwar Reddy. Genetic Evaluation of Children with Idiopathic Recurrent Acute Pancreatitis. Digestive Diseases and Sciences.2020 January 03. doi.org/10.1007/s1062 0-019-06026 -2*[Epub ahead of print]*

Authors aimed to analyze the genetic risk factors in children with idiopathic acute recurrent pancreatitis (IARP). All children (< 18 years) with ARP from January 2015 to May 2018 were prospectively enrolled in the study. Children with IARP underwent genetic testing for mutations/polymorphisms in genes known to predispose to pancreatitis. Genetic evaluation was available in 144 (70.6%) children with IARP. Overall, 89.5% (129/144) children had polymorphisms in at least one gene. Mutations/polymorphisms in at least 1 gene were identified in 89.5% (129/144) children including *SPINK1* in 41.9%, *PRSS1* (rs10273639) in 58.2%, *CTRC* in 25.6%, *CTSB* in 54.9%, *CLDN2* in 72.9%, and *CFTR* in 2.3%. There was no significant incidence of genetic mutations/polymorphisms in IARP with or without pancreas divisum.They have concluded that genetic alterations are present in the majority of the children with IARP. The incidence of genetic mutations is similar in children with or without pancreas divisum.

3.)Sumit Kumar Singh, Moinak Sen Sarma, Surender Kumar Yachha, Anshu Srivastava and Ujjal Poddar.Late-Onset Hepatic Failure in Children: Risk Factors that Determine the Outcome. Digestive Diseases.2020 January 15. DOI: 10.1159/000505124 *[Epub ahead of print]*

Late-onset hepatic failure (LOHF) is a subset of acute liver failure (ALF) which is a distinct entity in the group of intractable liver disease with limited pediatric experience.

The objective of this study was to identify etiology and risk factors that determine the poor outcome (death or liver transplantation within 160 days) of pediatric LOHF.Data of children diagnosed to have LOHF from January 2003 to December 2017 were extracted and analyzed.LOHF was defined as evidence of liver dysfunction in the form of encephalopathy with or without ascites occurring 5th–24th week after the onset of jaundice in the absence of pre-existing liver disease.47 children were enrolled in this study. Acute viral hepatitis was the most common etiology seen in 30 (64%), which included hepatitis A (n = 15), hepatitis B (n = 6), coinfection with hepatitis A and E (n = 7), hepatitis E (n = 1), and cytomegalovirus (n = 1). In 36% patients, no known cause of LOHF was identified and labelled as indeterminate. Univariate analysis showed indeterminate etiology, hepatic encephalopathy (HE), infection, acute kidney injury, and high PELD score determined poor outcome. On multivariate regression analysis, only PELD score with a cutoff 32 (area under curve 0.833, sensitivity 68%, specificity 92%) predicted poor outcome. Authors have concluded that indeterminate etiology, presence of HE, occurrence of infection at any site, and acute kidney injury lead to the PO. PELD score ≥32 can be utilized to optimize the listing for liver transplantation.

4.)Vikas Jain,Ujjal Poddar,Tajwer Singh Negi,Vivek A Saraswat, Narendra Krishnani, Surender Kumar Yachha and Anshu Srivastava. Utility and accuracy of transient elastography in determining liver fibrosis: a case-control study. European Journal of Pediatrics.2020 January 21. doi.:10.1007/s00431-019-03561-y *[Epub ahead of print]*

The objectives of this prospective case-control study were to determine liver stiffness (LSM) by transient elastography (TE) in children with newly diagnosed chronic liver disease (CLD) and to find out normal values in healthy Indian children. Two groups (A: 50 CLD who underwent liver biopsy and B: 50 healthy) aged 5–18 years were recruited prospectively. Liver biopsies were scored as per Metavir scoring and compared with TE. The median age of 100 recruited children was 13.6 years. In group B, normal LSM was 4.9 (2.5–7.3) kPa with significantly higher LSM in adolescent males (5.6 (4.1–7.3) kPa) as compared with females (4.3 (3.7–4.9) kPa). In group A, TE was excellent in discriminating significant fibrosis (≥ F2) at a cut-off value of 10.6 kPa and severe fibrosis at a cut off value of 15.05 kPa. The authors have also generated the normative data of LSM in Indian children between 5 and 18 years of age. Authors have concluded that TE is an excellent non-invasive tool to assess significant liver fibrosis in children and can be used as an alternative to liver biopsy. Normative value of TE in adolescent males is higher than in females.

February 2020

1.)Shreyas V. Kumbhare, Dhrati V. Patangia, Dattatray S. Mongad, Abhijeet Bora, Ashish R. Bavdekar and Yogesh S. Shouche. Gut microbial diversity during pregnancy and early infancy: an exploratory study in the Indian population.FEMS Microbiology Letters.2020 February 3. doi.org/10.1093/femsle/fnaa022*[Epub ahead of print]*

The gut microbial community is known to influence the human health and disease state and is shaped by various factors since birth. Authors have aimed to study the diversity of gut microbiota in pregnancy and infancy. They have analyzed gut microbial communities from 20 mother-infant dyads at different stages of pregnancy and early infancy. 80 fecal samples were analyzed for profiling the gut microbial community using 16S rRNA gene-based sequencing. Authors concluded that there was no significant alteration in the gut bacterial diversity during pregnancy. Significant alterations were observed during the period from birth to six months in infants, with a reduction in Staphylococcus and Enterococcus and an increase in Bifidobacterium and Streptococcus with a more stable microbial community at the age of six months.

2.)Aathira Ravindranath, Moinak Sen Sarma, Vinita Agrawal. A bite of truth through the teeth. Gastroenterology.2020.February 14. doi.org/10.1053/j.gastro.2020.02.050*[Epub ahead of print]*

Authors report 3 year old boy diagnosed with Langerhan cell histiocytosis.He presented swelling of gums,progressive jaundice,pale stools and pruritus in whom orthopantmogram gave a clue to diagnosis which was confirmed by histopathology of gum biopsy.

3.)Alec Reginald Errol Correa1, Neerja Gupta, Narendra Bagri1, Pandiarajan Vignesh, Seema Alam and Seiji Yamaguchi. Mevalonate Kinase Deficiency as cause of Periodic Fever in two siblings. Indian Pediatrics. 2020 February; 57: 180 – 182.

Authors report two siblings with mevalonate kinase deficiency (MVK), presenting with recurrent febrile illnesses, jaundice, hepatosplenomegaly, anemia and thrombocytopenia detected to have compound heterozygous variants in *MVK*.

March 2020

1.)Sailaja Valmiki, Kiran Kumar Mandapati, Leela Krishna Vamsee Miriyala, Chayarani Chandrashekhar Kelgeri,Mohamed Rela, Naresh P. Shanmugam and Durga Rao Vegulada.A case report of a novel 22 bp duplication within exon 1 of the

UGT1A1 in a Sudanese infant with Crigler-Najjar syndrome type I. BMC Gastroenterology 2020.March 6 doi.org/10.1186/s12876-020-01192-4 *[Epub ahead of print]*

Authors have reported a case of a 6 month old Sudanese female infant with Crigler-Najjar syndrome type I. Her molecular analysis revealed a novel homozygous 22 base pair duplication (c.55_76dup) in the coding exon 1 of the UGT1A1 gene. This 22 bp duplication causes a frame shift leading to a premature stop codon. She underwent a successful liver transplant at 7 months of age and was doing well at 1 year follow-up.

2.)Sadhna B. Lal , Vybhav Venkatesh , Surinder S. Rana, Neha Anushree ,Anmol Bhatia and Akshay Saxena. Paediatric acute pancreatitis: Clinical profile and natural history of collections. Pancreatology.2020 March 13. doi.org/10.1016/ j.pan.2020.03.007 *[Epub ahead of print]*

The authors aimed at analyzing the natural history and outcomes of pancreatic fluid collections (PFC) in children with acute pancreatitis (AP) (in accordance with the revised Atlanta classification). Medical records of all children with AP during the period from Jan 2015 to July 2019 were extracted and analyzed. 101 children with AP were included in the study of which 59.4% (60) were boys. Etiology was not found in 49.5% (idiopathic). The identifiable causes were trauma (15%), biliary (14%), infections (12%) and drugs (7%).37.6%, 60.4% and 2% had mild, moderately severe and severe AP. 61.4%(62) had PFC at diagnosis; 34%(21) acute pancreatic fluid collections (APFC) and 66%(41) acute necrotic collections (ANC). 52.3 %(11 of 21) of APFC evolved into pseudocysts & 68.2 %(28 of 41) of ANC into WON's. Drainage was required in 31%(12 of 39) of persisting collections, more frequently in children with traumatic AP. Percutaneous catheter drainage (PCD) was done in 6 children and endoscopic ultrasound (EUS) guided cystogastrostomy with placement of plastic or self expanding metal stents (SEMS) in 6 children. They have concluded moderately severe AP is common in hospitalized children with AP with PFC developing in 61.4%, majority being APFC. 48% of APFC and 32% of ANC will resolve and the rest evolve into pseudocyst or WON. Spontaneous resolution is more likely in children with non -traumatic AP having pseudocysts rather than WON's.

3.)Jagadeesh Menon Vengalil , Vybhav Venkatesh, Anmol Bhatia, Surinder S Rana and Sadhna B Lal. Ascites: an unusual presentation of eosinophilic gastroenteritis in a child. Tropical Doctor.2020.March 16.DOI: 10.1177/00494 75520911230 *[Epub ahead of print]*

Authors report an 11-year-old girl, presenting with massive abdominal distension and colicky abdominal pain. On examination she had ascites and evaluation showed peripheral eosinophilia, raised IgE levels and positive skin prick test. Abdominal sonography revealed massive ascites with thickening of the antro-pyloric region, duodenum, jejunum and proximal ileum.EUS showed presence of muscle layer thickening of both stomach and small bowel. Ascitic fluid analysis showed 8000/mm3, cells, 90% being eosinophils and the diagnosis of eosinophilic gastroenteritis was made.She responded well to steroids and montelukast.

4.)Snehavardhan Pandey,Vikrant Sood,Rajeev Khanna,Bikrant B. Lal, Arun Kumar Sood, S. K. Kabra and Seema Alam. Natural history, risk factors, and outcome of hepatopulmonary syndrome in pediatric liver diseases. Indian Journal of Gastroenterology.2020 March 18.doi.org/10.1007/ s12664-020-01015-0 *[Epub ahead of print]*

Authors aimed to study the natural history, risk factors, and outcome of hepatopulmonary syndrome (HPS) in biliary atresia (BA) and other chronic liver disease (CLD) subjects. All children (BA and other non-BA CLDs) older than 6 months of age were included in the study. HPS was diagnosed on the basis of standard international criteria. Fractional exhaled

nitric oxide (FeNO) was also measured at baseline. During the study period from January 2017 to December 2018, there were 42 children in BA and 62 in the CLD group. The overall prevalence of HPS was 42.3%: 57.1% in the BA group and 32.2% in the CLD group. Median age at HPS diagnosis was 14.4 months and 90 months in the BA and non-BA CLD groups, respectively. By the end of study period, the prevalence of HPS in the BA group further increased to 73.8% at 0.7% per month. Lower serum albumin ($p < 0.05$) in BA and higher splenic Z scores (p 0.013) in other CLDs were found to be significant risk factors for HPS. FeNO measurement did not reach diagnostic significance. They have concluded that prevalence of HPS is higher and also develops at an earlier age in the BA group compared to other CLDs. Also, risk of HPS development increases with increasing disease duration in BA. Lower serum albumin in BA and higher splenic Z scores in other CLDs may predict risk for HPS development.

5.)Vikrant Sood,Bikrant Bihari Lal,Shvetank Sharma, Rajeev Khanna,Manish K. Siloliya and Seema Alam. Gilbert's Syndrome in Children with Unconjugated Hyperbilirubinemia – An Analysis of 170 Cases. Indian Journal of Pediatrics.2020 March 20. doi.org/10.1007/s12098-020-03271-6 *[Epub ahead of print]*

Authors aimed to study the clinical spectrum, and laboratory profile of Indian patients with pediatric Gilbert's Syndrome (GS).Data of all pediatric (< 18 y of age at presentation) patients diagnosed with GS from year 2011 to 2018 were extracted and analyzed. 170 subjects were confirmed as having GS as per genetic analysis (133 with homozygous and 37 with heterozygous status).Majority were diagnosed in the adolescent age group (mean age 13.6 y). The median serum total bilirubin (TB) levels were around 3.3 mg/dl with maximum levels reaching upto 18 mg/dl. Around 15% subjects had an associated condition including hematological or hepatobiliary disease. They have concluded that GS is an important but under-recognised cause of unexplained unconjugated hyperbilirubinemia in Indian children. Extent of hyperbilirubinemia may fluctuate to levels much higher than what is usually described in current world literature, and thus, it should not be used to preclude diagnostic testing for GS in any subject.

6.)Gautham Pai, Moinak Sen Sarma and Rakesh Pandey. ***White-out duodenal mucosa: clue to a systemic diagnosis.*** **Gastroenterology.2020.March 24. doi.org/10.1053/j.gastro.2020.03.079** [Epub ahead of print]

Authors presented a A 4 year old Indian boy born of third-degree consanguinity presented with clinical steatorrhea from early infancy, gaseous abdominal distension, anemia and failure to thrive. Esophagogastroduodenoscopy showed an "unusually white" duodenal mucosa.Duodenal histology revealed preserved villous architecture with vacuolated enterocytes containing optically clear and foamy cytoplasm confirming the diagnosis of abetalipoproteinemia

7.)Diptaraj S. Chaudhari, Dhiraj P. Dhotre, Dhiraj M. Agarwal, Akshay H. Gaike,Devika Bhalerao, Parmeshwar Jadhav, Dattatray Mongad, Himangi Lubree,Vilas P. Sinkar, Ulhas K. Patil, Sundeep Salvi, Ashish Bavdekar et al.Gut, oral and skin microbiome of Indian patrilineal families reveal perceptible association with age. Scientific Reports 2020; March 30.doi: 10.1038/s41598-020-62195-5*[Epub ahead of print]*

In the present study, authors have utilized the patrilineal family arrangement to understand the association of age with the gut, oral and skin microbiome. They have characterized stool, oral and skin microbiome of 54 healthy individuals from six joint families by 16S rRNA gene-based metagenomics. Age-associated changes in the gut and oral microbiome of patrilineal families showed positive correlations in the abundance of phyla Proteobacteria and Fusobacteria, respectively. Genera *Treponema* and *Fusobacterium* showed a positive correlation with age while *Granulicatella* and

Streptococcus showed a negative correlation with age in the oral microbiome. Members of genus *Prevotella* illustrated high abundance and prevalence in the gut and oral microbiome. This study provides baseline data of the human microbiome from a healthy Indian sub-population, which could be used as a reference for further studies, including diabetes, obesity and inflammatory diseases.

April 2020

1.)Nitin Shah, MMA Faridi, Monjori Mitra, Ashish Bavdekar et al. Review of long term immunogenicity and tolerability of live hepatitis A vaccine. Human Vaccines & Immunotherapeutics. 2020 April 3. doi.org/10.1080/21645515.2020. 1741997 *[Epub ahead of print]*

In this article authors have reviewed the available long-term (≥10 years follow-up) published data on live attenuated hepatitis A (H2 strain) vaccine. The data from country of origin of the vaccine (China) and India were extracted and compared. Analysis established the long-term immunogenicity, protection, and tolerability of live attenuated hepatitis A vaccine. Based on the results of several clinical trials showing long term protection, authors have concluded that single dose of live attenuated hepatitis vaccine can be widely used to protect high-risk population against hepatitis A virus infection and related complications.

2.)Sanjiv Saigal, Subash Gupta,S. Sudhindran, Neerav Goyal,Amit Rastogi1, Mathew Jacob, Kaiser Raja,Anand Ramamurthy, Sonal Asthana, R. K. Dhiman,Balbir Singh, Rajasekhar Perumalla, Ashish Malik,Naresh Shanmugham and Arvinder Singh Soin.Liver transplantation and COVID−19 (Coronavirus) infection: guidelines of the liver transplant Society of India (LTSI). Hepatology International.2020.April 8. doi.org/10.1007/s12072-020-10041-1 *[Epub ahead of print]*

The guidelines are applicable to both deceased donor as well as living donor liver transplants. The key recommendations incuded moratorium on all non-urgent transplants whereas for ALF can be done as before and for ACLF decision for transplantation should be based on individual centre's discretion. Elective DDLT should be done only if donor is COVID-19 negative, and recipient is from the same city. LDLT should be done for urgent cases after thorough counselling. All donors (deceased and living donor) and recipients should be tested for COVID-19 at the time of urgent transplant. Standard immunosuppression should be followed in the post-transplant period.

3.)Anshu Srivastava, Durga Prasad, Ipsita Panda, Rajanikant Yadav, Manoj Jain, Moinak Sen Sarma, Raghunandan Prasad, Ujjal Poddar and Surender Kumar Yachha. Transjugular versus percutaneous liver biopsy in children: indication, success, yield and complications. Journal of Pediatric Gastroenterology and Nutrition. 2020. April DOI: 10.1097/MPG.0000000000002587. *[Epub ahead of print]*

Authors evaluated the indications, success rate, tissue yield and complications of transjugular liver biopsy (TJLB) in comparison to (percutaneous) PB in children. Electronic records of children (≤18 years) who underwent liver biopsy (LB) during 2013 to 2018 were reviewed. Clinic laboratory data including indication, type of biopsy, complications and tissue yield (length, number of complete portal tracts [CPT]) were noted and analyzed. PB was performed either by blinded, USG guided or plugged method. TJLB was performed according to the standard technique using ultrasound and fluoroscopic guidance. 540 children [age 36(1.0-216) months, 355 (65.7%) boys] subjected to LB (TJLB or PB) were enrolled. LB was done to determine etiology of neonatal cholestasis (n=232, 42.9%), chronic liver disease (n=236, 43.7%), non-cirrhotic portal hypertension (n=34, 6.3%), focal lesions (n=18, 3.3%) and others (20, 3.7%).Of the total 540 LB; 67(12.4%) were TJLB and 473 (87.6%) were PB. Amongst PB, 322 (68.0%) were by percussion method, 125 (26.4%) by real time

ultrasound guidance and 26 (5.5%) by plugged method. Technical success and complications are same with PB and TJLB, but tissue yield is poorer and cost is higher with TJLB at our centre. Tissue yield of >6 complete portal tracts is adversely affected by TJLB and presence of cirrhosis. Both percussion method and USG guided PB are similar in tissue yield, success and complications in infants and children. Authors concluded that LB is a safe procedure and only 12% children require TJLB due to contraindications of PB. Technical success and complications are similar but tissue yield is poorer in TJLB than PB. Presence of cirrhosis and TJLB adversely affected tissue yield.

4.)Aathira Ravindranath, Moinak Sen Sarma, Dimple Jain. Melena in neonates – Endoscopic surprise Gastroenterology.2020.April 13. doi.org/10.1053/j.gastro.2020.04.021 *[Epub ahead of print]*

Authors present the case of 2 neonates who presented present with melena in whom endoscopy clinched the diagnosis. esophagogastroduodenoscopy (EGD) of both babies showed multiple live worms –ankylostoma duodenale from second part of duodenum deep into jejunum .Both infants were treated with 50 mg mebendazole twice a day for five days

5.)John Matthai, Neelam Mohan, MS Viswanathan, Naresh Shanmugam, Lalit Bharadia, Shirish Bhatnagar and KP Srikanth. Therapeutic Enteral Formulas in Children. Indian Pediatrics.2020 April; 57: 343-348.

Therapeutic enteral formulas are those that are indicated in specific situations of disease or need and are not substitutes for breast milk. A variety of therapeutic enteral formulas for various diseases have become available in India in the last few years. Therapeutic enteral formulas, which are indicated in various disease states belong to four categories - lactose modified, hydrolyzed, MCT based and metabolic disease specific formulas. Lactose modified formulas which are used in temporary or permanent lactose intolerance and Galactosemia are either casein or soy protein based. Hydrolyzed formulas could be partially hydrolyzed, extensively hydrolyzed or amino acid based. Only extensively hydrolyzed formula should be recommended in milk protein allergy. Amino acid (elemental) formulas are mainly indicated in patients with diffuse intestinal mucosal disease. MCT formulas are used in chronic liver disease with cholestasis,and have 30 to 80% MCT. Formulas for inborn errors of metabolism are free of specific carbohydrate, amino acid or fatty acid. Proprietary formulas presently available in India with their specifications have been listed in this review article.

6.)Jogender Kumar, Debajyoti Chatterjee, Sadhna B Lal and Praveen Kumar. An infant with severe anemia and hypoalbuminemia.Indian Pediatrics. 2020 April; 57; 349-352.

In this clinicopathological conference, authors discussed the case of a two-month-old girl admitted with complaints of progressive pallor, generalized body swelling and pale colored stool since the neonatal period. On examination, severe pallor, chubby cheeks and moderate hepatomegaly were noted. Investigations revealed isolated anemia, transaminitis, conjugated hyperbilirubinemia, prolonged prothrombin time and hyperlipidemia. She died due to severe sepsis, shock, and pulmonary hemorrhage. An autopsy revealed characteristic histopathology findings of cystic fibrosis in the liver, lungs, and pancreas. Genetic analysis performed on autopsy tissue was positive for F508del compound heterozygous (WT/F508del) mutation, confirming the diagnosis of cystic fibrosis.

7.) Kriti Joshi, Rishi Bolia, Ujjal Poddar and Preeti Dabadgao. Consumptive hypothyroidism due to diffuse hepatic hemangiomas treated with propranolol therapy. Indian Pediatrics.2020 April 15; 57: 366 – 368.

Infantile hepatic hemangioma (IHH)-related consumptive hypothyroidism is rare and occurs as a result of excess thyroid hormone inactivating enzyme,

type-3 iodothyronine deiodinase. Authors have reported an infant with IHH-related hypothyroidism, in whom treatment with propranolol led to regression of tumor and subsequent euthyroid status.

8.) Manoja Kumar Das ,Narendra Kumar Arora et al. Intussusception in children aged under two years in India: Retrospective surveillance at nineteen tertiary care hospitals.Vaccine.2020 April 23. doi.org/10.1016/j.vaccine.2020.04.059 *[Epub ahead of print]*

A surveillance network was established to document the epidemiology of intussusception cases in Indian children in preparation for rota virus vaccine (RVV) introduction. Intussusception in children 2–23 months were documented at 19 nationally representative sentinel hospitals through a retrospective surveillance for 69 months (July 2010 to March 2016). For each case clinical, hospital course, treatment and outcome data were collected. Among the 1588 intussusception cases, 54.5% were from South India and 66.3% were boys. The median age was 8 months. The most common symptoms and signs were vomiting (63.4%), bloody stool (49.1%), abdominal pain (46.9%) and excessive crying (42.8%). The classical triad (vomiting, abdominal pain, and blood in stools) was observed in 25.6% cases. 96.4% cases were diagnosed by ultrasound with ileocolic location as the commonest (85.3%).Management was done by reduction (50.8%) and surgery (41.1%) and only 1% of the patients' died. Authors have concluded that intussusceptions cases have occurred in children across all parts of the country, with low case fatality in the settings studied. The progressive rise cases could indicate an increasing awareness and availability of diagnostic facilities

9.) Anil C. Anand, Bhaskar Nandi, Subrat K. Acharya, Anil Arora, Sethu Babu, Yogesh Batra, Yogesh K. Chawla, Abhijit Chowdhury, Ashok Chaoudhuri, Eapen C. Eapen, Harshad Devarbhavi, RadhaKrishan Dhiman, Siddhartha Datta Gupta, Ajay Duseja, Dinesh Jothimani, Dharmesh Kapoor, Premashish Kar, Mohamad S. Khuroo, Ashish Kumar, Kaushal Madan, Bipadabhanjan Mallick, Rakhi Maiwall, Neelam Mohan, Aabha Nagral et al.The INASL Task-Force on Acute Liver Failure. Indian National Association for the Study of the Liver Consensus Statement on Acute Liver Failure (Part 1): Epidemiology, Pathogenesis, Presentation and Prognosis. Journal of Clinical and Experimental Hepatology.2020 April 28. doi.org/10.1016/j.jceh.2020.04.012 *[Epub ahead of print]*

A roundtable discussion of the INASL task force on ALF which included experts from Pediatric Gastroenterology and Hepatology was held on 6th and 7th July 2019 to discuss, debate, and finalize the consensus statements on epidemiology, clinical presentation, pathology and prognostication of ALF.

In India, viral hepatitis is the most frequent cause of ALF, with drug-induced hepatitis due to antituberculosis drugs being the second most frequent cause. The clinical presentation of ALF is characterized by jaundice, coagulopathy, and encephalopathy. It is important to differentiate ALF from other causes of liver failure, including acute on chronic liver failure, subacute liver failure, as well as certain tropical infections which can mimic this presentation. The disease often has a fulminant clinical course with high short-term mortality. Death is usually attributable to cerebral complications, infections, and resultant multiorgan failure. Timely liver transplantation (LT) can change the outcome, and hence, it is vital to provide intensive care to patients until LT can be arranged. It is equally important to assess prognosis to select patients who are suitable for LT. Several prognostic scores have been proposed, and their comparisons show that indigenously developed dynamic scores (ALFED) have an edge over scores described from the Western world.

May 2020

1.) Giuseppe Indolfi, Bjo¨rn Fischler,Regino P. Gonzalez-Peralta,Mirta Ciocca, Gilda Porta, Mohan Neelam, Mohamed El-Guindi, Deirdre Kelly, Yen-Hsuan Ni, Anupan Sibal, Daniel H. Leung, and Mei Hwei Chang, Hepatitis Expert Team of the Federation of International Societies of Pediatric Gastroenterology, Hepatology, and Nutrition (FISPGHAN). Comparison of Recommendations for Treatment of Chronic Hepatitis C Virus Infection in Children and Adolescents: A Position Paper of the Federation of International Societies of Pediatric Gastroenterology, Hepatology, and Nutrition. Journal of Pediatric Gastroenterology and Nutrition. 2020 May; 70 (5): 711–717.

This position paper written by the Hepatitis Expert Team of the FISPGHAN aimed to systematically evaluate clinical practice guidelines (CPGs), medical consensus, and position papers on the use of direct-acting antivirals (DAA) to treat chronic hepatitis C virus (HCV) infection in adolescents and children in order to compare recommendations and provide the basis for developing a unified position statement. A total of 5 documents: 3 clinical practice guidelines, 1 medical consensus, and 1 position paper published during 2011-2019 were analysed and reached consensus on the main pillars for the therapeutic management of HCV infection in children. They concluded that adolescents (12–17 years old) should be treated with the appropriate and available DAA regimens and that interferon-based therapies should not be used in children. Specific recommendations regarding which DAA regimen to use and treatment duration varied significantly. The expert team have also commented that stakeholders need to convene to standardize therapeutic strategies at a global level if we are to eradicate HCV in children.

2.)Pandey Snehavardhan, Rajeev Khanna, Bikrant B. Lal, Vikrant Sood, Arun K. Sood,and Seema Alam. Comparison of two diagnostic criteria for hepatopulmonary syndrome–High prevalence in Biliary Atresia. JPGN 2020 May; 70 (5): 623–627)

The authors aimed to do a comparative study of hepatopulmonary syndrome (HPS) in pediatric liver diseases with respect to its prevalence using the available diagnostic criteria. This was done as a prospective observational study conducted from 2017 to 2018 where consecutive children with biliary atresia (BA) and other chronic liver diseases (CLDs) were studied. Prevalence of HPS was compared using the 2 available criteria: demonstration of intrapulmonary vascular dilatation along with either alveolar-arterial oxygen difference (P [A-a] O2) on arterial blood gas analysis of more than 15mmHg (criteria 1), or higher than age-appropriate calculated value for P (A-a) O2 (criteria 2). A total of 42 children in BA group and 62 in the non-BA CLD group were included. Using the criteria 1, the prevalence of HPS was 42.3%: 57.1% in the BA group and 32.2% in the CLD group, whereas using criteria 2, the prevalence was 48.1%: 61.9% in the BA group and 38.7% in the CLD group. Criteria 2 diagnosed 6 additional patients with HPS compared to criteria 1 (P value 0.405). BA subjects had higher risk (2.9–3 folds) of developing HPS compared to other CLDs. Authors have concluded that there is high prevalence of HPS in pediatric liver disease subjects. Age-appropriate formula for HPS diagnosis may be better applicable in pediatric population. BA subjects have a higher risk of developing HPS compared to other CLDs overall, irrespective of the severity of liver disease and/or portal hypertension

3.) Bikrant Bihari Lal, Vikrant Sood, Pandey Snehavardhan, Rajeev Khanna, Samba Siva Rao Pasupuleti,Manish Siloliya, Guresh Kumar Seema and Alam.A novel, bedside, etiology specific prognostic model (Peds−HAV) in hepatitis A induced pediatric acute liver failure. Hepatology International. 2020 May 5. doi.org/10.1007/s12072-020-10050-0 *[Epub ahead of print]*

Authors have conceptualized to develop and validate a HAV-etiology specific prognostic model in PALF. Children with HAV induced PALF (IgM HAV

reactive) were included and outcome was defined at day 28 in terms of death or native liver survival.120 Children with HAV induced PALF who presented between January 2012 to August 2019 were enrolled and there were 74 survivors with native liver and 46 deaths. The first 75 patients with HAV induced PALF (data retrieved from the records being maintained prospectively for another ongoing study on PALF) were used to identify the predictors of outcome and to develop the HAV specific prognostic model in PALF - Peds-HAV.This model was developed based on 3 independent predictors of death obtained on logistic regression analysis (INR > 3.1; jaundice to HE interval > 10 days and presence of grade 3–4 HE) in HAV related PALF. Presence of 2 or more of these criteria predicted death with 90% sensitivity, 81.4% specificity and 84.9% accuracy. Peds-HAV model was superior to existing prognostic models like PELD/MELD, KCH and PRISM III. In the validation cohort, Peds-HAV model predicted death with 83.3% sensitivity and 92.6% specificity. To assess the dynamicity of the model, Peds-HAV scores were also calculated for each day from admission to day 7 based on the INR and HE grade on that day. The sensitivity, specificity and accuracy of the Peds-HAV model, which were 83.3%, 84.7% and 84.3% respectively at baseline, improved to 84.2%, 97.2%, 94.5% at day 3 and further to 90%, 100% and 98.7% at day 7 respectively. Authors conclude that Peds-HAV model is a simple, bedside, dynamic, etiology (HAV) specific prognostic model based on 3 objective parameters with optimum sensitivity and specificity, hence should be used as liver transplant listing criteria in HAV induced PALF.

4.) Lalit Bharadia, Neha Agrawal and Nandan Joshi. Development and Functions of the Infant Gut Microflora: Western vs. Indian Infants. International Journal of Pediatrics.2020 May 7. doi: 10.1155/2020/7586264 *[Epub ahead of print]*

The gut microflora of infants from the two populations is more similar than expected. The temporal sequence of colonization remains the same, with aerotolerant and facultative anaerobes colonizing the gut first and paving the way for the growth of a predominantly anaerobic microflora later on. Presence of bifidobacteria and lactobacilli in infants in both populations, specifically in breastfed infants, has important clinical implications given that most probiotic formulations contain these two bacterial genera and most prebiotics are also formulated to stimulate their growth.

5.) Aathira Ravindranath. Chronic vomiting in children: Etiology, diagnosis, and management. Indian Journal of Gastroenterology.2020 May 08. doi.org/10.1007/s12664-020-01035-w *[Epub ahead of print]*

In this technical notes the author has reviewed the literature on chronic vomiting in children extensively and narrated exhaustively. Etiology of chronic vomiting in relation to the age of the child has been tabulated. Author advocates a step based approach in the evaluation to distinguish gastrointestinal versus extraintestinal cause, ascertain the location of pathology in the gastrointestinal tract and tailoring customized evalution based on clinical diagnosis. An outline of the management of common causes has been provided. Author concluded by commenting that vomiting in children encompasses a whole gamut of causes and reaching a clinical diagnosis guides further investigations for confirmation. Instead of searching for the needle in the haystack, a methodical approach will aid in making the right diagnosis and channelize the treatment.

6.)Jagadeesh Menon,Naresh Shanmugham,Mukul Vij,Sripriya Srinivas,Srinivas Reddy andMohamed Rela. Peribiliary pseudotumor like presentation of IgG4 related disease. The Indian Journal of Pediatrics.2020 May 8. doi.org/10.1007/s12098-020-03328-6*[Epub ahead of print]*

In this scientific letter authors describe pseudotumor like presentation of Ig G4 related disease (IgG4-RD) which is peribiliary and periportal rather than isolated

hepatic and is previously undescribed in pediatric literature.A 14-y-old boy with pain abdomen of two years duration had a firm splenomegaly on examination. His bilirubin was 0.5 mg/dl, aspartate aminotransferase (AST) 476 U/L (0–40 U/L), alanine aminotransferase 216 U/L (0–40 U/L) and gamma glutamyl transpeptidase 118 U/L (0–49 U/L). A sonography followed by MRI abdomen showed a soft tissue encasing the hilar bilar duct extending into the intrahepatic main hepatic ducts along the two branches of portal vein along with extrahepatic portal vein obstruction. Biopsy of the lesion showed intense inflammatory infiltrates with plenty of plasma cells and eosinophils along with obliterative phlebitis and storiform fibrosis. The number of IgG4 related plasma cells were 10/hpf. With a diagnosis of IgG4-RD, child was started on oral steroids at 40 mg once daily dosing. The child became asymptomatic after 1 wk with normalisation of liver function tests (LFTs). After 6 mo, the repeat MRI showed significant resolution of the soft tissue lesion. Azathioprine was added at 25 mg OD subsequently it for long term maintenance.

7.) Rohan Malik, Anshu Srivastava, Surender K Yachha and Ujjal Poddar.Chronic vomiting in children: A prospective study reveals rumination syndrome is an important etiology that is underdiagnosed and untreated. Indian Journal of Gastroenterology.2020 May 20.doi.org/10.1007/s 12664-020-01025-y*[Epub ahead of print]*

Rumination syndrome is frequently overlooked, and under-recognized; children are subjected to unnecessary testing and inappropriate treatment for a condition which can be diagnosed clinically and managed easily. The authors present a prospective study on children with chronic vomiting.50 children (5-18 years) were enrolled in the study. Authors have reported that diagnosis was rumination syndrome in 30, cyclical vomiting in 8, functional vomiting in 6, intestinal tuberculosis in 4 and intestinal malrotation and superior mesenteric artery syndrome in 1 child each. They have concluded that rumination syndrome was an important cause of chronic vomiting in children aged 5- 18 years and diagnosis was delayed and these children were often inappropriately treated. Therapy in the form of diaphragmatic breathing had a good success rate.

8.)Amey D. Sonavane, Abhijit Bagde, Vikram Raut, Shaji Marar, Ambreen Sawant,| Ketul Shah, Amruth Raj,Ashok Thorat, Harshit Chaksota,Vishnu Biradar,Suresh Vasanth, Aabha Nagral and Darius Mirza. Therapeutic coil embolization of dominant shunt in hepatopulmonary syndrome enhances post-liver transplant respiratory recovery. Pediatric Transplantation.2020 May 21. DOI: 10.1111/petr. 13729 *[Epub ahead of print]*

Authors have reported a three years and 5 month old boy who was diagnosed with Budd Chiari Syndrome (BCS) at 6 months of age when he presented with ascites. At 2 years of age, he developed progressive clubbing and significant hypoxia (Spo2- 65% on room air) and was diagnosed with hepatopulmonary syndrome (HPS). In view of progressive failure to thrive, worsening HPS and recurrent variceal bleeding, he was planned for living donor liver transplantation. Pre-operative CT angiogram revealed a large pulmonary shunt - a dominant arteriovenous (AV) shunt from a branch of the inferior division of the left pulmonary artery (LPA).He underwent super-selective cannulation of the segmental subdivision of the descending branch of the LPA and left lower zone pulmonary AV fistula embolization was accomplished using platinum coils. Post-embolization, his oxygen saturation improved to 74% on room air and liver transplantation procedure was uneventful.

9.)Parijat Ram Tripathi, Moinak Sen Sarma, Surender Kumar Yachha, Richa Lal, Anshu Srivastava and Ujjal Poddar. Gastrointestinal polyps and polyposis in children: experience of endoscopic and surgical outcomes. Digestive Diseases.2020 May 25. DOI: 10.1159/000508866 *[Epub ahead of print]*

Authors aimed to study the clinical behaviour of gastrointestinal (GI) polyps in children with emphasis on therapeutic outcomes of polyposis syndrome. They have extracted and analyzed the retrospective data of 240 children with proven GI polyps on endoscopy. GI polyps were classified into single polyp, multiple polyps and polyposis syndrome. They have observed that there were no significant differences between single (52.5%, n=126) vs. multiple polyps (27.5%, n=66) with respect to age, symptoms, histology and recurrence. Polyposis syndrome (20%, n=48) presented with complex symptoms (50%) and had higher family history, significantly lower hemoglobin, total protein and albumin as compared to single and multiple polyps. 97.5% patients had juvenile hamartomatous polyps in histopathology. Associated adenomatous changes were not statistically significantly in single polyp, multiple polyps and polyposis syndrome groups. Dysplasia was present in 10% of polyposis syndrome, 4.5% multiple polyps and 3.3% single polyp groups and none had malignant transformation. 19 polyposis patients with favourable clinico-endoscopic criteria were endoscopically eradicated for polyps in 3 (1-4) sessions with sustenance of laboratory parameters at 1 year and 30% symptomatic recurrence at follow-up of 23.5 (7-40) months. There were no major endoscopic complications. 19 patients required proctocolectomy with improvement in laboratory parameters 6 months post-surgery. Authors have concluded that multiple polyps behave similar to single polyps in children and colectomy may be effectively deferred in a large proportion of polyposis syndrome patients if maintained on an endoscopic protocol.

10.)Nida Mirza, Ravi Bharadwaj, Smita Malhotra and Anupam Sibal. Progressive familial intrahepatic cholestasis type 4 in an Indian child: presentation, initial course and novel compound heterozygous mutation. BMJ Case Reports 2020.May 30. doi: 10.1136/bcr-2019-234193 *[Epub ahead of print]*

Authors have reported a 15-year- old boy, born to third degree consanguineous parents who had history of prolonged pruritus and jaundice. On evaluation by next generation sequencing a novel heterozygous missense variation in exon 17 of the TJP2 gene (chr9: g.71854869T>C; depth: 138×) that results in the amino acid substitution of proline for leucine at codon 822 (p.Leu822Pro; ENST00000539225.1) was detected. This confirmed progressive familial intrahepatic cholestasis type 4 as the aetiology of cholestatic liver disease.

June 2020

1.)Ramkiran Cherukuru,Jagadeesh Menon, Kinisha Patel, Ravikumar Thambidurai, Komalavalli Subbiah, Naresh P Shanmugam, Mettu Srinivas Reddy, Mohamed Rela. Uncommon presentation of a recurrent diaphragmatic hernia after pediatric liver transplantation. Pediatric Transplantation. 2020 June 5. DOI: 10.1111/petr. 13790 *[Epub ahead of print]*

Diaphragmatic hernia (DH) is a rare but well-recognized complication of pediatric liver transplantation (PLT). However, a recurrent DH in the setting of PLT has not been reported. Authors have reported a child who had previously undergone a DH repair early after PLT and presented more than two years later with atypical findings of severe sepsis and a tender abdominal swelling indicating recurrence of DH.Authors conclude that a protocol of screening ultrasound, chest X-ray or even MRI should be considered to detect recurrence early to prevent acute presentations.

2.)John Matthai, Naresh Shanmugam and Prasanth Sobhan. Coronavirus Disease (COVID-19) and the Gastrointestinal System in Children. Indian Pediatrics.2020 June 15; 57; 533-535.

This is a special article published on behalf the ISPGHAN and Pediatric Gastroenterology Chapter of Indian Academy of Pediatrics

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV2), though primarily a respiratory pathogen, also involves the gastrointestinal tract. Similar to the respiratory mucosa, angiotensin converting enzyme-2 (ACE-2) receptor and transmembrane serine protease 2 (TMPRSS2) co-express in the gastrointestinal tract, which facilitates viral entry into the tissue. Less than 10% of children with infection develop diarrhea and vomiting. Prolonged RT PCR positivity in the stool has raised the possibility of feco-oral transmission. Elevated transaminases are common, especially in those with severe coronavirus disease (COVID-19). Children with inflammatory bowel disease and post liver transplant patients do not have an increased risk of disease, and should remain on medications they are already on. Children with chronic liver disease should continue their medications as usual. All elective procedures like endoscopy should be postponed.

3.)Manoj Madhusudan, Radhika Raman and Malathi Sathyasekaran. Acrodermatitis enteropathica as a presentation of cystic fibrosis in an infant. Indian Pediatrics.2020 June 15; 57: 573.

In this clinical case letter authors described a seven-month-old girl born to third degree consanguineous parents who presented with non-healing perianal skin lesions, steatorhhoea and failure to thrive and with no history of respiratory infections. Acrodermatitis enteropathica was suspected at 7 months of age. Serum zinc levels were low (46 µg/dL). A detailed family history revealed two siblings deaths in early infancy with recurrent respiratory symptoms. Genetic analysis showed homozygous mutation on exon 14 of the *CFTR* gene (p.Arg709Ter), which was deemed pathogenic for cystic fibrosis (CF). Authors concluded that CF is associated with a wide range of presenting features which includes acrodermatitis enteropathica.

Publications inadvertently missed in the previous issues –

1.) Shruti Sharma, Sadhna B. Lal, Manupdesh Sachdeva, Anmol Bhatia and Neelam Varma. Role of granulocyte colony stimulating factor on the short term outcome of children with acute on chronic liver failure. Journal of Clinical and Experimental Hepatology.2019 October 16 doi:10.1016/j.jceh. 2019.10.001 *[Epub ahead of print]*

Acute-on-chronic liver failure (ACLF) in the paediatric age group is a syndrome with a high mortality rate without liver transplant. Granulocyte colony–stimulating factor (GCSF) therapy has been shown to significantly improve liver function and reduce short term mortality in adults with ACLF. The aim of this study was to evaluate the role of GCSF on short-term outcome of children with ACLF in a nontransplant unit from North India. Children (aged > 1 year) diagnosed with ACLF from January 2017 to March 2018 were randomised. Group A (n=15) was given GCSF therapy at 5mcg/kg/day for 5 days along with standard medical care (SMC) and group B (n=15) was given only SMC. The outcome was evaluated as survival at 30 and 60 days of therapy. It was observed that GCSF at a dose of 5 mcg/kg/d for 5 days may result in an early improvement of disease severity and early survival benefit, when given to children with ACLF without advanced grades of hepatic encephalopathy. There was no significant difference in the overall survival on day 30 and 60.Authors have concluded that GCSF therapy at 5 mcg/kg/day for 5 days was ineffective in improving the survival outcome on day 30 and 60 of therapy.

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