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Message from Editorial Board

Welcome to the Fourth issue of PGLJ! We hope that the first three issue of PGLJ did stand up to your expectations. We will continue to strive and work hard so that PGLJ becomes a resource that you can depend on to keep up with the rapidly evolving field of Pediatric Gastroenterology.

The fourth issue of PGLJ brings you a steady supply of high-quality, peer reviewed papers that are relevant and readable.

The highlight of this issue is Guidelines review of important topic like **Hepatitis B and C in children , nutrition in CLD and Autoimmune Pancreatitis**

This third issue is has a **social edge** commentary on Liver Transplatation in India. Liver transplantation we all know is the only therapeutic option to many liver disease in children and should be within the reach of all sections of society .

- **Invited Review article** this time is to Introduce our readers with Deep Learning and Block chain system in relevance to Pediatric Gastroenterology .
- We have one C**ase Report** where in authors have provided us unique case on Chronic button battery ingestion in a child.
- Section of **Journal Watch** has two parts. First section dealing with international publications related to different aspects of Pediatric Gastroenterology. The second section incorporates article published by ISPGHAN members in between September 2019 - December 2019. We would request all members to send us information about their publication so that we can continue to incorporate them in future issues.
- **ISPGHAN Kaleidoscope**: Section deals with activities done under the ISPGHAN banner both at state and national level. We have included awardees and experience from the ISPGHANcon 2019 at Chennai. Apart from that many other activities were conducted throughout the country which has been shared through this section with the rest of the pediatric community.

We would like to take this opportunity to thank all the reviewers for the effort and expertise that they have contributed to reviewing, without which it would be impossible to maintain the high standards of peer-reviewed journals.

We request you the reader to become an author and share your thoughts and research with the national and international community through this journal. We also request you to pass on the message to Trainees (DMs, FNBs, PDCCs, and Fellowships) for it will be a great place for them to start their academic venture.

As this the last journal by the current editorial board we would like to bid adieu on a positive note. We understand that we may not have done a perfect job and some errors or mistakes might have been committed unknowingly. However our readers have always helped us to improve by giving positive feedback. We hope that the new editorial board of 2020 will take the journal to new heights and achieve what we had dreamt off a year back

Kindly submit your contribution in MS word only at: *pglj.ispghan@gmail.com*

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REVIEW ARTICLE

Deep Paediatric Gastroenterology With Blockchain

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Key Words:

Deep learning, Artificial Intelligence, Block chain, Bitcoin, Paediatric Gastroenterology, Paediatric Endoscopy, Artificial neural networks.

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Introduction:

Deep learning and Block chain are the systems where one can generate and explore further medical sciences. Current medical systems and its developmental process are restricted to randomised control trials and their associates. Both deep learning and block chain are underused either due to ignorance or fear. Block chain can give trust to the developed deep learnt algorithms .Both can speed up medical science without biases and can take clinical subjects to their full potential.

What is Deep Learning?

Deep learning is the part of machine learning based on artificial neural networks .It uses algorithms to derive conclusions from the given inputs. Deep medicine, a concept now accepted has three stages[1]. First is data gathering or deep pheno-typing which includes detail history, clinical exam finding, investigations, and genetic records in digitised form. Deep learning in the developed neural networks is the second component. The third component is machine learnt result applications. The resultant output would give us the probabilities and certainties of the clinical condition that would explore the natural history of progression of disease.

Deep learning in clinical medicine is composed of algorithms that permit software to train itself to perform tasks by processing multi-layered network of clinical data giving us results[2] .These results needs further applications. Clinical data is fed through the layers of computations. Deeper the layers of computation subjected more are the derived inferences. Thus Deep learning enables computers to learn from data for better inferences.[3]

Endoscopic images, histopathology slides, clinical images, associated history and clinical findings are the raw data subjected to deep neural networks. Image segmentation, clinical data correlation can be done easily with the well-described neural network. The application of deep Paediatric Gastroenterology in field of metabolic liver disease is worth considering .Enzyme analysis, genetic/epigenetic results, histopathological liver findings, clinical phenotypes and genetic variable expression of metabolic liver diseases; all can be studied by artificial intelligence. Histopathological diagnosis like non specific colitis and non specific duodenitis can be revised with machine learning. More answers are expected on progression of disease with deep neural networks in very early onset inflammatory bowel disease and celiac disease. Deep learning tools for histopath slide analysis for liver fibrosis are now well studied[4]. Deep learning of medical images is undertaken by companies like Enlitic, Merge, health care, Zebra medical vision, RAD logic. Mobile apps like Ada, Your MD, and Babylon use artificial intelligence. Buoy health app draws clinical data from 18000 clinical publications, 1700 medical conditions, more than 5 million patients. More the clinical data be digitised and fed to neural networks more would be the accuracy. Face 2 gene app can help a hepatologist to make diagnosis in syndromic liver/genetic diagnosis.

Published & Proposed Applications:

The University of Tokyo has worked on convolution neural network for liver CT mass calcification with 84% accuracy [5]. Deep neural network can avoid error and biases. Essential collaboration with data scientist can help endoscopist to develop image (endoscopic) interpretation in real time. Dynamic real time imaging can be fortified with AI (Artificial Intelligence) for decision making e.g. site identification for mucosal biopsy for better diagnostic yield or appropriate haemo-clip application location with least chances of dislodgement. It can also help endoscopist to

demarcate the mucosa for polypectomy or POEM with least complications. Multi-center study to determine the diagnostic accuracy of EndoBRAIN, an artificial intelligence-based system that analyzes cell nuclei, crypt structure, and micro-vessels in endoscopic images distinguishes neoplastic from non-neoplastic lesions with 96.9% sensitivity, 94.3% specificity ,96.0% accuracy , 96.9% positive-predictive value, and a 94.3% negative-predictive value.[6] Krishnan et al.[7] classified nine types liver disorders with help of neural networks in ultrasound images with accuracy of 79 %. Novel AI diagnostic system which compiles Java and C++ to the application of deep learning algorithm on mobile devices with Android platform [8] are proposed and tested for cholelithiasis. Specific learning modules with teaching aids can help budding endoscopist in dynamic endoscopic image interpretation. Watson for Genomics (WfG) curated actionable gene list identified additional genomic events of potential significance (not discovered by traditional MTB curation) by 32% using cognitive computing [9]. Deep learning can also help endoscopist in not missing polyps while doing endoscopy as shown in various studies.[10, 11, 12]The neural network has demonstrated 90.5% accuracy rate in identifying celiac disease from endoscopic images [13] .

Comparative performance of the machine learning prediction model with pre-endoscopic clinical risk scoring systems the Glasgow-Blatchford score [GBS], admission-Rockall score, and AIMS 65 by Shung D L et al revealed better determining risk in patients with gastrointestinal bleeding (UGIB) by artificial intelligence [14]. Machine learning model can increase identification of low-risk patients who can be safely discharged earlier. Supervised learning algorithm is studied and used to analyze laboratory data and to build a prediction model for diagnosis of appendicitis based on relevant biomarkers .The study revealed that a biomarker signature based on learning algorithms is capable of becoming the gold standard for the diagnosis of paediatric appendicitis.[15] AI base - Multi-parameter model is also capable of discriminating between complicated and uncomplicated appendicitis with specificity of 67%, a sensitivity of 93%, accuracy of 90% .Another decision making study [16] for diagnosis of appendicitis with artificial neural networks (ANN) noted 91% sensitivity with a specificity of 85% and 100% sensitivity with a specificity of 97% .

Study comparing the performance[17] of unsedated ultrathin transoral endoscopy, unsedated conventional EGD (Esophagogastroduodenoscopy), and sedated EGD, with or without the use of an artificial intelligence (AI) system; notes blind spot rate with AI-assisted sedated Conventional -EGD is significantly lower. Convolution neural network (CNN) system based on deep learning can reduce the reading time of endoscopists without oversight of abnormalities in the capsule-endoscopy [18] Machine algorithm can also help in diagnosing Chronic liver disease based on AI supported algorithms [19] on ultrasound. Deep learning neural networks can study motility disorders [20] with better accuracy. More validation studies are needed. Deep AI neural network can contribute to personalised nutrition. The paper published [21] on personalised nutrition by prediction of glycemic responses used machine learning in analysis; highlights variable individual food responses to the same food. Thus deep learning can help in studying cow's milk protein allergy, gluten hypersensitivity, unexplained phenomenon of non celiac gluten sensitivity and probiotics and their interactions. Systematic literature review and meta-analysis methods remain time-consuming and labor-intensive. Machine learning directed meta-analysis [22] can reduce the labour as well as costs.

Deep learning in Paediatric gastroenterology can help a gastroenterologist by incorporating all patient data. Analysis can be improved without personal biases. Deep Paediatric Gastroenterology would not substitute but help gastroenterologist in future for right decision making.The major limitation of deep learning is the data feeding .If inaccurate data is provided to deep neural networks;we can get wrong interpretation .Trials comparing specific deep neural network with clinical trials would help in optimising/ personalising the treatment of patients. Once established; the combination can be secured with block chain.

Pediatric Gastroenterology Block Chain.

Block chain is software which cannot be changed or hacked [23]. It is based on predominantly distributed network. The basic purpose of block chain is to group digital information into group of collections called as blocks. Blocks are joined together as cells or nodes.

Every node is connected with each other. Altering one node would not be possible without change in pattern of chain. This block chain is represented as Hash. More the nodes of digital information blocked better is the work done by block chain.

Bitcoin [24] is the first generation block chain with basic concepts of data mining and proof of work. Ethereum, Hyperledger, Corda and Ripple are second generation block chain with programmable smart contract, security and added features. IOTA ;Internet of things is third generation block chain which is block-less, secured, quantum proof, scalable, open source with fee less transaction system. It has no separate validator of data blocks. Each user has to validate previous two transactions. IOTA can help each endoscopic processor to have unique identity. It can transmit images over the cloud for multiple interactions. All of the generations of block chains can communicate with Microsoft Co. Data stored on different block chains can communicate and transact with each other with better speed. Multi-centric clinical data analysis with direct endoscopic/ histopathological image processing would be easier.

Use of block chain in clinical paediatric gastroenterology is add- on to digital neural networks. One of the best uses of block chain in paediatric gastroenterology can be for research. Once data is digitised and blocked one cannot change it. The trust-worthy nature of trial is reinforced. Endoscopic images can be digitised and blocked making them easier to access and their originality is preserved. Medical records/ confidential information also can be stored in nodes making it unalterable. Storage of personal identification in each patient case cannot be challenged. Issues of intellectual property or trademark would not arise. Algorithms approached in each case would be preserved. Clinical decision making protocol can be standardised and used for comparison. Biases would minimize. Result of each clinical trial can be tied to the methods. More specific outcome in a given clinical situation can be meta-analysed with large data. Patient confidentiality can easily be preserved on block chain.

The major limitation of block chain is the information supplied to each block is taken for granted as truth. Hence once mistake is blocked; results would be difficult to analyse. Block chain are slow at present, need lot of electricity and nodal validation.

Combining deep learning and block chain would definitely make field of paediatric gastroenterology interesting both in research and clinical sciences. The way of Meta analysis and Meta review would change. Guidelines would be more uniform and populations specific. Multiple point coordination would be easily possible .Generating library of blocks which are trustworthily managed with block chain is easily possible in future. Integrated decision making by Clinical data, histopathological data, endoscopic images and radiological pattern in disease in specific manner would give more clarity on patient state. Both systems would work as a support to clinical sciences .Only underlying condition necessary is the truth of data mining and data entry.

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Pediatric Liver Transplantation In India- Social Aspects

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One of the marvels of modern medicine has been the evolution of liver transplantation (LT) as an established therapy in the last 5 decades. In the US alone over 7.5 lac liver transplants have been performed of which about 54000 have been in children [1]. In the 80's and 90's LT in India seemed unthinkable till the first successful pediatric liver transplant was performed in 1998 at Indraprastha Apollo Hospital, Delhi [2]. The progress was slow over the next decade due to scarcity of trained personnel, poor awareness amongst primary care doctors, reservations regarding donor safety and the huge financial implications. By 2007 only about 318 LT's had been performed in India [3]. However, the last decade has seen a phenomenal growth with the advent of multiple liver transplant centres. Presently about 1700 liver transplants are performed in India yearly with about 10% being in children. The growth has primarily comprised living donor liver transplant (LDLT) though cadaveric donation is picking up, primarily in the Southern part of the country.

Many challenges still exist. There is still a lack of awareness and faith in the modality amongst many primary care paediatricians who are sceptical about the results, morbidity and need for long term care especially amongst those from smaller towns. This becomes all the more pronounced when disease is advanced, or child presents in acute liver failure with high risk of mortality with delayed referral. LT in India is largely limited to the private sector and this healthcare structure does not follow a specific referral pattern, thus limiting the opportunity to provide uniform level of primary, secondary and tertiary care. Awareness among general practitioners about the indications and success of transplant plays a vital role in timely referral. Dissemination of success stories of individual patients who receive constant input from their LT centres in an effort to enhance joint care with their referring units can greatly help in confidence building and promote early referral. Acceptance for LT needs to be boosted through more publications and CME's.

Early transplantation in children avoids growth failure and loss of schooling, and its associated downstream impact on both individual and societal development. Families need to be committed to the cause, as a young child will need the support of a caregiver for the greater part of his childhood. Children with liver transplantation have lower health related quality of life compared to normal individuals, these impairments are comparable, if not better, to those of children with other chronic health conditions [4]. Sadly, the commitment with its implications of investments in time, emotion, effort and money is more readily forthcoming for male offspring. The covert or overt bias against the girl child was reflected in our data as 72.2% of the recipients were male in the initial decade but the ratio has tended to equalise with 51.7% boys and 48.3% girls undergoing LT at our centre in the second decade of the programme. The changing social milieu is also evidenced by fathers coming forward in greater numbers as donors [5].

From the donor's perspective, the risk of not only morbidity but also mortality cannot be entirely denied. Also, donors do go through a lot on the physical, emotional and social front in addition to time lost away from their occupation. Donor safety concerns are a still a major factor limiting transplant despite stringent donor selection criteria being applied by transplant centres. However, in a patriarchal society like ours, increasing numbers of fathers as donors reflects encouragingly on the increasing acceptability for LT in our society.

Financial constraints continue to be the biggest challenge and the the most crucial limiting factor has been the prohibitive cost of LT. The concept of universal health care insurance is still evolving, and most insurance companies do not provide cover for perinatal onset or genetic diseases. Many charities and crowd funding programmes have actively helped poor families save their children by raising funds for their transplants. Many corporates support transplant programmes as part of their CSR budgets. Discounted packages have been offered by a few centres. The advent of crowd funding platforms has been a boon for the the needy as funds can be raised in a short period of time [6]. That strangers come together on the internet to fund a medical catastrophe for an unknown person is heart-warming and provides an insight into the social responsibility that the community is eager to take up when transparency is assured. This has enabled families with limited means to avail of lifesaving transplants even when they could pitch in only marginal amounts. Nearly 20% of our transplant patients in the last 3 years bore an individual expense of only 1.5 lac rupees. Campaigns for children evoke an emotional outpouring of help. This brings with it tremendous responsibility on institutions to use these funds judiciously for subsidised programmes only to maintain credibility and avoid a reputation of “commercialisation of transplantation”.

LT in India remains largely living related and encouraging deceased donor transplantation (DDLT) is the need of the hour. Southern states esp Tamil Nadu have robust DDLT programmes that contribute about a third to half of their total transplants. Increasing DDLT is also being reported from a few other states but remains minimal in Northern India. Society needs to be educated about cadaveric donation through multiple strategies right from education in schools, social media and other mass media campaigns, support from celebrities and hospital awareness programmes.

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Chronic Hepatitis B management in Children

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Abstract

Abstract

Chronic hepatitis B in children is mostly due to mother-to child transmission and risk of chronicity is highest when exposed in early infancy. The infection passes through different phases depending upon the degree of activation of immune system and status of HBeAg. Accurate assessment of each phase requires measurement of HBeAg, HBV-DBA and ALT. Treatment is indicated in those who are in HBeAg positive or negative hepatitis, in those with cirrhosis and extra-hepatic manifestations. Peg IFN and nucleos(t)ide analogues (NA) are the mainstay of treatment. Peg IFN though has a finite duration of treatment has many side effects. NA therapy with high barrier against resistance have fewer side effects but duration of therapy should ideally be until loss of HBsAg as even after HBeAg seroconversion chances of seroreversal or HBeAg negative hepatitis are there. Children undergoing immunosuppression should be screened not only with HBsAg but also with AntiHBc and NA prophylaxis should be initiated in those cases with high risk of reactivation.

Introduction

India remains a region of intermediate endemicity as hepatitis B virus (HBV) prevalence is about 3% in the general population. Mother-to-child transmission accounts for almost 2/3 of all cases of chronic hepatitis B in children. The risk of chronicity after exposure to hepatitis B is 90% in the newborn, 30% in children < 5 years and 5% in adolescents. Though chronic hepatitis B is seemingly innocuous during childhood, risk of cirrhosis is 3 to 5% and risk of hepatocellular carcinoma (HCC) is 0.01 to 0.03% even before reaching adulthood. Additionally, all these children carry the burden of the disease into adulthood when the risk of cirrhosis is 2 to 3% annually and that of HCC in those with cirrhosis is 3 to 8% per year.[1] Therefore, understanding the dynamics of chronic hepatitis B in childhood is essential to decide preventive and therapeutic strategies.

Natural history of chronic hepatitis B

Natural history of chronic hepatitis B is described using the new nomenclature based on the HBeAg status, HBV DNA (Hepatitis B virus deoxyribonucleic acid) and alanine aminotransferase levels (ALT) as a marker of liver inflammation. These phases result from the dynamic interaction between the virus and host immune system. The duration and outcome of each phase depend on a number of factors, the most important being the age of acquisition of infection.

1. HBeAg-positive chronic HBV infection: This phase was previously referred to as the immune-tolerant phase owing to the dormancy of immune system against the virus, thus allowing uncontrolled replication of HBV. This phase is characterized by HBeAg positivity, very high HBV-DNA and normal ALT signifying minimal or no liver inflammation. Perinatally acquired HBV or transmission of HBV in the first 2 years of life will have a prolonged HBeAg-positive chronic HBV infection which may last for 1 to 4 decades. Transplacental transmission of HBeAg induces immune tolerance thus explaining establishment of infection without any inflammation. Though there is hardly any parenchymal inflammation there is continuous integration of HBV-DNA into the hepatocytes and formation of covalently closed circular (ccc) DNA which forms the transcription template. Because of the random insertion of viral DNA into the host genome, a fertile background for development of hepatocellular

carcinoma (HCC) is formed. Even without evident features of inflammation, 1.7 to 4.5% of children infected at birth have cirrhosis on liver biopsy.[7]

2. HBeAg-positive chronic hepatitis B: In this phase there is activation of the immune system against the virus and is characterized by elevation in ALT, fluctuating levels of HBV-DNA and HBeAg positivity. Liver histopathology will show varying degree of necroinflammation. This phase was termed as the immune-active phase previously. This phase of active hepatitis is akin to a double edged sword. Activated immune system can cause HBeAg seroconversion in 65 to 90% in the long run. However, repeated flares of inflammation lead to progression of fibrosis. In children, early seroconversion is a risk factor for developing HCC as the severe necroinflammation forms an ideal background for carcinogenesis.

3. HBeAg-negative chronic HBV infection: After seroconversion majority will enter the "inactive carrier phase" which is now termed HBeAg-negative chronic HBV infection. In this phase ALT levels are normal, HBV-DNA is usually < 2000IU/L and Anti HBe is positive. Necroinflammatory activity is low and risk of progression to cirrhosis is low. Once this phase is reached there is a 1 to 3% chance of HBsAg loss annually. However, some may develop chronic hepatitis and move on to the next phase.

4. HBeAg-negative chronic hepatitis B: This phase is typified by elevated ALT, negative HBeAg, positive Anti HBeAg and moderately high HBV-DNA. Liver biopsy would show changes of inflammation and fibrosis. These patients have mutations in the core and pre-core regions that prevent HBeAg expression and still allow replication. Though only 10% children with chronic hepatitis B are in this phase there can be disease progression and higher risk of HCC. Adult studies have shown that those who have quantitative HBsAg level >1000IU/L have higher chances of reactivation.

5. HBsAg-negative phase: This phase is characterized by HBsAg negativity, Anti-HBs may or may not be detectable, Anti-HBc positivity, normal ALT and undetectable HBV-DNA. This phase was previously referred to as "occult HBV" phase. If this phase occurs before development of cirrhosis there is hardly any risk of disease progression or HCC. Annual risk of HCC after spontaneous HBsAg clearance is 0.55%. However, persistence of cccDNA in the hepatocytes would lead to reactivation when exposed to immunosuppression.

The summary of diagnosing hepatitis B in different phases of infection is given in Table 1.

Treatment

The ultimate goal of treatment is eradication of hepatitis B virus which in turn will stall disease progression and HCC development. Nevertheless, this will remain a utopian goal with the available treatment options presently. HBsAg loss signifies intense suppression of viral replication and is a desirable goal as disease progression correlates with viral replication. HBeAg seroconversion is a less desirable end point as there still remains the risk of seroreversion and HBeAg-negative chronic hepatitis.

Indications for treatment

As per the European Association for Study of Liver (EASL) recommendations for adults with chronic hepatitis B, all patients with HBeAg positive or negative hepatitis ought to be treated. These patients classically have ALT > ULN, HBV-DNA > 2000IU/L and moderate necroinflammation on liver biopsy. Irrespective HBV-DNA level, all patients with cirrhosis (compensated or decompensated) should be treated. Patients with HBeAg positive or negative chronic HBV infection are not offered treatment unless they have extrahepatic manifestations, family history of HCC or cirrhosis or if they are more than 30 years of age. In children, a decision to treat should take into account the slow progression of the disease in children, risk of complications later and the side effects of prolonged treatment. As patients with lower transaminases have lower chances of achieving seroconversion, only when the ALT is elevated more than 1.5 times the upper limit treatment can be considered. ALT can remain elevated for 6 months during spontaneous seroconversion hence, it is prudent to wait for 6 months before embarking on treatment. The cut-off for HBV-DNA is well established in adults as 2000IU/ml but until robust data in pediatric patients is available it is best to use the same cut-off though in some studies 20000 IU/ml has been used. Liver histopathology showing at least moderate necroinflammation or fibrosis would have better response to antivirals. However, there are some studies that have shown benefit of treatment even in the HBeAg positive chronic hepatitis B infection in children.

Treatment options

The two classes of drugs approved for treatment of chronic hepatitis B in children are pegylated interferon (Peg IFN) and nucleos(t)ide analogues

(NA) which include lamivudine, adefovir, telbivudine and entecavir, tenofovir disoproxil fumarate. Tenofovir alafenamide is a newer analogue that is approved in adults but not yet in children. Peg IFN based therapy has an immunomodulatory role which enhances host immunity against the virus and also has anti-viral effect. The advantages of Peg IFN therapy is the finite duration (180ug/1.73m^2/week for 6 months) of therapy, high barrier against resistance, moderate HBeAg and HBsAg loss and low risk of relapse. Drawbacks of this treatment are the numerous adverse effects, need for subcutaneous injections and contraindication in decompensated cirrhosis. Commonly used NAs are lamivudine (3 mg/Kg OD[Maximum 100 mg/day], < 2 years of age), entecavir (> 2 years of age) and tenofovir (>12 years of age). Entecavir (0.015mg/kg/day) and tenofovir (300mg/day) have high barrier against development of resistance, have fewer side effects but HBeAg and HBsAg loss is slow, duration of therapy is not defined (ideally until HBsAg loss) and there is risk of relapse on cessation of therapy. After achieving HBeAg seroconversion and undetectable HBV-DNA, NAs should be continued for at least 12 months more to consolidate the treatment. In those who do not seroconvert or in those with HBeAg negative chronic hepatitis B therapy with NAs should be continued indefinitely. As most of the children are in HBeAg positive chronic HBV infection phase they do not fulfill the traditionally defined criteria for treatment. Nevertheless, they have very high HBV-DNA levels, are at risk HCC development and are a source of transmission. Thus, some authors treated children in this phase with lamivudine for 2 months followed by combination of lamivudine and conventional interferon for 10 months and showed HBeAg seroconversion in 22% and HBsAg loss in 17%. Similarly an Indian study showed HBeAg loss in 39% and HBsAg loss in 20%.[18] The results are contradictory in another study which showed that sequential therapy is of no benefit in the immune-tolerant phase. Another recent study that used Peg IFN and entecavir showed that only 3% achieved HBeAg loss. Thus, with presently available evidence treatment in the HBeAg positive chronic hepatitis B infection (immune-tolerant phase) cannot be recommended.

Liver transplantation

Children undergoing liver transplantation for decompensated liver disease due to chronic hepatitis B should receive NA and Hepatitis B immunoglobulin (HBIG) after transplantation which reduces the chances of graft infection to < 5%. If the patient is HBV-DNA negative at the time of transplantation HBIG can be discontinued but NA's to be continued. But if HBV-DNA is positive prolonged therapy with NA and HBIG would be required. If a child with any other cause of liver disease is undergoing liver transplantation from a donor who is positive for Anti-HBc IgG, lifelong NA should be continued to prevent reactivation with immunosuppression.

Children undergoing immunosuppression

All children ought to undergo screening with HBsAg, Anti-HBs and Anti-HBc IgG before commencement of immunosuppression.

HBsAg – negative, Anti-HBs – positive, Anti-HBc – negative: Can proceed with immunosuppression

HBsAg – negative, Anti-HBs – negative, Anti-HBc – negative: Reinforced vaccination

HBsAg – positive, Anti- HBs – negative, Anti-HBc – positive: Prophylaxis with NA has to be started and continued until 12 months after completing immunosuppression (18 months in case of rituximab based immunosuppression). It has to be discontinued only if the disease is in remission. During prophylaxis liver functions have to be monitored every 3 months and 12 months after discontinuation.

HBsAg – negative, Anti-Hbs – negative, Anti-HBc – positive: The decision to start NA prophylaxis would depend on the risk of reactivation which is based on the immunosuppressive regimen.

- High risk of reactivation (>10%): In those who receive rituximab or stem cell transplantation, NA prophylaxis has to be given and continued for 18 months after cessation of immunosuppression with monitoring for at least 12 months after prophylaxis withdrawal.
- Moderate (1 to 10%) or low risk (<1%): HBsAg and HBV-DNA monitoring has to be done every 1 to 3 months as there is risk of seroreversion. If HBV-DNA becomes detectable or HBsAg becomes positive NA therapy has to be initiated.

Conclusion

In children with chronic hepatitis B phase of the disease has to classified based on HBeAg, Anti-HBe, HBV-DNA and ALT levels with or without liver biopsy. Cases with HBeAg positive or negative hepatitis need to be treated with anti-virals. More studies are needed to justify therapy in the HBeAg positive chronic HBV infection (immune-tolerant) phase.

Table 1: Phases of infection in chronic hepatitis B

	HBeAg positive chronic infection (Immunetolerant)	HBeAg positive chronic hepatitis (Immuneactive)	HBeAg negative chronic infection (Inactive carrier)	HBeAg negative chronic hepatitis
HBeAg	Positive	Positive	Negative	Negative
HBV-DNA (Copies/ml)	>20000	2000-20000	<2000	>2000
ALT	Normal	>ULN	Normal	>ULN
Liver histopathology	Normal	Moderate to severe necroinflammation/fibrosis	Minimal activity	Moderate to severe necroinflammation/fibrosis
Treatment	No	Yes	No	Yes

HBV-DNA: Hepatitis B virus-deoxyribonucleicacid, ALT: alanine aminotransferase, ULN: upper limit of normal

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Chronic Hepatitis C management in Children

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Background

3.5 to 5 million children are estimated to have chronic hepatitis C virus (HCV) infection all over world while prevalence in pediatric population is 0.15% (0.6% in high income and 0.3% in low income countries).[1,2] In Indian studies HCV prevalence among all age groups is 1-1.9%.[3] In a recent population based study, in 5-18 years age group HCV seroprevalence was 0.7% while RNA positivity was 0.4%.[4] Main route of HCV acquisition in children is from mother to child vertical transmission. In children as compared to adults, HCV infection leading to cirrhosis (1-4%) is uncommon and hepatocellular carcinoma is rare.[5] Weather to treat HCV in childhood has been a point of debate due to lower HCV related complication in childhood and higher side effects due to interferon based treatment regimens. With the approval of safer and more efficacious direct acting antivirals (DAAs) in pediatric population, now treatment is recommended by ESPGHAN (European Society of Paediatric Gastroenterology, Hepatology and Nutrition)[5] and AASLD-IDSA (American Association for the Study of Liver Diseases-Infectious Diseases Society of America)[6] in all HCV infected children above ≥ 3years age.

Investigations and diagnosis of chronic HCV infection in children

All infants born to HCV positive mothers should undergo antibody based test (anti HCV antibody) at 18 months age, as maternal antibodies can be found before this age in serum of the child. If antibody test is positive then HCV RNA should be performed at 3 years age, as 25-50% children may spontaneously clear the prenatally acquired HCV infection by this time.[1] To allay the parental anxiety or if loss to follow up is a concern, RNA based test can be performed as early as 2 months age.[6]

In other children suspected of HCV infection should undergo serology, if positive then RNA estimation.

HCV genotyping is not recommended in adults anymore due to approval of pangenotypic DAAs. Although in pediatric patients genotyping should be performed as pangenotypic DAAs are yet not approved for all age groups.

Routine liver function test should be performed at diagnosis and then yearly in asymptomatic children. Before starting treatment, it is not mandatory to perform tests for assessment of liver fibrosis like liver biopsy or fibroscan except in patients where advanced liver disease is suspected.[5]

Children with cirrhosis should undergo hepatocellular carcinoma (HCC) [ultrasound with or without serum alpha-fetoprotein (AFP) every 6 months] and endoscopic surveillance for variceal status (at screening and then every 3 yearly thereafter).[6]

Tests for active hepatitis B infection (HBsAg, anti-HBc, and anti-HBs) should be done before starting HCV DAA therapy due to risk of reactivation during or after treatment.[6]

Indication of HCV treatment in children

Treatment for HCV infection is not recommended in < 3 years age. All treatment naïve and experienced children (≥ 3-18 years) should be considered for treatment irrespective of liver disease status. In children with significant fibrosis or cirrhosis or extrahepatic manifestations treatment should be considered without delay. Similarly in patients planned for solid organ/hematopoietic stem cell transplant and on immunosuppressant treatment, there should be urgency to start anti HCV treatment.

After recent FDA approval of DAAs in ≥ 3 years age, therapy can be offered to all children above 3 years age. In case of unavailability of DAAs, risks and benefits of interferon based therapy or to wait till DDAs become available should be compared and discussed with parents before instituting treatment. In general PEG interferon and ribavarin based treatment can be deferred till DAAs become available.

Treatment of Chronic HCV infection

Goal of treatment

Goal is to cure HCV infection to prevent progression of HCV related liver disease. End point of therapy is undetectable HCV RNA in blood at 12 weeks [sustained virological response (SVR 12)] after end of DAAs treatment and at 24 weeks (SVR 24) after end of PEG IFN and ribavarin treatment.[5]

Following drugs are approved in children for HCV treatment (Table 1 and 2)

Ledipasvir and Sofosbuvir

This combination is now recommended from ≥ 3-18 years for genotypes 1, 4, 5 and 6 in patients without cirrhosis or with compensated cirrhosis.[5,6]

Sofosbuvir and ribavarin

Recently this combination is also approved by FDA for use in children ≥ 3 years for genotype 2 and 3.[6] Presently this is the only DAA combination approved in ≥ 3-11 years age for genotype 2 and 3. Clinical trials are underway evaluating weight-based dosing of sofosbuvir/velpatasvir and glecaprevir/pibrentasvir and that may lead to FDA approval of these drugs soon in children aged 3 - 11 years.[6,7,8]

Glecapravir and Pibrentasvir

This is first pangenotypic combination approved by FDA in age group ≥12 years or ≥45kg.

As per AASLD HCV guidance panels if there is no compelling evidence to start immediate antiviral treatment in 3-11 years age then to wait till pangenotypic regimens are approved.[6]

PEG interferon (IFN) and ribavarin

ESPGHAN guidelines 2018 recommended that PEG IFN based therapy can be deferred till DAAs are available in that age cohort (3-11 years). With approval of DAAs across all age cohorts now there is no role of PEG IFN based therapy anymore unless DAAs are not available and treatment is strongly needed.

Other considerations for children with HCV infection

Hepatotoxic drugs should be used with caution in children with chronic hepatitis C after assessment of potential risks versus benefits of treatment. Use of corticosteroids, cytotoxic chemotherapy, and/or therapeutic doses of acetaminophen are not contraindicated in children with chronic hepatitis C. Solid organ transplantation and bone marrow transplantation are not contraindicated in children with chronic hepatitis C.

Adolescents with chronic HCV infection and their families should be guided regarding potential risks of alcohol for progression of liver disease.

Conclusion:

All children with chronic HCV infection ≥ 3 years age should be considered for treatment even if liver functions are normal. With approval of DAAs, treatment is now highly effective and safe in children. Long term safety data are still not available. Availability of age/weight appropriate dose combinations of DAAs and high cost are the issues that need attention in developing countries like India.

Table 1: Drugs approved for children in HCV infection

Drug	Genotype	Dose
Ledipasvir and Sofosbuvir (Oral)	1,4,5,6	<17kg : 33.75mg/150mg 17 to <35 kg: 45mg/200mg >35kg : 90mg/400mg
Sofosbuvir and Ribavarin (Oral)	2,3	Sofosbuvir <17kg : 150mg 17 to <35 kg: 200mg >35kg : 400mg Ribavarin < 47kg : 15mg/kg 47-49kg : 600mg 50-65kg : 800mg 66-80 kg: 1000mg >80kg : 1200mg
Glecaprevir and Pibrentasvir (Oral)	Pangenotypic	300mg/120mg OD (≥12 years or ≥45 kg)
Interferon α-2b (subcutaneous)	Pangenotypic	6 X 10^6 IU/m^2 3 times a week (3-18 years)
Pegylated Interferon α-2a	Pangenotypic	100mg/ m^2 per week (5-18 years)
Pegylated Interferon α-2b	Pangenotypic	1.5mg/kg per week (3-18 years)

Table 2: Direct acting antivirals (DAAs) approved in children

Age	Drugs	Genotype	Duration
3-18years	Ledipasvir and Sofosbuvir	1,4,5,6 1	12 weeks* 24 weeks (treatment exposed# without or with compensated cirrhosis)
	Sofosbuvir and ribavarin	2	12 weeks*
		3	24 weeks*
12-18 years	Glecaprevir and Pibrentasvir	Pangenotypic 1,2,4,5,6 3	8 weeks* 12 weeks (treatment exposed§ without or with compensated cirrhosis) 16 weeks(treatment exposed§, without or with compensated cirrhosis)

* normal liver or compensated cirrhosis
# Interferon and/or protease inhibitor experienced
§ Interferon and/or Sofosbuvir experienced

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Recent Recommendations for Diagnosis and Management of Autoimmune Pancreatitis in Childhood: Consensus From INSPPIRE

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Autoimmune pancreatitis (AIP) is a distinct, infrequent form of pancreatitis in children. In recent years, the disease of pediatric AIP (P-AIP) has been increasingly recognized but many questions remain regarding its physiopathology, diagnosis, and treatment.

International **S**tudy Group of **P**ediatric **P**ancreatitis: **I**n search for a cu**RE** (INSPPIRE) is the first and largest international multicenter effort studying children with acute recurrent and chronic pancreatitis. INSPPIRE has enrolled more than 400 patients with acute recurrent and chronic pancreatitis since 2012, from 22 different sites worldwide with the goal to study the risk factors, natural history, and outcome of the disorders in children.

The INSPPIRE P-AIP working group recently drafted 15 statements including definition, diagnosis, and management of P-AIP following the review and appraisal of collected data. In contrast to adult AIP (A-AIP), there are no established guidelines directing a common diagnostic and therapeutic approach for P-AIP. In fact, most previous published case series have relied on adult criteria for P-AIP management decisions. INSPPIRE P-AIP working group has made use of the expertise of a large panel of pediatric pancreatologists to develop pediatric-focused clinical recommendations for the definition, diagnosis, and treatment approach of P-AIP.

Working Definition of Autoimmune Pancreatitis

- AIP in children is a distinct subtype of pancreatitis associated with pancreatic parenchymal changes including lymphoplasmacytic and/or neutrophilic infiltrates and/or parenchymal fibrosis. A feature of the disease is the prompt clinical response to steroids.

Clinical Presentation

- Children with AIP may present with acute onset of abdominal or back pain, jaundice, fatigue, and/or weight loss.

Diagnosis

- As a form of pancreatitis, P-AIP is associated with elevated amylase and lipase. However, due to a common subacute presentation, these may have already normalized at the time of diagnosis.There is lack of data to associate a diagnosis of P-AIP with increased gammaglobulin levels or autoantibodies such as antinuclear antibody (ANA), rheumatoid factor, or anti– Saccharomyces cerevisiae antibody (ASCA).
- Transabdominal ultrasound serves as an important first line imaging technique in children presenting with symptoms suggestive of pancreatitis and/or obstructive jaundice. However, high suspicion for AIP, a hypoechoic parenchyma, diffuse or focal enlargement of the pancreas, a pancreatic mass lesion with/or without a dilated common bile duct in absence of choledocholithiasis, should prompt a magnetic resonance imaging (MRI)/MRCP.
- MRI/MRCP findings seen in P-AIP include focal, segmental, or global pancreas enlargement; hypointense pancreas on T1-weighted images; hypointense capsule-like rim on T2-weighted images; main pancreatic duct irregularities or stricture; common bile duct stricture or dilatation of the common bile duct which tapers toward an enlarged pancreatic head. Although most of these features are not specific for P-AIP, the presence of more than one should raise the suspicion for P-AIP.
- Histological findings of acute and/or chronic inflammatory cell infiltration around pancreas acinar periductular and/or presence of IgG4-positive plasma cells with or without pancreas fibrosis is suggestive for the diagnosis of P-AIP.
- A tissue diagnosis should ideally be obtained before initiating therapy. Barriers, however, exist to recommend routine EUS-guided biopsies for all children (eg, limited number of EUS-skilled pediatric endoscopists and pediatric pathologists, inadequate biopsy needles). If these barriers cannot be overcome, we suggest that the diagnosis of P-AIP can be made based on the clinical and imaging findings, because the risk for pancreatic cancer in children is extremely low.
- More data are needed to determine the utility of major papilla biopsies for the diagnosis of P-AIP

Therapeutic Options and Response to Therapy

- Some P-AIP patients may have symptom resolution without any therapy. There are, however, no long term data comparing complication or recurrence rate with and without treatment. Thus, as per adult literature and reports of P-AIP, treatment with oral prednisone is recommended for symptomatic patients after establishing the AIP diagnosis.
- Oral prednisone, 1 to 1.5mg /kg/day to a maximum of 40 to 60 mg given in 1 or 2 divided daily doses for 2 to 4 weeks is recommended as first-line treatment in PAIP. Prednisone should then be tapered.
- Treatment response to corticosteroid therapy should be assessed as clinical response within 2 weeks after starting corticosteroid therapy, imaging response by imaging such as transabdominal US, MRI/MRCP, or EUS about 3 months after starting corticosteroid therapy. In case of AIP relapse, a new course of prednisone may be tried.
- The introduction of an immunomodulator such as 6- mercaptopurine, azathioprine, mycophenolate mofetil, or infliximab (in patients with a concomitant diagnosis of inflammatory bowel disease) can be an alternative to prednisone in biopsy-proven P-AIP patients if maintenance therapy is required. There is insufficient data to suggest one immunomodulator over another.

Other Organ Involvement

- Children with a diagnosis of AIP are at greater risk to develop other autoimmune or inflammatory diseases.

Mid- and Long-term Outcome

- There is currently insufficient data about the long term risk of complications such as EPI and diabetes. Hence, patients with P-AIP should be monitored regularly by pediatric gastroenterologists, and when reaching adulthood, by adult gastroenterologists.

In this article, a working definition of the disease and recommendations for the diagnosis and therapy of P-AIP is provided. The goal is to provide a standardized approach to diagnose, treat, and follow patients with P-AIP, bring uniformity to patient care and facilitate future research.

Commentary

AIP is the only form of CP for which targeted (anti-inflammatory) treatment is available hence its identification is vital. At the present time, pediatric gastroenterologists rely on the adult AIP guidelines to diagnose and manage AIP in children and that exclusive use of adult criteria may lead to underdiagnosis of AIP in children. AIP in adults is classified into two subgroups, AIP type 1 (lymphoplasmacytic sclerosing pancreatitis) & AIP type 2 (idiopathic duct-centric pancreatitis). A definitive diagnosis of idiopathic duct-centric pancreatitis requires histologic examination (predominant type seen in children), whereas lymphoplasmacytic sclerosing pancreatitis can be diagnosed without it. Diagnosis of AIP in children can be established based on the combination of specific clinical symptoms at presentation and distinct findings on cross-sectional imaging, and ideally with histology. Clinical presentation of AIP is different in children compared with adults. In literature, majority of children had symptoms of abdominal pain and/or obstructive jaundice in combination with focal pancreas enlargement, main pancreatic duct irregularities, and distal CBD narrowing on cross-sectional imaging. Infact abdominal pain, weight loss, and fatigue are more consistently reported in children than in adult AIP patients who present with painless jaundice.A time-limited corticosteroid treatment course to treat the acute symptoms of pancreatitis, which may also prevent long-term complications of pancreatic insufficiency, is justified. However, further studies are needed to determine whether the advantages of steroid therapy outbalance the potential side effects of this therapy, particularly in children. In this regard, it will be helpful to obtain control imaging about 3 months after starting corticosteroids to evaluate for normalization of the pancreatic imaging findings, confirming the diagnosis of AIP.

Nutrition Support of Children with Chronic Liver Diseases :

A Joint Position Paper of the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition and the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition

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Introduction: Malnutrition is a known as well as a common complication of childhood chronic liver diseases (CLD) including cholestatic and end-stage liver diseases. It is associated with increased morbidity and mortality of the patients with CLD. Identification of the nutritional deficiency is of utmost importance especially in children with end-stage liver disease requiring transplantation, as optimized pre-transplant nutrition may hasten post-transplant recovery while simultaneously decreasing complications.

Aims:

1. To summarizes the available literature on various aspects of nutrition in children with chronic liver diseases (CLD).
2. To discuss the challenges and approaches in the nutritional assessment of children with CLD
3. To summarize the pathophysiology of the malnutrition in the context of CLD and to treatment recommendations and future research focus

Pathophysiology of malnutrition in children with chronic liver disease:

There are various risk factors associated with development of malnutrition in children with cholestasis and end-stage liver disease and are summarized in figure 1. Children with cholestatic liver diseases suffer from maldigestion and malabsorption of nutrients from the very early stage of disease. Later on, with the progression to end-stage liver disease, the factors such as anorexia, nausea and vomiting, abnormal nutrient metabolism, increased energy expenditure and iatrogenic factors also come to the play making the process more complex.

Nutritional Status Assessment

- History: daily oral/enteral intake, medication history, socioeconomic factors, such as access to food and vitamins or supplements.
- Physical Examination: Anthropometry (weight, height, mid upper arm circumference (MUAC), triceps skin folds (TSF). Look for features of protein, essential fatty acid, and fat-soluble vitamin deficiencies,
- Frequency of assessment depends on the severity of malnutrition, ranging from every 2 weeks in severe to every 3 months in mild degree of malnutrion

Functional assessment of nutritional status

- Handgrip strength: It can be easily measured at the bedside and has been used in adults with liver disease. Normative data for pediatric handgrip strength exist for children 4 years of age and older but its use in children with liver disease needs further studies.
- Frailty: It reflects nutritional status. It is a measure of 5 components namely slowness, weakness, shrinkage, exhaustion and diminished activity and has been found to correlate with the morbidity and wait-list mortality in adults with ESLD. A modified version of frailty for pediatric use has been developed which includes 6 minute walk for slowness, TSF for shrinkage, handgrip strength for weakness, PedsQL questionnaire for exhaustion and a physical activity questionnaire to assess diminished activity

Imaging Approaches to Determine Nutritional Status

- Dual-energy X-ray Absorptiometry, Bioelectrical impedance and Air-displacement plethysmography: These modalities provide a measure of fat and fat-free mass. However, the accuracy is decreased in fluid overload state
- Sarcopenia: It is defined as severe muscle depletion and acts as a marker of poor nutritional status. It is determined on the basis of cross-sectional imaging of psoas muscle. Sarcopenia has been shown to be associated with waitlist as well as post liver transplant mortality in adults with end-stage liver disease.

Assessment and challenges in nutritional support of children with cholestasis and end-stage liver diseases

Energy Expenditure: The energy requirements of patients with liver disease depend on their resting energy expenditure (REE), their activity level, and the severity of their maldigestion/malabsorption and disease severity. Indirect calorimetry is ideal to measure the REE but when not available, World Health Organization/United Nations University equation, can be used.

Fat: The fat requirements depend on the nutritional status as well as the presence and severity of maldigestion/malabsorption. Requirement can be assessed with serial measurement of TSF and signs of essential fatty acid deficiency (dry, rough skin, poor growth, numbness, paresthesias, and vision impairment). Total fatty acid profiles in the red blood cells can be used to test for essential fatty acid deficiency.

Protein: Requirement is increased in view of protein loss, increased amino acid oxidation, and poor nutritional status. Assessment of protein status based on markers like albumin, prealbumin, transferrin, and retinol-binding protein may be inaccurate due to their decreased synthesis or increased losses (in stool, urine or the interstitial space). Similarly, blood urea nitrogen is affected by hydration status, and the capacity of the liver to make urea. Other parameters, such as measures of sarcopenia (discussed above), may be more useful indirect indicators of chronic protein depletion.

Carbohydrates:

Usually patients receive 50% to 65% of their total calories in the form of carbohydrates. Hyperglycemia and hypertriglyceridemia may suggest insulin resistance, but former may also indicate excess carbohydrate provision. Conversely, there is risk of hypoglycemia which may go unnoticed particularly in young infants.

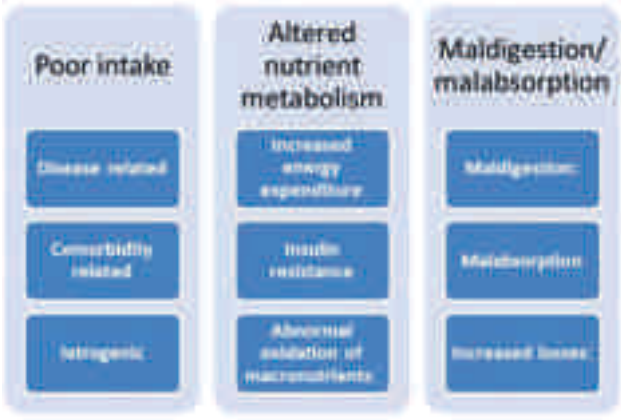

Figure 1: Pathophysiology of malnutrition in chronic liver disease

Vitamin A

Vitamin A status is usually assessed by measuring serum retinol and retinol binding protein levels but may be inaccurate with advanced liver disease. If serum retinol is <20 mg/dL, a modified relative dose response test can be used to confirm the result. Ophthalmologic assessments have poor sensitivity and specificity to detect vitamin A deficiency.

Vitamin E

Vitamin E deficiency manifests predominantly with neurologic symptoms, which may be irreversible. Screening should be done by measuring ratio of vitamin E to total lipids (triglycerides, phospholipids, and total cholesterol) in serum. The cut-off is 0.6 mg of serum vitamin E/g of total lipids in those 1 to 12 years of age and 0.8 mg/g in older children and adults.

Vitamin K:

International Normalized Ratio (INR) is used routinely in clinical practice to assess vitamin K status. However, it may be normal in cholestasis with vitamin K deficiency. Plasma PIVKA-II (protein induced in vitamin K absence) levels may assist in determining vitamin K deficiency in such patients followed by further work-up including measurement of serum parathyroid hormone, calcium, and phosphate levels.

Vitamin D

Vitamin D deficiency manifests as osteopenia and rickets. Both cholestasis and noncholestatic patients are also at risk for VDD, particularly in the context of advanced liver disease. Serum parathyroid hormone, calcium, and phosphate levels should be measured in children with suspected deficiency of vitamin D.

Zinc

Zinc deficiency manifests as skin rashes and diarrhea. In children with cirrhosis, serum zinc levels do not correlate with tissue zinc content and, as such, clinicians should have a high index of suspicion. A low alkaline phosphatase levels may be suggestive of zinc deficiency but need to be interpreted with caution in patients with cholestasis and/or bone disease, which cause elevations in this biomarker.

Recommendations of nutritional support in children with cholestasis: It should focus on providing increased total calories, lipids, and protein, while avoiding extended periods of fasting. Correction of fat-soluble vitamin deficiencies can be challenging in view of global shortage of supplements with enhanced absorption. Recommendations are summarized in table 1.

Table 1: Recommendations for nutritional support in children with cholestasis

Energy/Nutrient	Requirement	Comments
Energy	130% of requirement for age	• Account for losses associated with maldigestion/malabsorption • Monitor MUAC and TSF every 2-4 weeks • Use NG/NJ feeding if unable to meet energy goals for more than 2 weeks
Protein	~130-150% of requirements for age	•Account for losses associated with maldigestion/malabsorption
Carbohydrates	40-60% of total calories	• Hyperglycemia can occur due to insulin resistance • Hypoglycemia can also occur
Fat	• 30-50% of total calories • Start with MCT/LCT ratio of 30%/70% of total fat calories • Provide a minimum of 3% of total kcal from LA and 0.7-1% from αLA	• Increase MCT if suboptimal growth with LCT • MCT may be added in the form of both MCT oil, and MCT-containing formula. •Development of steatorrhea may suggest excessive MCT supplementation • Monitor for EFAD • Dietary sources of EFA include soy, canola, corn, walnut or fish oils, egg yolks
Vitamin A	• <10 kg – 5,000 IU/day • >10 kg – 10,000 IU/day	• Adjust based on results of monitoring labs
Vitamin D	• Cholecalciferol: 2,000-5,000 IU/day	• Larger weekly doses (e.g. 50,000 IU/once per week) are used in some centers; limited available data preclude formal recommendations re: weekly dosing • Calcitriol can be used in patients with rickets/osteoporosis in the context of cholestasis/cirrhosis; limited data in paediatrics.
Vitamin E	• TPGS: 15-25 IU/kg/day	• Adjust based on results of monitoring labs
Vitamin K	• 2-5 mg per day	• 1-10 mg IV may be required • May also be given IM
Iron	• Meet DRI for age	• Adjust based on results of laboratory investigations • Note that hepatotoxicity from iron overload can occur; clinicians should carefully consider the need for IV iron provision
Calcium	• Meet DRI for age	• Adjust based on results of laboratory investigations • Increase calcium and decrease oxalate intake in cholestatic patients with oxalate stones
Sodium	• 1-2 mEq/kg/day	• Restrict if fluid overloaded
Potassium	• 2 mEq/kg/day	• Adjust based on results of laboratory investigations

αLA= a-linolenic acid; DRI = dietary reference intake; EFA = essential fatty acids; EFAD= essential fatty acid deficiency; IM =intramuscular; IU= international units; IV= intravenous; kcal= kilocalories; LA= linoleic acid; LCT= long-chain triglycerides; MCT= medium chain triglycerides; MUAC = mid-upper arm circumference; NG = nasogastric; NJ =nasojejunal; REE = resting energy expenditure; TPGS= D-alpha-tocopheryl polyethylene glycol 1000 succinate; TSF = triceps skin folds.

CASE REPORT

Chronic button battery ingestion

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Abstract

Abstract: Button battery ingestion is a hazardous condition, which is associated with the increasing technology in household products. Most of these ingestion are unwitnessed so parent`s unawareness of potential lethal outcomes may delay the doctor visit. Most cases of button battery ingestion end uneventfully. However, those batteries that lodge in the esophagus can result in serious complications. Very few case report are available where button battery has been lodged in esophagus without causing major complication. This case presents a child who had a button battery in the esophagus for a substantial duration of 3 months with negligible consequences referred to the Pediatric department of Vivekananda polyclinic and institute of medical sciences, Lucknow

1. Introduction

Battery ingestion in children is an emerging hazard. With the use of button batteries in toys and easy accessibility to these batteries, the incidence of accidental ingestions is increasing. National Capital Poison Center data show a 6.7 fold increase in the percentage of button battery ingestions from 1985 to 2009 [1]. Most children who ingest a disk battery remain asymptomatic and pass the battery in their stool within 2-7 days [5]. Only 10% of patients who ingest disk batteries report symptoms, which are predominantly GI problems. Most common place where disk batteries become lodged, resulting in clinical sequelae, is the esophagus. Esophageal damage can occur in a relatively short period of time (2-2.5 h) when a disk battery is lodged in the esophagus. [1, 3]. Prompt removal of button battery from esophagus is indicated to prevent feared complications of esophageal perforation, tracheoesophageal fistula, perforation, mediastinitis and vocal cord paralysis. Therefore, a rapid and accurate diagnosis is critical. Prolonged lodgment of button battery in esophagus is unlikely to present without any major complication. In this article, a case of neglected button battery lodgment in the esophagus with unusual presentation as gastritis is highlighted.

2. Case report

A 3 year old previously healthy girl child presented with complaint of dull aching abdominal pain, localized to epigastric region for last three months. Pain was not associated with nausea, vomiting or fever. She was evaluated and managed as a case of gastritis in various health center, but symptom did not improve. Then she visited a private nursing home where her CT abdomen was done which showed foreign body in lower third of esophagus. Child was then referred to Paediatric department of Vivekananda polyclinic and institute of medical sciences, Lucknow for further management. On general examination, the patient was well appearing and tolerating her secretions. Her vital signs were: temperature 36.6°C, blood pressure 111/73 mm Hg, pulse 122 beats/min, respiratory rate 24 breaths/min, and pulse oximetry 100% on room air. On head and neck exam, her trachea was midline and there was no subcutaneous emphysema. Lungs were clear to auscultation bilaterally and she demonstrated no difficulty with respirations. The remainder of the physical exam was unremarkable. Her chest X-ray (fig 1) showed an opaque foreign body consistent with button battery in lower esophagus. Patient was taken to operating room and button battery was retrieved endoscopically (fig 2). Circumferential mucosal ulceration was evident at site of impaction, though there was no transmural burn. Patient was discharged without further complication and regular follow up was adviced. On follow up the patient was completely normal, with no complaints of dysphagia or abdominal pain. She was eating foods of all consistencies without aspiration or difficulty. Repeat endoscopy after two months didn't reveal any perforation, fistula or any other major complication (fig 3).

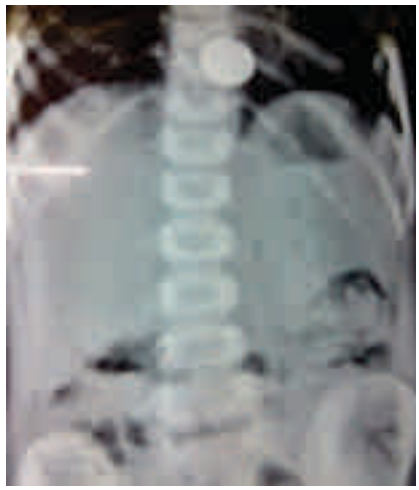

Fig 1 Plain X- ray abdomen showing a round disc battery in lower esophagus

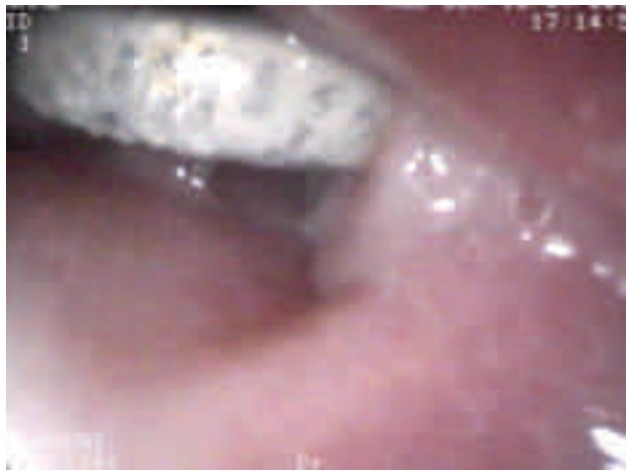

Fig 2 upper GI endoscopy showing impacted button battery a round disc battery in esophagus

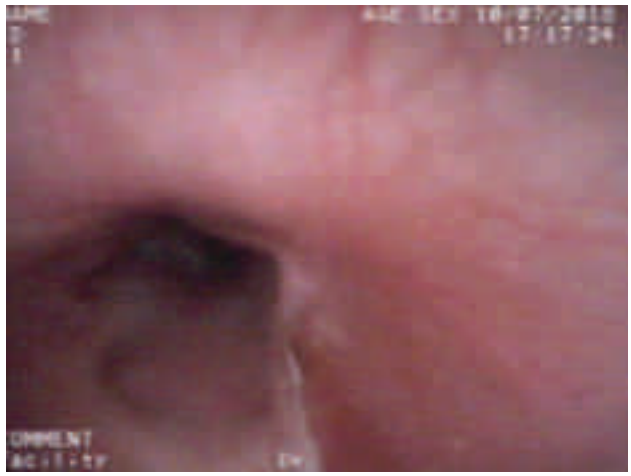

Fig 3 follow up upper GI endoscopy showing healthy esophagus

3. Discussion

Foreign body ingestion is a common encounter in pediatric emergency department. It is estimated that 80% of all cases of swallowed foreign bodies occur in children between 6 months and 6 years of age . Most of them, 90%, pass through the gastrointestinal tract without any complication . The frequency of battery ingestion has been increasing in recent years due to greater accessibility from electronic toys and adult devices. Most important predictors of clinically significant outcome were battery diameter greater than 20 mm and a patient age less than 4 years . Lovits and coworkers noticed a 6- to 7-fold increase in the rate of major or fatal outcomes by battery ingestion over three-year period (0.443% in 2007–2009) compared with (0.066% in 1985–1987 [3]. Button battery ingestion can cause injury in three primary ways: leakage of caustic alkaline electrolyte; ischemic necrosis caused by direct pressure; and production of external electrolytic current that hydrolyzes tissue fluids creating hydroxide at the negative pole [3]. The esophagus is susceptible to foreign body retention because of its anatomic areas of narrowing and weak peristalsis [1]. Unfortunately, battery ingestion often goes unwitnessed leading to severe damage by the time of presentation. Foreign body ingestion (including batteries) can be very difficult to diagnose without a radiograph as symptoms of cough, fever, decreased oral intake, difficulty swallowing, sore throat, and vomiting are symptoms of common viral infections .

In the case described above, the patient presented with three months of abdominal pain and was ultimately diagnosed with an ingested button battery lodged in her esophagus. Upon removal, there was surprisingly limited injury despite long-term ingestion of a button battery sized 20 mm in diameter.

Guidelines for management of button battery ingestion[2,8,9,10,11]

- Index of suspicion should be high because many cases are asymptomatic.
- Plain radiography of chest and abdomen not only confirms the diagnosis but also locates the site of the battery. The battery can be distinguished from a coin with the help of a double ring or halo sign seen in a X-ray.
- After diagnosis, endoscopy should be performed as soon as possible to remove the battery and

perform a complete exploration of the esophagus to rule out early complications.

- The battery located within the esophagus should be removed within 2 h of ingestion because of the potential to cause mucosal injury. This is much shorter time period compared to previous reports, as lithium batteries have higher capacitance and voltage.
- Hemorrhage occurs within 12–14 h of ingestion and may be fatal
- Batteries which have passed into the stomach need not to be extracted on emergent basis. Such batteries must be removed if they fail to cross pylorus in 8 h, if patients have GI symptoms or when the size of the battery is large.
- Specific complications like tracheoesophageal fistula and aortoesophageal fistula occur between 9 and 18 days of ingestion, depending upon the location of negative pole.
- Length of observation, duration of esophageal rest, and need for serial imaging and endoscopy/ bronchoscopy are determined based on the location and severity of injury
- Complications include esophageal perforation, tracheoesophageal fistula, mediastinitis, vocal cord paralysis, tracheal stenosis, aspiration pneumonia, empyema, abscess, pneumothorax, spondylodiscitis, and perforation into large vessels

4. Conclusion

We present this atypical case to increase awareness surrounding this diagnosis amongst primary care physicians. Button battery ingestions that remain in the esophagus can result in severe complications and death within hours to days. This case presents a child who had a button battery in the esophagus for 3 months. It is important for physicians to keep ingestion of button batteries in their differential for children presenting with vomiting, coughing or gagging, refusal to eat, and complaints of abdominal or chest pain. Clinical suspicions should be confirmed by a plain radiography followed by an emergency endoscopy if it reveals a round opaque foreign body. The earlier the diagnosis is made, the less serious and devastating complications occur.

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GUESS THE DIAGNOSIS

Zaheer Nabi, Sundeep Lakhtakia, Upender Shava, Rangarao Devarasetty, D. Nageshwar Reddy
Asian Institute of Gastroenterology, Hyderabad, India

A 5-year-old child presented to the hospital because of a history of recurrent episodes of abdominal pain. Evaluation revealed elevated transaminases (alanine aminotransferase, 340 IU/L; aspartate aminotransferase, 400 IU/L).

An Ultrasound was performed. (Fig 1a) Thereafter based on the findings an endoscopic cholangiography (ERC) was performed. (Fig 1b).

What is the diagnosis?

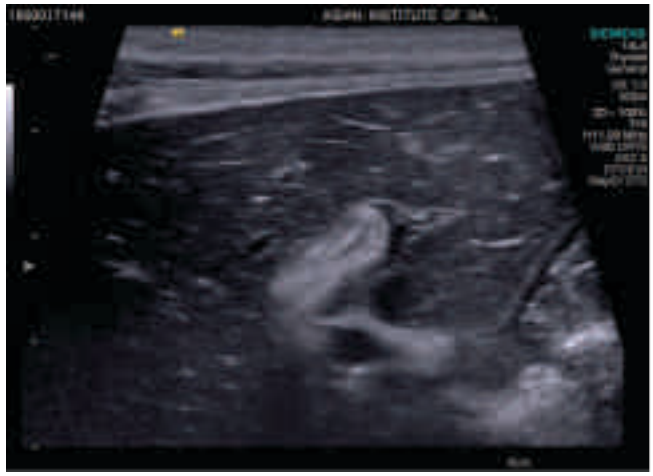

Fig 1a

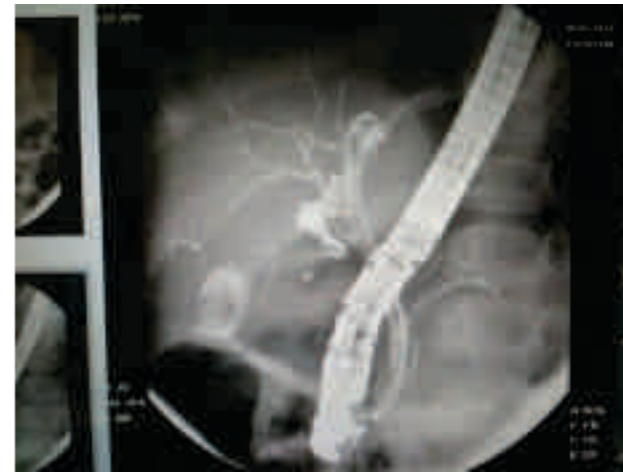

Fig 1 b

Answer

Biliary Ascariasis

Ultrasound revealed dilatation of the common bile duct (6.6 mm) with a curvilinear echogenic structure. The central portion of this structure was anechoic, and there was no shadow effect. These findings were suggestive of *biliary ascariasis*. The Ascaris worm could be traced up to the intrahepatic duct. Cholangiography showed a linear filling defect in the common bile duct. Endoscopic sphincterotomy was performed, and a live worm was extracted from the bile duct with a biliary balloon, followed by its removal from the duodenum with rat-tooth forceps (Fig. 2)

Hepatobiliary and pancreatic ascariasis (HPA) is caused by entry of the nematode, Ascaris lumbricoides from the duodenum in to the biliary and pancreatic ductal lumen. It is prevalent worldwide with an overall prevalence of 25%. An estimated 1.4 billion people are infected. Ascariasis is ubiquitous in the Indian subcontinent.

The natural habitat of an ascaris is the jejunum. HPA is initiated by proximal movement of the organisms in to duodenum. Heavy worm-load is the main factor for forward march of the ascarides.

HPA is a disease of adults (mean age 35 years, range 4 to 70 years) with female predominance (female: male ratio 3:1). Ascariasis is more often prevalent in children, however, HPA is seen less often in children. This may be due to smaller size of the ampullary orifice

HPA can cause six distinct clinical presentations including - biliary colic, acute cholangitis, acalculous cholecystitis, hepatic abscess, acute pancreatitis and recurrent pyogenic cholangitis.

Diagnosis of HPA can be made by ultrasonography, duodenoscopy and ERCP. Of late, MRI and MRCP can help in diagnosis of HPA and may replace ERCP if therapeutic procedure is not envisaged. On ultrasound it appears as a thick long linear or curve non-shadowing echogenic strip containing a central longitudinal anechoic tube (four-line sign), representing the digestive tract of the worm.

The treatment for HPA is to give appropriate treatment for clinical syndromes along with effective anthelmintic therapy. Anthelmintic drugs which are very effective include pyrantel pamoate, mebendazole, albendazole and ivermectin

Endotherapy should be performed in case patient's symptoms do not subside on intensive medical treatment and/or ascrides fail to move out of the ductal lumen up to 3 wk of follow up.

Further Reading

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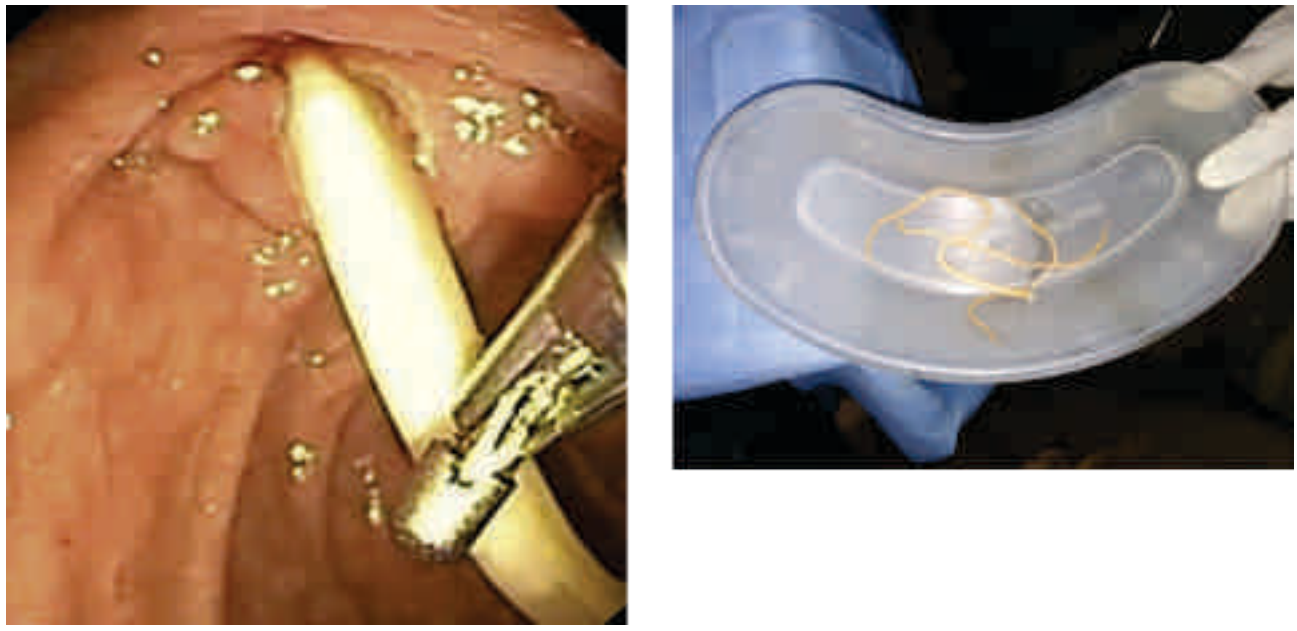

(Fig. 2)

STUDY 1 : Hepatology :Whom to do Kasai – Genetic signature?

Luo, Z., Shivakumar, P., Mourya, R., Gutta, S., & Bezerra, J. A. (2019). Gene Expression Signatures Associated With Survival Times of Pediatric Patients With Biliary Atresia Identify Potential Therapeutic Agents. Gastroenterology. doi:10.1053/j.gastro.2019.06.017

Factors that affect outcomes of patients with biliary atresia were studied in this paper. Liver biopsies and clinical data obtained from infants with cholestasis and without liver disease. Messenger RNA (mRNA) was isolated randomly assigned to discovery (n=121) and validation sets (n=50), and analyzed by RNA sequencing.14-gene mRNA expression pattern predicted shorter and longer survival times in both the discovery (n=121) and validation sets (n=50) of children with Biliary atresia. Gene expression signature combined with level of bilirubin at 3 months after hepato-portoenterostomy, identified children who survived for 24 months. Many mRNAs expressed at high levels in liver tissues with good survival had enriched scores for glutathione metabolism suggesting the importance of N acetyl Cysteine. While mRNAs encoding proteins that regulate fibrosis genes were increased in liver tissues from infants who did not survive for 2 years. For evaluation of surgical success, importance of underlying genetic factors is underscored. Thus 14-gene signature has the potential to change our approach to children with biliary atresia.

STUDY 2: Luminal Gastroenterology: What's the level of Calprotectin?

Kennedy, Nicholas A. et al. Association Between Level of Fecal Calprotectin and Progression of Crohn's Disease .Clinical Gastroenterology and Hepatology, Volume 17, Issue 11, 2269 - 2276.e4 https://doi.org/10.1016/j.cgh.2019.02.017

918 patients with Crohn's disease (CD) were examined retrospectively. Clinical data and fecal calprotectin measurements were analyzed .Median follow-up was of 50.6 months. A calprotectin level cut-off of 115 mcg/g was identified as optimal for separation of those with and without disease progression. Earlier studies have identified a cut-off value of 250 mcg/g as being useful to distinguish active from inactive disease. In this study a lower threshold of 115 mcg/g was identified suggesting that lower levels of inflammatory activity still may be associated with an adverse outcome.

STUDY 3: Hepatology: Interesting NASPGHAN Scientific abstract worth considering?

Machine learning models to predict waitlist mortality among pediatric liver transplant candidates: an update to PELD. Sonja Swenson , John Roberts , Emily Perito Pediatrics, University of California, San Francisco, Palo Alto, CA; Surgery, University of California, San Francisco, San Francisco, CA

No studies till now have examined whether Machine Learning techniques that could improve prediction modeling for pediatric liver transplant candidates. UNOS Standard Transplant Analysis and Research (STAR) data was used in the study. Machine Learning identified patterns and interactions in data that can improve prediction accuracy. 16 objective variables were evaluated for inclusion. Cohort included all U.S. liver transplant candidates. A Refit PELD was built with a multivariate Cox Proportional Hazards (PH) model using current PELD components. PELD+ was derived by backward stepwise regression as an expanded Cox PH model. RSF is a ML model that creates many independent decision trees; each form a unique data subset to determine the final model. Random Forest RSC (Rv.3.5.3) .It is used to produce 1000 trees grown under log-rank competing risks splitting. RSF's C-index was significantly higher than that of Refit PELD or PELD+. RSF's most important

predictors were bilirubin, INR, height z-score, age, albumin, creatinine, ascites and weight z-score. Thus ML techniques could improve mortality predictions for children awaiting liver transplant.

STUDY 4: Luminal Gastroenterology Monogenic vs Non-monogenic IBD: APPROACH?

Lega, S., Pin, A., Arrigo, S., Cifaldi, C., Girardelli, M., Bianco, A. M., ... Bramuzzo, M. (2019). Diagnostic Approach to Monogenic Inflammatory Bowel Disease in Clinical Practice: A Ten-Year Multicentric Experience. Inflammatory Bowel Diseases. doi:10.1093/ibd/izz178

Patients with VEO-IBD and early onset IBD with severe/atypical phenotypes (EO-IBD s/a)(n= 93) managed between 2008– 2017 who underwent a genetic workup were studied. In 13% a genetic diagnosis was confirmed. Candidate sequencing (CS) was performed in 50%, and next generation sequencing (NGS) was performed in 90%. Candidate sequencing had a good diagnostic performance when guided by clinical features specific for known monogenic diseases. NGS helped finding new causative genetic variants. 59% of patients in group <2 years of age.59% were males .8% had family history of IBD.Extra-intestinal manifestations were present in 43%.

Monogenic IBD group had <1 month onset .They were predominantly Boys .The coexistence of extraintestinal manifestation was noted in this group .Both Colonic and small bowel and/or perianal involvement was present. Sanger sequencing helped in diagnosis .Bone marrow transplant was useful in specific cases. Nonmonogenic IBD had later onset without gender bias. Extraintestinal manifestations were less likely.NGS: next generation sequencing helped in diagnosing these cases.

Add on: Common Genetic variants that cause VEOIBD are XIAP, IL10RA,G6PC3,MEFV, LRBA, FOXP3,and TTC7A. Genetic variants ZAP70, RAG2, IL2RG, LIG4, ADA, DCLRE1C, CD3G, are generally associated with immunodeficiency. New sequencing technologies are diagnosing more genetic variants which are associated with VEOIBD. Streamlining investigations would be helpful in resource poor settings. Easy availability of NGS may help in diagnosis in most cases with possibility of missing a few. Judicious approach based on clinical tell-tale signs with endoscopic findings may integrate both the approaches in future.

STUDY 5: Luminal Gastroenterology: Epigenetics in Celiac Disease: Mucosal biopsy?

Romero-Garmendia I, Garcia-Etxebarria K, Hernandez-Vargas H, et al. Transcription Factor Binding Site Enrichment Analysis in Co-Expression Modules in Celiac Disease. Genes (Basel). 2018;9(5):245. Published 2018 May 10. doi:10.3390/genes9050245

Transcription factor binding site enrichment analysis[5] in co-expression module in celiac disease was studied by Irati Romero-Garmendia et al .It is the first whole genome co-expression analytical study that tests the effect of gliadin in duodenum biopsies of pediatric patients. (n = 18) .Duodenal biopsies samples were immediately stored in liquid nitrogen. RNA was extracted later. In-vitro culture (with or without gliadin) of biopsy portion on two set of patients' viz. Celiac diagnosed on gluten free diet and celiac disease patient at diagnosis were studied. They noted transcription factor like IRF1, ELKI, NFKB1 and CREB1 were significantly up regulated in celiac disease. These were the key molecules which control gene expression. ELK1 transcription factor was over expressed at mRNA level in active celiac disease. ELK1 had an important role in deciding intestinal permeability.

Celiac disease is multi-factorial in etiology. Transcription factor analysis helps us to understand important role of epigenetics in pathophysiology.

Compiled by : Dr. Yogesh Waikar

Publications by ISPGHAN members
(September – November, 2019)

September

1. *Sood V, Lal BB, Gupta E, Khanna R, Siloliya MK, Alam S. Hepatitis A Virus-related Pediatric Liver Disease Burden and its Significance in the Indian Subcontinent. Indian Pediatr. 2019 Sep 15;56(9):741-744.*

Hospital records of 431 children (age <18 y) diagnosed to be suffering from acute HAV infection during 2011 to 2018 were extracted and analyzed. Additionally, a seroprevalence study was done on 2599 participants (696 children and 1903 adults). The authors concluded that HAV infection is the major contributor the overall pediatric liver disease burden. A significant proportion of subjects remain susceptible to HAV infection even after 10 years of age. Population-based studies are required to further delineate the epidemiology of HAV infection in India for deciding introduction of HAV vaccine in the national immunization schedule

2. *Das MC, Srivastava A, Yadav RK, Yachha SK, Poddar U. Optic nerve sheath diameter in children with acute liver failure: A prospective observational pilot study. Liver Int. 2019 Sep 24. doi: 10.1111/liv.14259. [Epub ahead of print]*

Early detection of raised intracranial pressure (ICP) improves outcome in acute liver failure (ALF). The authors evaluated the feasibility of bedside, ultrasound-guided measurement of optic nerve sheath diameter (ONSD) in normal and ALF children and correlation of ONSD with grade of hepatic encephalopathy (HE), international normalized ratio (INR) and blood ammonia (BA). Forty-one ALF and 47 healthy children (5-18 years) were prospectively enrolled and 12 hourly clinical evaluations was done. The authors concluded that ONSD can be safely and easily measured in ALF children and correlates with HE grade, INR and BA. Normal ONSD in children (>4 years) is <4.5 mm and value of >5.1 mm in ALF requires urgent attention.

3. *Tripathi PR, Poddar U, Yachha SK, Sarma MS, Srivastava A. Efficacy of Single Versus Split Dose Polyethylene Glycol for Colonic Preparation in Children: A Randomized Control Study. J Pediatr Gastroenterol Nutr. 2019 Sep 20. doi: 10.1097/MPG.0000000000002511. [Epub ahead of print]*

Polyethylene glycol (PEG) is the most effective colon cleansing agent but volume related adverse effects are common. Though split-dose PEG is used in adults, no pediatric study so-far has compared split-dose with single-dose PEG. The authors aimed at comparing the efficacy and tolerability of split-dose versus single-dose PEG for bowel preparation in children. In this study consecutive children (1-18 years) were randomized into either single-dose or split-dose PEG. Single-dose group received 4000 mL/1.73mPEG solution day before colonoscopy while split-dose group received half dose day before and the remaining half on the day of colonoscopy. The conclusion drawn was that split-dose PEG is more effective than single-dose regimen for bowel preparation with better tolerability and improved sleep quality in the pediatric population.

4. *Maji P, Malik R, Lodha R, Bagga A. Sickle Cell Intrahepatic Cholestasis with Acute Liver Failure and Acute Kidney Injury: Favourable Outcome with Exchange Transfusion. Indian J Pediatr. 2019 Sep 13. doi: 10.1007/s12098-019-03071-7.[Epub ahead of print]*

Sickle cell disease may present with a life threatening complication of intrahepatic cholestasis. Bilirubin may be very high (> 50mg/dL) in this condition. Exchange transfusion maybe life-saving.

5. *Neupane N, Krishnamurthy S, Jagadisan B, Dhodapkar R. Hepatitis B Seroprotection in Pediatric Nephrotic Syndrome. Indian Pediatr. 2019 Aug 15;56(8):659-662.*

The authors concluded that children with nephrotic syndrome, in general, and steroid-resistant nephrotic syndrome in particular, show poor seroprotection with Hepatitis B vaccination.

6. *Menon J, Kumar A, Vaiphei K, Lal S. An interesting cause of chronic abdominal pain in a child. Trop Doct. 2019 Sep 17:49475519876422. doi:10.1177/0049475519876422. [Epub ahead of print]*

Chronic abdominal pain without red flag signs is usually functional abdominal pain and does not require investigation. The authors encountered an eight-year-old boy who was subsequently diagnosed with a retroperitoneal ganglioneuroma. In view of the rarity of this tumour and its presentation, the authors were prompted to report this case.

7. *Valamparampil JJ, Reddy MS, Shanmugam N, Vij M, Kanagavelu RG, Rela M. Living donor liver transplantation in Alagille syndrome-Single center experience from south Asia. Pediatr Transplant. 2019 Sep 30:e13579. doi: 10.1111/petr.13579.[Epub ahead of print]*

To analyze the clinical characteristics and the outcomes of living donor liver transplantation in children with Alagille syndrome (AGS). Clinical data of children with AGS who underwent liver transplantation between July 2009 and May 2019 in the authors unit were retrospectively analyzed. Primary end-points were patient and graft survival. Ten children with AGS underwent living donor liver transplantation at a median age of 28 months (range, 12-84 months). The most common indication for transplantation was severe pruritus with poor quality of life. They reported 100% patient and graft survival at a mean follow-up of 32 months (range 3-72 months). This is the first series of LDLT for Alagille syndrome in the Indian sub-continent. They report excellent post-transplant outcomes in contrast to outcomes reported from Western literature.

8. *Ravindranath A, Sen Sarma M, Yachha SK. Bile acid synthetic defects: Simplified approach in a nutshell. Hepatobiliary Pancreat Dis Int. 2019 Sep 12.pii: S1499-3872(19)30181-X. doi: 10.10 16/j.hbpd.2019.09.003. [Epub ahead of print]*

In this review the authors present a simplified approach to bile acid synthetic defects.

October

1. *Snehavardhan P, Lal BB, Sood V, Khanna R, Alam S. Efficacy And Safety Of Sodium Benzoate In The Management Of Hyperammonemia in Decompensated Chronic Liver Disease of the Childhood- A Double Blind Randomised Controlled Trial. J Pediatr Gastroenterol Nutr. 2019 Oct 22. doi: 10.1097/MPG.0000000 000002521. [Epub ahead of print]*

It was a prospective, interventional, double-blinded randomized controlled trial conducted from August'2017 to December'2018. The objective was to evaluate the efficacy and safety of sodium benzoate in the management of hyperammonemia and hepatic encephalopathy in decompensated chronic liver disease (CLD). The authors concluded that the addition of sodium benzoate significantly reduced the ammonia levels on the first 2 days of therapy but the effect was not sustained till day 5. The effect of sodium benzoate would probably be more sustained, if higher dosage (400 mg/kg/day) could be used under monitoring of benzoate levels. There was no effect on resolution of HE. Sodium benzoate caused an increasing trend of adverse events with no effect on short-term survival.

2. *Ravindranath A, Sen Sarma M, Yachha SK, Lal R, Singh S, Srivastava A, Poddar U, Neyaz Z, Behari A. Outcome of portosystemic shunt surgery on pre-existing cholangiopathy in children with extrahepatic portal venous obstruction. J Hepatobiliary Pancreat Sci. 2019 Oct 25. doi: 10.1002/jhbp.692. [Epub ahead of print]*

This study was performed to assess the effect of porto-systemic shunt surgery (PSS) on portal cavernoma cholangiopathy (PCC) in children with EHPVO. Children with EHPVO and PCC (unfit for Meso-Rex shunt) underwent Magnetic resonance cholangiogram (MRC) and Magnetic resonance portovenogram (MRPV) before non-selective PSS. Those with patent shunt were re-evaluated at least 6 months after surgery with MRC, MRPV and compared with pre-shunt images. The authors concluded that non-selective PSS decompresses esophago-gastro-splenic venous circuit effectively but fails to ameliorate cholangiopathy and

peribiliary collaterals. Peristence of cholangiopathy is attributable to SMV block.

3. *Ravindranath A, Srivastava A, Yachha SK, Poddar U, Sarma MS, Saraswat VA,Mohindra S, Yadav RR, Kumar S. Childhood pancreatic trauma: Clinical presentation, natural history and outcome. Pancreatology. 2019 Oct 31. pii: S1424-3903(19)30762-8. doi:10.1016/j.pan. 2019.10.008. [Epub ahead of print]*

The objective of this study was to study the presentation, management strategies and long-term natural history of children with pancreatic trauma. Children admitted with pancreatic trauma were analyzed for their presentation, management and outcome. 36 children [29 boys, age 144 (13-194) months] presented at 30 (3-210) days after trauma. Management consisted of various combinations of nasojejunal feeds [n = 17,47.2%], TPN [n = 5,13.8%], octreotide [n = 13,36%], pseudocyst drainage [radiological (n = 18,50%), endoscopic (n = 3,8.3%)] and ERCP [n = 12,33.3%]. Surgical intervention was done in 2 (5.5%) cases. Of the 32 cases in follow-up, 19 (59.3%) recovered and 13 (40.6%) developed CP, with half (6/13) of them being symptomatic with recurrent pain. The authors concluded that multi-disciplinary non-operative management is effective for managing pancreatic trauma in 94.4% of children, with 75% requiring radiological or endoscopic intervention. 40% developed structural changes later but only half were symptomatic.

4. *Karunakaran P, Kochhar R, Lal S, Nampoothiri RV, Varma N, Varma S, Malhotra P. High Prevalence of Celiac Disease in Patients with Immune Thrombocytopenia. Indian J Hematol Blood Transfus. 2019 Oct;35(4):722-725*

Celiac disease (CD) is known to be associated with several autoimmune disorders. The authors studied the prevalence of subclinical CD among patients with immune thrombocytopenia (ITP) as compared to general population. Four patients of primary ITP (4/79) were positive for both serology as compared to 2 (2/316) healthy controls [odds ratio 8.37 (CI 1.50-46.47, $p < 0.005$)]. Among the ITP cases only one had clinical symptoms of CD while none of the healthy controls had symptoms of CD. There is a significantly higher prevalence of subclinical CD in patients with ITP.

5. *Menon J, Shanmugam N, Vij M, Reddy MS, Rela M. Cutaneous Leishmaniasis Presenting As Macrocheilitis In A Post Liver Transplant Pediatric Patient. J Pediatr Gastroenterol Nutr. 2019 Oct 29. doi: 10.1097/MPG.0000000 000002545. [Epub ahead of print]*

A 3-year-old boy, who underwent living donor liver transplantation at 1 year age for biliary atresia presented during his routine follow with painful perioral swelling of two months duration. Considering cellulitis, he was treated with intravenous antibiotics for 5 days, but with little improvement. Kaposi sarcoma was considered in immunosuppressed patient and lip biopsy was done which suggested Leishmaniasis

6. *Ahlawat R, Parikh NS, Jhaveri A. Triple Diagnosis of Crohn's Disease, Celiac Disease, and Eosinophilic Esophagitis in a Child With Siderius-Hamel Syndrome. WMJ. 2019 Oct;118(3):140-142*

The authors present a case of a child with Siderius-Hamel syndrome who had characteristic findings of all these conditions - Crohn's disease, celiac disease, and EoE-an occurrence that to our knowledge has not been reported previously.

November

1. *Shankar S, Bolia R, Foo HW, D'Arcy CE, Hardikar N, Wensing M, Hardikar W. Normal Gamma Glutamyl Transferase Levels at Presentation Predict Poor Outcome in Biliary Atresia. J Pediatr Gastroenterol Nutr. 2019 Nov 14. doi:10.1097/MPG.0000000000002563. [Epub ahead of print]*

Gamma-glutamyl transferase levels (GGT) are typically elevated in biliary atresia (BA), but normal GGT levels have been observed. This cohort of 'normal GGT' BA has not been described nor has the prognostic value of GGT level on outcomes in BA. Infants diagnosed with BA between 1991 - 2017 were

retrospectively analysed. Outcomes were defined as survival with native liver, liver transplantation (LT) and death. Patients were categorised into normal (<200IU/L) or high GGT groups based on a mean of three consecutive GGT values done prior to Kasai portoenterostomy (KPE). Baseline parameters, age at surgery, clearance of jaundice and outcomes were compared between the two groups. The authors concluded that 12.3% of infants with BA had normal GGT levels at diagnosis. Low GGT levels at presentation in biliary atresia was associated with a poorer outcome.

2. *Nabi Z, Ramchandani M, Chavan R, Darisetty S, Kalapala R, Shava U, Tandan M,Kotla R, Reddy DN. Outcome of peroral endoscopic myotomy in children with achalasia. Surg Endosc. 2019 Nov;33(11):3656-3664*

Achalasia cardia is rare in children and optimum endoscopic management options are not well known. Peroral endoscopic myotomy (POEM) is a novel treatment modality for achalasia with excellent results in adult patients. The long-term outcomes of POEM are not well known in children. In this study, the authors evaluated the outcome of POEM in children with idiopathic achalasia. A total of 44 children (boys-23, girls-21) with mean age of 14.5 ± 3.41 years (4-18) were diagnosed with achalasia during the study period. POEM was successfully performed in 43 children (technical success-97.72%). Intra-operative adverse events occurred in 11 (25.6%) children including retroperitoneal CO2 (7), capno peritoneum (3), and mucosal injury (1). Clinical success at 1, 2, 3, and 4 years' follow-up was 92.8%, 94.4%, 92.3%, and 83.3%, respectively. Erosive esophagitis was detected in 55% (11/20) children. On 24-h pH study, GER was detected in 53.8% (7/13) children.

3. *Malik I, Bhatia V, Kumar K, Sibal A, Goyal N. Pediatric Hepatic Venous Outflow Tract Obstruction: Experience from a Transplant Center. Indian Pediatr. 2019 Nov 15;56(11):965-967.*

The authors carried out a review of case records of children diagnosed with hepatic venous outflow tract obstruction at their center in last 10 years. Out of 11 cases identified, 6 had variable blocks in the hepatic venous system and 4 had combined hepatic venous and inferior vena cava (IVC) block. One child with paroxysmal nocturnal hemoglobinuria (PNH) had isolated IVC involvement. Angioplasty was attempted in 3 patients; among them 2 had successful outcome. Seven children with advanced liver disease underwent transplantation, which was successful in six. With availability of modalities like interventional radiology and transplantation, the overall prognosis of hepatic venous outflow tract obstruction seems to be good when managed in a well-equipped center.

4. *Deswal S, Dewan V, Ahuja A, Singh S, Tiotia R, Vani Narayani K, Anwar S. Endo-gastric Teratoma - A Rare Cause of Upper GI Bleeding in an Infant! Indian J Pediatr. 2019 Nov 11. doi: 10. 1007/s12098-019-03097-x. [Epub ahead of print]*

The authors report a rare cause of upper gastrointestinal bleeding in an infant - An endo-gastric teratoma.

5. *Chang MH, Fischler B, Blauvelt B, Ciocca M, Dhawan A, Ekong U, Ni YH, Porta G, Sibal A, DAgostino D, Wirth S, Mohan N, Schwarz KB. Survey of Impediments to Prevention of Mother-to-infant Transmission of Hepatitis B Virus by International Societies. J Pediatr Gastroenterol Nutr. 2019 Dec;69(6):648-654*

Mother-to-infant transmission (MIT) is the leading cause of hepatitis B virus (HBV) infections globally. The aim of this international study was to assess the impediments to prevention of (MIT) of HBV. cross-sectional survey was developed by the Federation of the International Societies for Pediatric Gastroenterology, Hepatology and Nutrition(FISPGHAN). The survey was sent to HBV experts of the 5-member societies of FISPGHAN, and 63 of 91 countries/regions responded. Among the participating countries/ regions, 11% did not implement infant HBV immunization programs. The first dose of vaccine was given >24 hours in 36% of the total countries and 100% of African countries. The recommended birth dose was unavailable for outborn neonates in 45% of the total countries, including 92% of African and 50% of Latin American countries/regions. During pregnancy, 44% countries do not screen maternal viral markers, and 46% do not provide third trimester antiviral therapy for highly viremic pregnant mothers.

Publications inadvertently missed in the previous issues –

1. *Meena DK, Akunuri S, Meena P, Bhramer A, Sharma SD, Gupta R. Tissue Transglutaminase Antibody and Its Association with Duodenal Biopsy in Diagnosis of Pediatric Celiac Disease. Pediatr Gastroenterol Hepatol Nutr. 2019 Jul;22(4):350-357*

This study aimed to evaluate a possible association between the anti-tissue transglutaminase antibody (anti-tTG) titer and stage of duodenal mucosal damage and assess a possible cut-off value of anti-tTG at which celiac disease (CD) may be diagnosed in children in conjunction with clinical judgment. The authors concluded that There is an association between the anti-tTG titer and stage of duodenal mucosal injury in children with CD. An anti-tTG value of 115 AU/mL (6.4 times the upper normal limit) had 76% sensitivity, 100% specificity, with a 100% PPV, and 17% NPV for diagnosing CD (95% CI, 0.75-1). This cut-off may be used in combination with clinical judgment to diagnose CD.

2. *Malik I, Kumar K, Hussain H, Bhatia V, Sibal A, Malhotra S. Celiac disease: What the Indian pediatricians know about the disease. Indian J Gastroenterol. 2019 Jun;38(3):263-267*

To ascertain the knowledge, awareness, and practices pertaining to celiac disease (CD) among the Indian pediatricians. A survey link containing a questionnaire was shared through electronic mail using a pediatric database. The survey was kept active for 6 months; all responses received at the end of the survey were analyzed. Two hundred and seventy one pediatricians out of more than 10,000 chose to respond to the survey. Most pediatricians agreed that more patients with CD are being diagnosed than earlier. Most pediatricians opined that clinical manifestations which prompted to a diagnosis of CD were failure to thrive (96.2%) and chronic diarrhea (81.4%). Knowledge about atypical manifestations of celiac disease was low. Though knowledge about the common association of CD with type 1 diabetes (62.1%) and autoimmune hepatitis (55.8%) was there, awareness about its association with other uncommon conditions was lacking. A trial of gluten-free diet (GFD) was thought to be a logical step if serology was positive by 31.3% of respondents. While 87.7% of pediatricians advocated lifelong adherence to GFD, 12.3% felt that GFD could be discontinued in the future. This web-based survey revealed that though pediatricians are seeing increasing number of celiac disease patients, there is a need to increase awareness regarding the disease, its associated conditions, the need for mucosal biopsy to confirm the diagnosis and the necessity of lifelong adherence to GFD.

3. *Nabi Z, Basha J, Lakhtakia S, Shava U, Pal P, Ramchandani M, Gupta R, Kalapala R, Darisetty S, Tandan M, Reddy DN. Disconnected Pancreatic Duct in Children With Walled OFF Necrosis: Impact on Outcomes of Endoscopic Drainage. J Pediatr Gastroenterol Nutr. 2019 Jul;69(1):116-119*

Disconnected pancreatic duct syndrome (DPDS) is frequently encountered in cases with walled off necrosis (WON). The impact of DPDS on the outcomes of pancreatic fluid collections (PFCs) is not well known. In this study, the authors aimed to evaluate the incidence of DPDS and its clinical impact on the outcomes of endoscopic ultrasound (EUS)-guided drainage of PFC in children. The authors concluded that majority of the children with DPDS do not develop a symptomatic recurrence of PFC after the removal of cystogastric stents. DPDS may be a risk factor for the development of new-onset diabetes. However, future prospective studies are needed.

4. *Ravindranath A, Srivastava A, Seetharaman J, Pandey R, Sarma MS, Poddar U,Yachha SK. Peritoneal Lymphomatosis Masquerading as Pyoperitoneum in a Teenage Boy. ACG Case Rep J. 2019 Jun 17;6(6):e00116.*

A 16-year-old boy presented with 1 month of fever, abdominal pain, and distension. The ascitic tap drained pus-like fluid, and ultrasonography showed diffuse thickening of the omentum and mesentery with echogenic ascites. The ascitic fluid appearance deceptively resembled pus, but further analysis revealed atypical lymphocytes. Omental and bone marrow biopsies confirmed Burkitt lymphoma. Awareness of this rare presentation is imperative for making a correct diagnosis.

Compiled by : Dr. Rishi Bolia

ISPGHAN Literature Festtival -2019: 23rd & 24th November, Raipur, Chhattisgarh

Dr Rimjhim Shrivastava, Consultant, Pediatric Gastroneterology and Hepatology, Raipur, Chhattisgarh

"Learning is a treasure that will follow its owner everywhere. Always walk through life as if you have something new to learn and you will."

Every year, medical grassland is flooded with new researches and knowledge. Keeping a track of these new developments is the only way to be the authority in that domain.

ISPGHAN Literature Fest is a similar platform for learning, where the Pediatric –Gastro fraternity get enlighted among themselves.

The successful paradigm of Literature festival laid by Dr Yogesh Waiker in 2018 at Nagpur, consists of only academic affairs, with literature reviews on various topics and sharing of clinical experiences in a closed group.

ISPGHAN Literature fest-2019 was organized in Raipur, Chhattisgarh on 23rd & 24th November. A total of 18 delegates participated in this. In this two days meet latest advancements were discussed.

Following are the important take home messages by the different speakers:

I. Updates on diagnosis and Management of Wilson's disease : Dr Aabha Nagral

1) Modified Leipzig score > 4 as described by the INASL, ISPGHAN and Movement Disorders Society of India consensus meeting (J of Clin and Exp Hepatology 2019) is a useful score for diagnosing Wilson's disease as no single parameter is diagnostic. Serum copper, Penicillamine challenge, Liver copper have little role in diagnosis of Wilson's disease.
2) Relative exchangeable copper reflects free copper and its measurement seems promising in the diagnosis and management of the disease
3) Trientine is now manufactured and available in India
4) Earlier switch from d-penicillamine to zinc once clinical improvement is achieved seems to be effective in symptomatic Wilson's disease.
5) AARC-ACLF score > 11 predicts 90 day mortality in decompensated WD the best (compared to NWI, HD score, PELD, CLIF-SOFA).
6) Plasmapharesis seems effective in acute presentation of liver failure as a bridge to liver transplantation.
7) Liver transplantation has good long term results including with heterozygous donors, however should be avoided in severe neuro Wilson's Disease

II. Celiac Crisis Vs. Refeeding Syndrome : Dr L K Bharti

1) Celiac crisis and Refeeding syndrome are closely mimicking clinical conditions.
2) Celiac crisis can be precipitated by general immune stimulus due to many factors like malnutrition, bowel infection, and poor compliance to GFD, post surgery.
3) About half of the patients of celiac crisis respond to only GFD and nutritional management. So

steroids are required only in other half of patients with Celiac Crisis who didn't responds to standard GFD and nutritional support.

4) In Refeeding syndrome there is potential fatal shifts of electrolytes and mineral in malnourished child who are abruptly refed by enteral, parenteral routes.
5) Low and slow feeding with gradual increase along with monitoring of electrolytes and mineral is the key to prevention of Refeeding syndrome.

III. Evolving Practice and Changing Phenotype in Pediatric Autoimmune Liver Disease and Diagnostic Scoring : Dr Somshekhar

1) Pediatric AILD's diagnosed more frequently than in the past, because of enhanced awareness, real increase in their prevalence, and/or decrease in viral hepatitis-related disease. Juvenile sclerosing cholangitis is being increasingly diagnosed
2) Hyaline droplets-Histological feature is specific for AIH
3) Parenchymal inflammation responds satisfactorily to standard immunosuppressive treatment – azathioprine, both in AIH and ASC; UDCA improves numbers in ASC, but effect on long term survival questionable
4) In ASC, the bile duct disease progresses in about 50% of cases, leading to ESLD requiring LT more frequently than in AIH. Both AIH and ASC can recur after LT, recurrence being more common in ASC than in AIH
5) De novo AIH after LT for non-autoimmune conditions responds to the classical treatment of AIH, but not to standard antirejection treatment
6) Scoring systems – Any diagnostic score, based on the ease of use, may be used to support diagnosis of AILD

IV. Newer advances in the diagnosis and treatment if Celiac disease : Dr Shipra Agarwal New diagnostic guidelines in ESPGHAN 2019:

1) No role of HLA DQ2/8 in diagnosis for patients with positive TTg IgA, if they qualify for CD diagnosis with biopsy or if they have TTg >10x ULN and EMA IgA positivity
2) CD can be diagnosed in asymptomatic patients using same algorithm as those with symptoms. Decision as whether to perform duodenal biopsy should be shared decision with the parents**.** (Conditional recommendation)
3) Testing for EMA, DGP, or AGA for initial screening is not recommended
4) **Assessment of dietary compliance:**Detection of gluten immunogenic peptides in urine or stool of the patients on GFD is a potential future tool for detection of inadvertent gluten intake. It has good correlation with histology. As small as 25 mg gluten intake can be detected in the urine.
5) **Newer pharmacological approaches : Latiglutenase** (gluten digesting enzyme): in preliminary studies, it has shown to protect intestinal mucosa compared to placebo. **Larazotide** (modulator of tight junctions): Has been shown to be effective in improving the symptoms compared to placebo.
6) **Vaccines (NexVax):** Phase 2 trial ongoing.

V. Case of IBD : Dr Bijal Mistry

1) Patients of Ulcerative colitis who are on steroids/ immunosuppresants are at higher risk of active tuberculosis than general population
2) However, other bacterial causes of consolidation has to be ruled out in these patients
3) Causes of necrotic lymph nodes other than Tuberculosis have to be considered before starting Anti-Tuberculous treatment- eg. squamous cell carcinoma metastasis, lymphoma, leukemia, viral lymphadenitis eg. herpes simplex lymphadenitis, bacterial lymphadenitis, non-tuberculous mycobacterial adenitis, fatty nodal metaplasia, systemic lupus erythematosus (SLE), Kawasaki disease
4) Decision to start AKT in unresponsive cases has to be taken based on the antibiotics dose and duration, clinical condition, duration of immunosuppresants or steroids, high incidence of tuberculosis in developing countries like India and treated as 'Clinically diagnosed Tuberculosis'
5) Anti-fungals may be added in unresponsive patients with sepsis

VI. Challenges and Updates in management of ALF including newer modalities : Dr Malathi

1) Pediatric ALF an **acute onset of liver disease** with **no evidence of chronic liver disease** and **hepatic-based coagulopathy** (INR 2) not corrected by parenteral vitamin K with or without hepatic encephalopathy or a hepatic-based coagulopathy (INR 1.5– 1.9) with HE.
2) The high mortality reported in ALF has decreased with the advent of tailored, prompt and appropriate ICU care and liver transplant.
3) PICU plays a pivot role in management of ALF and provides support for failing organs, simultaneously allows time for hepatic regeneration, optimization of liver status if liver transplant is required.

4) The variables which prognosticate ALF are age of child, etiology (paracetamol, ischemic, hepatitis A). At present there are no perfect PALF prognostication models which can predict whether the child will survive or die without liver transplant
5) The two artificial liver support systems which act as a bridge either to recovery or to transplant are continuous renal replacement therapy (CRRT) and plasmapheresis.

VII. Chronic pancreatitis in children: Prevention and treatment: Dr Vibhor Borkar

1) Newer conceptual model of chronic pancreatitis needs to be defined to understand pathophysiology and plan early intervention to halt progress of pancreatitis.
2) In children with genetic causes of pancreatitis with two genes affected, pose a faster risk of progression to chronic pancreatitis.
3) In children with chronic pancreatitis and pain with intraductal stones in head and neck region; long term endotherapy is safe and viable option.
4) Absence of IgG4 elevation, doesn't rule out autoimmune pancreatitis. Active efforts for tissue diagnosis should be made in children who are suspected to have autoimmune pancreatitis.
5) Total pancreatectomy with islet auto-transplantation (TPIAT) in children has demonstrated excellent outcomes including relief from chronic opioid use, as well as improved mental and physical quality of life with good glycemic control.

VIII. Preparation and Prerequisite for Endoscopy in children : Dr Bhushan Miraje

1) Almost all GI procedure are performed under moderate or deep sedation and general Anesthesia.
2) Informed consent and preprocedure health evaluation and resuscitative equipment should be obtained.
3) Routine oxygen administration during Pediatric procedures are recommended.
4) Use of split dose bowel cleansing regimen is strongly recommended.
5) Polyethylene glycol with electrolyte via nasogastric tube in hospital setting for 24 hr before procedure is safe and appropriate regimen

IX. Recent papers on treatment of IBD: Dr Bhaswati Acharya

1) EEN is once again emphasised to be effective in mild to moderate Crohn's Disease affecting small bowel and /or colon
2) Stopping standard treatment carries risk of relapse
3) Vedolizumab is effective with reduced immunosuppression and is being used
4) Biological use pre and peri-operatively does not impose more operative risks
5) EEN and PN before any surgery in IBD reduce morbidity.
6) Newer agents like Ustekinumab & oral agent Ozanimod are promising
7) NAC in IBD needs more research
8) Biosimilar of Adalimumab used in India is equally effective as proved in a recent multicentre study from India

X. Biliary atresia : Factors influencing time of diagnosis, Pre and Post Kasai challenge:Dr Bikrant Bihari

1) The emphasis of ongoing and future research is on diagnosing and doing Kasai surgery before 30 days of life *(JPGN 2018, JPGN 2019)*.
2) Newborn conjugated/direct bilirubin has emerged as an excellent screening tool. However, stool colour chart/app remains more cost effective in general population *(NEJM 2016, J Med Screen 2019)*.
3) Serum MMP7 levels is a very promising marker to differentiate biliary atresia from other causes of neonatal cholestasis *(Hepatol 2018, J Pediatr 2019)*.
4) Steroids and other medications have failed to show a consistent beneficial role post kasai. Prevention and treatment of cholangitis remains key *(Pediatr Surg Int 2016)*.
5) N-acetylcysteine is being studied as adjunctive therapy after recent discovery that mRNA of glutathione synthesis were upregulated in biliary atresia long term survivors. *(Gastroenterology 2019)*.

XI. CMPA and Food Protein-induced Enterocolitis Syndrome and role of milk substitute: Dr Viswanathan MS

1) Avoid other mammalian milks, such as goat's milk or sheep's milk, in patients with cow's milk allergy because of highly cross-reactive allergens.
2) No clear relationship exists between digestibility and protein allergenicity. Milk allergens are known to preserve their biologic activity even after boiling, pasteurization, ultra-high-temperature processing, or evaporation for the production of powdered infant formula.
3) FPIES is a Non-IgE mediated gastrointestinal food hypersensitivity. Incidence - 0.015 to 0.7

percent. Most commonly caused by cow's milk (CM) or soy protein, although other foods can be triggers.

4) Specific IgE to cow's milk (SIgE) and Skin prick test (SPT) are especially helpful in predicting prognosis & time interval until the next challenge. Infant with negative SIgE/SPT at the time of diagnosis become tolerant to Cow's milk protein at a much younger age
5) Partially hydrolysed formula should not be used in the treatment of CMPA. Extensively hydrolysed formula is the preferred therapeutic formula of treatment in CMPA. Soy milk can be used in infants more than 6 months of age if there is tolerance to it.
6) In FPIES, introduction of green vegetables and then fruits at four to six months of age instead of cereals is suggested because approximately one-third of infants with cow's milk or soy FPIES develop solid-food FPIES. Reactions to rice and other grains represent the most common types of solid-food FPIES.

XII. Newer Advances in Endoscopy : Dr Rimjhim Shrivastava

1) In the past few years, endoscopy has undergone a major advancements resulting in impressive impacts on diagnostic accuracy. These advancements were mainly established for adult patients, but like variceal band ligation and ERCP, these new technologies are being adapted for the pediatric population as well.
2) Pediatric population has limitations like small size; relatively low indications of certain conditions as Barret's Esophagus, metaplasia etc; and lack of training amongst the pediatric gastroenterologists, which limits the use of new technologies.
3) High definition endoscopy with narrow band imaging is developing as the new standard of care.
4) Single Targeted biopsy in celiac disease with narrow band imaging has high sensitivity though , has low specificity.(*Digestive and Liver Disease 46 (2014) e71–e84*)
5) ERCP is safe and effective in infants and older children with biliopancreatic disorder. (*Indian Pediatr 2019;56: 196-198*)
6) EUS provides important information that impacts management in children with pancreatobiliary disease and submucosal lesions of esophagus and stomach. ESGE/ ESPGHAN recommend endobronchial ultrasonography in children weighing <15 kg. It has replaced diagnostic ERCP in children and has important therapeutic roles as well.(Indian J Gastroenterology (*January-February 2016) 35(1:14-19))*
7) POEM is emerging strongly for Achalasia with excellent long term outcomes and minimal risks. (*J Pediatr Gastroenterol Nutr 2018;66:43-47*)
8) Double balloon eneteroscopy, confocal laser endomicroscopy , molecular endosopy, wide-view full spectrum endoscopy etc are some of the forthcoming technologies with high accuracy and wider diagnostic territory .

XIII. Diagnosis and management of Pediatric achalasia: Dr Sakshi Karkara

1) High resolution manometry(HRM) and High resolution impedance manometry(HRIM) are considered as a gold standard for diagnosis and classifying subtypes of achalasia as well for predicting the outcome of treatment.
2) Timed Barium swallow(TBS) instead of barium swallow should be done as it has a role in diagnosis as well as in prognosticating the disease outcome post procedure.
3) Laparoscopic Hellers Myotomy(LHM) with Partial fundoplication has excellent results in children and can be considered as first line treatment after explaining the parents of other modalities like Pneumatic dilatation (in more than 5 years of age) and their outcome.
4) Per Oral Endoscopic Myotomy(POEM) definitely shows promise as it avoids surgery, saves cost and hospital stay with almost similar results as LHM with slightly more GERD incidence which needs addition of PPI but needs expertise and we lack long term results.
5) POEM should be preferred over LHM as treatment for type III achalasia as the length of the myotomy can be decided while doing the procedure and specially after the advent of EndoFLIP (functional luminal imaging probe) the outcomes are better with lesser complications.

XIV. NAFLD: Recent Advances: Dr Yogesh Waikar

1) The newer terminology MPFL: metabolic dysfunction predominant fatty liver justifies the etiology and underlying disease process.
2) Persistent elevated ALT for more than 3 months twice the upper limit of normal, ALT > 80 U/l and reducing ALT after intervention suggests improvement. Normal ALT don't rule out diagnosis.
3) ELF score > 10.50 suggest advance liver fibrosis and early referral to specialist .Of many score ELF score is only useful score correlating with LIVER PATHOLOGY as per NICE guidelines.

4) Different genetic mutations have different implications. some are responsible for fibrosis while some would stay always at steatosis.
5) USG score =/>2 saverymuttu score and USFLI > 6 helps in screening.
6) Controlled attenuation parameter (CAP) > 241 dB/m :STEATOSIS,
7) Liver stiffness measurement by fibro-scan > 5.5 Kpa :FIBROSIS
8) MRI – PDFF and add on MRS is best noninvasive test for FATTY LIVER.
9) UDCA no role. Vitamin E may help , titrate it with ELF score.Metformin helps in ballooning but no change is steatosis , fibrosis.Lap sleeve Gastrectomy reverses fibrosis in properly selected cases.
10) Before staring treatment Liver biopsy is must.

XV. Current understanding and management of GERD: Dr Nishant Wadhwa/Dr Kanan Ramaswamy

1) Vomiting before seven days and after six months of life is never due to GERD. It is important to know is what is not GERD and for that always look for red flags. Over rather than under diagnosis a major problem in today's clinical practice.
2) Extra- esophageal symptoms does not correlate with reflux studies. Hence PPI should not be given empirically. However, empirical treatment with PPI for children above 1 year is acceptable before doing work up.
3) In special circumstances like neurologically impaired and post surgical GERD cases, duration of PPI therapy is usually longer and reassessment at regular intervals required.
4) Impedance pH monitoring is incorporated in distinguishing functional reflux variants as per Rome IV criteria.
5) Hydrolysate infant formulas should be tried for treatment of reflux symptoms in infants prior to a detail investigation.

Celiac Awareness Program-Jaipur

Celiac disease has taken the form of an epidemic in North India. Apparently 1% of general population suffers from it. This translates to more than seven lac patients in Rajasthan itself. Though the awareness level today is better than what it was a decade ago, still there is lot of confusion regarding the correct diet and there are several myths associated with it. A common disease like this certainly needs regular awareness to improve diagnoses and treatment.

Santokba Durlabhji Memorial Hospital (**SDMH**) at Jaipur organizes regular awareness program on Celiac disease. SDMH organized 4th anuual **Celiac awareness program** on Sunday, 15th Dec 2019. In the

morning half – **Celiac workshop** was organized in which more than 100 Celiac children with their family members assembled on a chilly morning at 9 am. Faculty included Dr. S M Mittal, Dr. Sushma Narayan and Dr. Deepak Goyal from New Delhi, Dr. P C Khatri from Bikaner, Dr. Namita Bhandari from Jodhpur and several experts from Jaipur. Day started with Kids participating in Celiac Quiz while Parents learned their share through Recipe Contest and Poster Competition. Everyone then participated in Slogan competition on a slogan wall. Today 2nd edition of book "Celiac disease – guide to parents" (authored by Dr. Sushma Narayan – Secretary General of Celiac Support Organisation and Dr. S K Mittal Former Prof & Head, Pediatrics at Maulana Medical Collge, New Delhi) was launched by the Secretary of SDMH- Shri

Yogendra Durlabhji along with all faculty. There were lectures on Celiac disease – rising incidence, myths and social and psychological issues related to Celiac disease. An open panel discussion was held in which parents participated and got their queries addressed. Winners were awarded prizes at the end and Gluten free meal was served to all.

In the second half we organized a **Celiac CME** where 50 pediatricians and Nutritionist participated. Experts in Homeopath were invited. Newer guidelines (2019) on Celiac were discussed along with role of GFD beyond Celiac. Role f alternative medicine was also discussed and then a panel discussion where several issues related to the disease was discussed.

Dr Moinak Sen Sarma Assistant Professor, SGPGIMS Lucknow felicitated with ISG Om Prakash Award 2018 at ISGCON Kolkata 2019 for achieving excellence in gastroenterology at young age

ISPGHAN Representation at UP Pedicon 2019 at Aligarh

Prof Yaccha, Dr Shrish, Dr Rajiv, Dr Jaya and Dr Moinak along with Organising Secretary Dr Sanjeev Kumar

Awards at ISPGHANcon 2019, Chennai

CP MITTAL AWARD			
SL. NO	TOPICS	PRESENTER NAME	PRIZE
1	EFFICACY AND SAFETY OF SODIUM BENZOATE IN THE MANAGEMENT OF HYPERAMMONEMIA IN THE DECOMPENSATED CHRONI LIVER DISEASE OF CHILD HOOD: A DOUBLE BLIND RANDOMISED CONTROL TRIAL	DR. SNEHAVARDHAN PANDEY , ILBS NEWDELHI	1
2	OUT COME OF PORTO SYSTEMIC SHUNT SURGERY ON PRE-EXISTING CHOLANGIOPATHY IN CHILDREN WITH EXTRA HEPATIC PORTAL VENOUS OBSTRUCTION	DR. JAYENDRA SEETHARAMAN, SGPGI	2
GI PLENARY			
1	TACROLIMUS HAS SUPERIOR EFFICACY IN THIOPURINE NAIVE IN COMPARISON TO THIOPURINE EXPERIENCED CHILDREN WITH STEROID DEPENDANT OR REFRACTORY COLITIS	DR. SAHANA SHANKAR , ROYAL CHILDREN'S HOSPITAL	1
2	EFFICACY AND TOLERABILITY OF SINGLE DOSE VS. SPLIT DOSE POLYETHYLENE GLYCOL FOR COLONIC PREPARATION IN CHILDREN:A RANDOMIZED CONTROL STUDY	DR. PARIJAT TRIPATHI, SGPGI	2
LIVER PLENARY			
1	ROLE OF GRANULOCYTE COLONY STIMULATING FACTOR ON THE SHORT TERM OUT COME OF CHILDREN WITH ACUTE ON CHRONIC LIVER FAILURE	DR. SHRUTI SHARMA , PGIMER CHANDIGRAH	1
2	CHANGED IN OPTIC NERVE SHEATH DIAMETER WITH MANAGEMNET OF INTRACRANIAL HYPERTENSION IN PEDIATRIC ACUTE LIVER FAILURE	DR. PRITI VIJAY, ILBS	1
3	A CLINICO - VIROLOGICAL STUDY TO EXPLORE THE DYNAMIC OF CHRNIC HBV INFECTION IN THE IMMUNOTOLERANT PHASE	DR. GAUTAM RAY , IPGMER	2

E- POSTER: GASTROENTEROLOGY , PANCREAS			
1	PANCREATIC, HEPATOBILIARY (HPB) AND GASTROINTESTINAL (GI) MANIFESTATION OF CYSTIC FIBROSIS - A RETROSPECTIVE STUDY FROM A TERTIARY CARE CENTRE IN SOUTH INDIA	DR. LEENATH THOMAS , CMC, VELLORE	1
2	EFFICACY OF ORAL PSYLLIUM VERSUS PLACEBO IN PEDIATRIC IRRITABLE BOWEL SYNDROME: A DOUBLE BLIND RANDOMZED CONTROL TRIAL	DR. JAGADEESH MENON, PGIMER CHANDIGARH	2
3	CELIAC AND SUPERIOR MESENTERIC ARTERY PSEUDOANEURYSMS IN CHILDREN : CLINICAL PROFILE, MANAGEMENT ANDN OUT COME	DR. JAYENDRA SEETHARAMAN, SGPGIMS	2
E- POSTER: LIVER			
1	A STUDY OF EFFECT OF LONG - TERM ORAL STEROIDS ON INTRAOCULAR PRESSURE IN CHILDREN WITH AUTOIMMUNE HEPATITIS	DR. DURGA PRASAD, SGPGIMS	1
2	ABO- INCOMPATIBLE DECEASED DONOR PAEDIATIC LIVER TRNASPLANTATION: NOVEL TITRE - BASED MANAGEMENT PROTOCOL	DR. SHARATH VERMA : MAX SUPERSPECIALITY HOSPITAL	2
3	EVALUATION OF THE PROTOCOL BASED IDAGNOSTIC APPROACH FOR METABOLIC LIVER DISEASE	DR.PIYUSH UPADHYAY, ILBS	2
4	INCIDENCE OF GALL BLADDER DYSFUNCTION IN CHILDREN WITH CELIAC DISEASE AT PRESENATATION AN DPOST GLUTEN WITHDRAWAL - CORRELATION OF ULTRASONOGRAPH (USG) AND HEPATOBILIARY (HPB) SCINTIGRAPHY	DR. SUBHAMOY DAS, PGIMER	
INTERESTING CASE SCENARIOS			
1	HEPATOLOGY (METABOLIC)	DR. SHIVANI DESWAL , PGIMER & DR RML HOSPITAL	1
2	AN INTERESTING CASE OF CROHNS DISEASE WIT A MYCOTIC ANEURYSM	DR. AYESHA , KKTCH	2
3	AN UNUSUAL CAUSE OF CHRONIC DIARRHEA IN A ADOLESCENT - A CASE REPORT	DR. JAYENDRA SEETHARAMAN , SGPGIMS	
VIDEO DIGEST			
1	ENDOSCOPIC DILATATION OF DUODENAL DIAPHRAGM :	DR. SRINIVAS S , KKTCH	1
2	1 YEAR OLD BOY WITH MULTIPLE FOOD BOLUS IMPACTION	DR. RHIMJIM SRIVASTAVA	2

Glimpses of ISPGHANcon 2019 at Chennai

ISPGHANcon 2019, Chennai

Experience summary at ISPGHAN 2019 as a delegate

It gives me immense pleasure to share my experience as a delegate at our prestigious Pediatric Gastroenterology society meeting, ISPGHAN, held in Chennai 2019. I would like to first congratulate the organizing team (Malathi Ma'am, Naresh Sir and other team members) for their tireless efforts and hospitality in making this a grand success and giving each of us an unforgettable experience to cherish. It was a great learning platform to meet and interact with our esteemed teachers, seniors and colleagues from all over the country. The scientific sessions of the program were wonderful; I got opportunity to learn so many new and innovative things. The academic presentations such as oral, poster and audio-visual sessions for the audience and students were very encouraging and extra ordinary. I cannot forget to share about 'the gala dinner", the evening was blooming and beaming with such great energy from all teachers, seniors and lovely friends. Last but not least, I won first prize for best poster presentation in the Liver category, which made my memories extra special.

Thank you all

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Apollomedics Super Speciality Hospital, Lucknow 226012, India
Email:durgambbs03@gmail.com

ISPGHANcon 2019, Chennai

Packed in-between Dussehra and Diwali 2019, the stage was set for the biggest academic extravaganza in Pediatric Gastroenterology in India, the ISPGHANCON.

The sixth annual meet of ISPGHAN (Indian Society of Pediatric Gastroenterology, Hepatology, and Nutrition) and the annual meeting of the Pediatric Gastroenterology chapter of IAP was held from the 18th to 20th October at the ITC Grand Chola Hotel in Chennai, India. And believe us, the meeting ticked the 'excellent' boxes in all categories. Starting with the venue, the rain gods were very kind with light showers preceding the conference dates, making the Chennai weather surprisingly pleasant. The 'Grand Chola' too was exemplary in its ambience, and all the delegates & faculty enjoyed the magnificence of this 'seven star' atmosphere to the hilt.

Day One of the conference focused on workshops (Pre-conference workshops) conducted at different hospitals within Chennai city. They were well attended, and involved video-teaching, hands on training, and skill enhancement in Upper & Lower GI endoscopy, Endotherapy, usage of Endoscopic accessories, PEG (Percutaneous Endoscopic Gastrostomy) and discussions on GI emergencies. The workshops were followed by the evening symposium (at the conference venue) on Pancreatitis in children, which had a guest lecture, a panel discussion, and case presentations by the local ISG members too. With the “who's who” of Pediatric Gastroenterology from the country and renowned foreign delegates attending the meeting, the high quality academic discussions kick-started the grand event in style!

The subsequent two days of the meeting covered almost all aspects pediatric luminal gastroenterology, hepatology, pancreatology and nutrition, including liver & intestinal transplantation, genetics, recent developments, and much more. The success of any academic meeting is often judged by the invited faculty, delegate attendance, interaction by the audience, and the enthusiasm of the trainees, not to mention the numbers present in the sessions. ISPGHANCON 2019 has unanimously excelled in all these areas. Eighty-one abstracts were presented (Oral & Posters) in the meeting, and the quality of research presented in these sessions had high academic quality, as commented by the judges (National & Overseas)! Day One ended with the General Body meeting, followed by the gala banquet, where one & all had a great time, dancing to some exhilarating Tamil music.

Apart from the core Pediatric GE topics, day two had a parallel session for general Pediatricians, where common office & hospital scenarios in Pediatric GE were discussed by leaders in the field. It was extremely heartening to see the main hall filled to capacity till the end.

As they say, all good things must come to an end. The meeting ended with the valedictory session & prize distribution ceremony. All of us are extremely thankful to 'Team Chennai' (Prof Mohamed Rela, Prof VS Sankaranayanan, Dr Malathi Sathiyasekaran, Dr Naresh Shanmugam, Dr Bhaskar Raju, Dr S Srinivas, Dr MS Viswanathan, Dr Dhanaseker, Dr D Nirmala, Dr Jaganathan, Dr Jagdish Menon, Dr B Sumathi, Dr John Mathai, Dr S Balasubramaniyan, Dr Somasekar, Dr P Ramachandran, and all others who were involved in any capacity in the organization of the conference) for this top-notch academic extravaganza!

Dr. Gautam Ray
Asst. Professor,
Pediatric Gastroenterology,
School of Digestive and Liver Diseases,
IPGMER, Kolkata

Indian Society of Pediatric Gastroenterology, Hepatology and Nutrition (ISPGHAN)
(Registered under Tamil Naidu societies registration act, 1975, 81 No-361of 2013)

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Kindly enroll me as a Life Member/ Associate Life Member/Affiliate Foreign Member of the Indian Society of Pediatric Gastroenterology, Hepatology and Nutrition. Eligibility of member category is given in this form*(see page 2).

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5. Field of medicine connected with Pediatric Gastroenterology
(Specify here specialty such as Surgery, Pathology, Radiology, Psychiatry etc.)

6. Attachment to the Hospitals:.....
7. Modes of Payment: Either by NEFT (preferred) or by multicity cheque
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Membership Criteria

Membership Categories	*Eligibility criteria	Current Membership fee
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Affiliate Foreign Member	Affiliate Foreign Membership shall be open to members of the medical profession who are not ordinarily residents of India, and have a postgraduate degree in Pedaitric, Pediatrics gastroenterology or Gastroenterology recognized in their respective country of residence	US dollar 100

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PG Students. Rs 1000/-
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- Gene therapy in Wilson Disease

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