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INDIAN SOCIETY OF PEDIATRIC GASTROENTEROLOGY, HEPATOLOGY AND NUTRITION

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Message from the President ISPGHAN

Dear Friends,

It gives me a great joy to see the release of our first e journal an official publication of our society ISPGHAN. I appreciate the dedicated and sincere effort of the editors and the contributors who have worked as a team to bring out this journal. Our society is blessed with excellent academicians, brilliant teachers, astute clinicians and hard core researchers. I am sure they will continue to share their knowledge with us through this journal because "knowledge shared is knowledge gained."

There may be small hurdles during the beginning but as we run the race with the strong support of all our members both seniors and juniors this new endeavor will be a solid teaching and learning ground in Pediatric gastroenterology and hepatology. I sincerely request all the members to contribute to this journal.

I wish the editorial team the very best in their efforts.

Dr. Malathi Sathiyasekaran

Message from the Secretary ISPGHAN

Greetings from the secretary's desk to all the members. I congratulate you all for the publication of the first issue of "Pediatric Gut and Liver e Journal", the official quarterly e journal of ISPGHAN. Ours is a young, growing society with ~230 members, including residents in GI fellowship program as well as paediatricians with interest in the speciality. This journal will give an opportunity to our members to publish their work and also initiate the trainees into the process of research methodology and scientific writing. We would like to add features like diagnostic challenges, images and clinic-pathological conferences in this journal to educate young trainees in clinical aspects of our speciality. I request the senior members to support this activity by contributing review articles on various contemporary topics of interest and participating in the peer review process of submitted manuscripts.

Although it is an e journal, we would like to conform to the international standards and maintain quality from the start. This e journal will give us a platform to address the problems that are more specific and relevant to our population. The e journal will be circulated widely through our website, email to members as well as through WhatsApp groups. This enhanced accessibility will certainly be beneficial for our community as it will raise awareness about relevant topics and ignite comprehensive and involved discussions.

I would like to congratulate and thank the editorial team of Shirish Bhatnagar, Rajeev Khanna, Yogesh Waikar and Rishi Bolia for taking on this responsibility. I promise my full hearted support and also of the whole society towards this endeavour. I hope that with active contribution from all of us, they will be successful in regularly publishing this e-journal and in the near future move towards a print journal as well.

Dr. Anshu Srivastava

Message from Editorial Board

Welcome to the first issue of PGLJ! We hope that PGLJ will become an essential part of your professional life, a resource that you depend on to keep up with the rapidly evolving field of Pediatric Gastroenterology. PGLJ will bring you a steady supply of high-quality, peer reviewed papers that are relevant and readable.

The Editorial Board wants to create a balanced journal that appeals both to general pediatric fraternity and of course to the pediatric gastroenterologist. We dream of making PGLJ an international forum for sharing the best ideas in coming times.

We have planned the following sections:

- **Invited Review article** will include a comprehensive write-up on common topic of pediatric gastroenterology which is of interest among both paediatricians and pediatric GI specialist. This time the topic is Constipation a problem which is faced by many paediatricians and this review article will be ready reckoner for them.
- **Clinico Pathological Conference** where in authors objectively summarize both clinical and pathological findings to ascertain the sequence of events leading to death. This provides an in depth learning about the disease. This time we deal with a 3 months old child who presented with liver failure.
- We have 2 **Case Reports** where in authors have provided us unique cases and rare presentations of common disease that will enhance our knowledge.
- We have one section on **Guess the Diagnosis-** A Pictographic Trivia.
- Section of **Journal Watch** has two parts. First part covers important international publications related to different aspects of Pediatric Gastroenterology. The second section is a unique section as part of journal watch where in we have incorporated all article published by ISPGHAN members in last six months (September 2018 – February 2019) so that publications of our own members get there due highlight. We would request all members to send us information about their publication so that we can incorporate them in future issues.
- **ISPGHAN Kaleidoscope**: Section deals with activities done under the ISPGHAN banner both at state and national level. Our society is growing and actively doing many activities throughout the country which needs to be shared with the rest of the pediatric community.

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.

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

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Functional Constipation in Children

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Abstract

Currently, the knowledge and awareness among paediatricians in India regarding diagnosis and treatment strategies of chronic constipation are far from satisfactory, creating barriers to optimal disease management. Recently the Indian Society of Paediatric Gastroenterology, Hepatology and Nutrition (ISPGHAN) have proposed guidelines on constipation for use in Indian children. Constipation is a common problem among children; the commonest cause is functional (95 %). An elaborate history and meticulous physical examination to exclude red flags is the key to make a diagnosis of functional constipation. Management consists of disimpaction, followed by maintenance therapy with osmotic laxative, dietary modification and toilet training. Stimulant laxatives should be reserved only for rescue therapy. A regular follow-up with slow tapering of laxative is essential for successful treatment outcome.

Introduction

A normal pattern of stool evacuation is thought to be a sign of good health in children of all ages. Especially during the initial years of life, parents pay keen attention to the frequency and the characteristics of their children's defecation. Any deviation from what is thought by any family member to be normal for children may trigger an appointment with the paediatrician. Various studies from across the globe have shown that approximately 3% of general paediatric outpatient visits and 25% of paediatric gastroenterology consultations are related to a perceived defeacation disorder.

Chronic constipation is a source of anxiety for parents who worry that a serious disease may be causing the symptom and is a real challenge for the paediatrician to understand and to treat it in a convincingly effective manner. The chronic nature of constipation and common misconceptions about the symptoms and pathophysiology of constipation can lead to frustrating experiences for patients and families. Beyond the neonatal period, the most common cause of constipation is functional and only a small minority of children have an organic cause for constipation.

A recent study concluded that 25% of children with functional constipation continued to experience symptoms at adult age, suggesting that referral to specialized clinics at an early stage for children who are unresponsive to first-line treatment may help improve outcomes. This warrants a meticulous and evidence based approach to manage a child or an adolescent with constipation.

Definitions

Defining constipation remains a challenge because stooling patterns are highly variable in childhood. Generally, infants have an average of three to four stools per day and a toddler may have two to three stools per day. By the age of 4 years, children have a pattern and frequency of bowel movements that are similar to those of adults.

A delay or difficulty in defecation sufficient to cause significant distress to the patient is defined as constipation. When the duration of constipation is less than 4 week, it is labelled as acute constipation and when the duration is more, it is labelled as chronic constipation.

Recently the Indian Society of Paediatric Gastroenterology Hepatology and Nutrition (ISPGHAN) have proposed a definition for chronic constipation for application in Indian children (Box 1)

Box 1 : ISPGHAN definition of chronic constipation

Duration of more than 4 weeks for all ages; and Presence of more than 2 of the following: (*a*) defecation frequency less than 2 times per week, (*b*) faecal incontinence more than 1 times per week after the acquisition of toileting skills, (*c*) history of excessive stool retention, (*d*) history of painful or hard bowel movements, (*e*) presence of a large mass in the rectum or on per abdomen examination, (*f*) history of large-diameter stools that may obstruct the toilet *(This may not be elicitable for majority of Indian children who do not use the Western type of toilet).*

Faecal incontinence is defined as passage of stools in the undergarment. Fecal incontinence is classified as: (a) constipation-associated fecal incontinence and (b) non-retentive fecal incontinence: diagnosed only if there is no constipation and normal anal sphincter tone, and symptoms last for more than 2 months in a child with a developmental age of more than or equal to 4 years.

Refractory constipation: constipation not responding to optimal conventional treatment for at least 3 months, despite good compliance. These patients should be referred to a pediatric gastroenterologist for evaluation.

Pathogenesis

Faecal continence is maintained by involuntary muscles, internal anal sphincter and voluntary muscle contractions in perineum. The external anal sphincter is under voluntary control. The urge to defecate is triggered when stool comes in lower rectum. If a child doesn't want to defecate, he or she tightens the external anal sphincter and squeezes the gluteal muscle pushing feces higher in the rectal vault and reduce the urge to defecate. In response to the urge, they refuse to sit on the toilet, rise on their toes, cross their legs, scream and turn red. These actions are termed as withholding manoeuvre which parents mistake as an attempt to defecate. The longer that faeces remain in the rectum, the harder it becomes due to continued absorption of water. Passage of a hard or large stool may cause a painful anal fissure. The cycle of avoiding bowel movements because of a fear of painful defecation may progress to stool retention and infrequent bowel movements, a condition that is termed functional constipation. With prolonged duration of constipation, liquid stool from the proximal colon may percolate around hard retained stool and pass per rectum involuntarily called as fecal incontinence. If left untreated, chronic constipation can lead to other significant clinical issues, such as enuresis, frequent urinary tract infections and urinary symptoms, rectal prolapse, pelvic dyssynergia and rectal bleeding.

Causes of chronic constipation

Functional constipation is the commonest cause (90%), which is constipation not due to organic or anatomical cause or intake of medication.

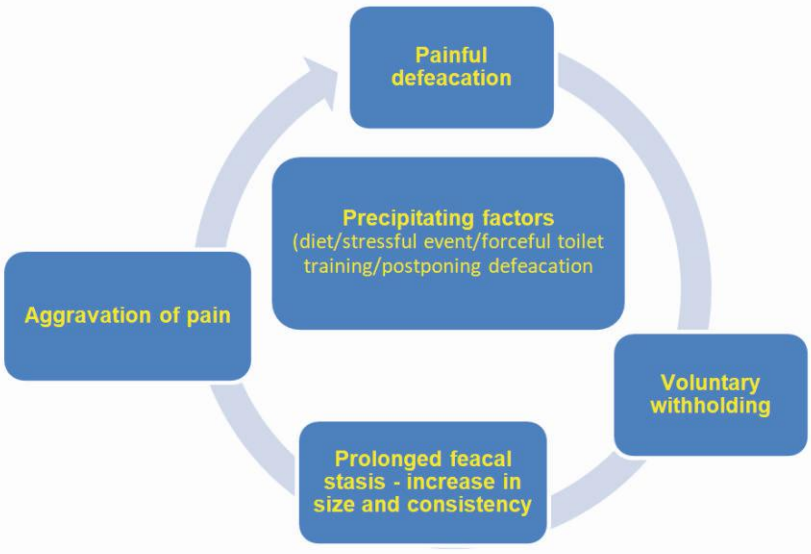

Figure 1 – Pathogenesis of functional constipation

Surgical	Medical
Local anal pathology – anal fissure Hirschsprung's disease(HD) Spina bifida Tethered cord Meningomyelocele Anterior displaced anus	Drugs – anticholinergics,anticonvulsants,antacids Mental retardation,hypotonia Hypothyroidism Hypercalcemia,hypokalemia

Table 1 – Causes of chronic constipation

Approach to constipation

The clinical history should include a description of stool frequency and quality, associated symptoms such as abdominal pain and rectal bleeding, growth pattern, continence and toilet training, presence or absence of withholding behavior, and symptom onset and duration.

It is important to enquire about dietary habits of the child. Consumption of excess of milk, juices and or other drinks, junk foods and bakery products may lead to constipation. In the modern era children largely depend on low fiber diet and this becomes important factor for onset of constipation. Less consumption of cereals, pulses, vegetables and fruits can result into constipation.

Delayed passage of meconium should raise suspicion for HD.Thin, ribbon like stools also may suggest HD compared to the large bulky stools that often are found with functional constipation.

Faecal incontinence should be directly assessed in terms of frequency and quality because it may be concurrent with constipation due to leakage of liquid stool around a firm rectal stool mass. Symptoms of overflow incontinence typically are small-volume liquid stools, often passed in the afternoon or during activities and sometimes unrecognized or

ignored by the child. Specific questions, including family history, should be directed toward exclusion of diagnoses other than functional constipation.

Standardized measures such as the modified Bristol stool chart (figure 2) allow for a common language and description of stools.

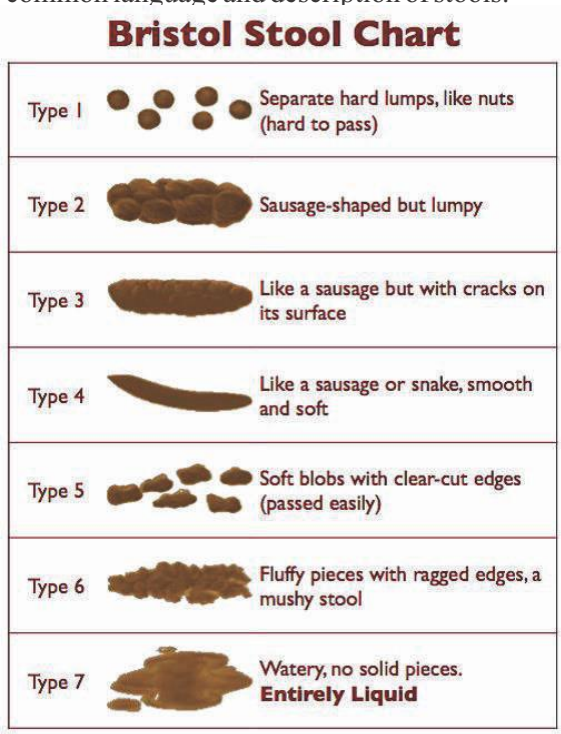

Figure 2 – Bristol Stool Chart

Physical examination should explore both the severity of constipation and potential causes. Ideally, a growth chart contains data spanning the onset of constipation to determine current parameters as well as past growth velocity.

External anal inspection can assess for anal atresia and displacement and may identify anal fissures, skin tags, or external haemorrhoids. It may also be useful to assess sphincter tone visually or identify faecal material around the anus or in the underwear. In addition, examining the back for sacral dimples or spinal deformities and assessing lower extremity motor tone, strength, and deep-tendon reflexes can indicate whether additional assessment for neurologic pathology is indicated.

Digital rectal examination (DRE) is important in specific circumstances but is not always necessary to diagnose functional constipation. Palpation of a firm or large rectal stool mass on rectal examination often confirms clinical suspicions, abnormalities in sphincter tone may indicate anal stenosis, and an empty rectal vault with expulsion of stool on finger withdrawal is a classic but infrequently seen finding in HD.

Laboratory evaluation is not warranted for constipation unless warning signs are present or other aspects of the history or physical examination suggest systemic disease.

Constipation rarely is the sole presenting symptom of hypothyroidism, electrolyte abnormalities, lead toxicity, or celiac disease, and routine screening for these diseases is not recommended. Routine allergy testing is also not recommended in evaluation of constipation, and cow milk protein restriction in young children for a limited time to assess the clinical response remains controversial.

A plain abdominal radiograph may help to visualize the amount of retained stool. Barium enema is suggested but not required when constipation is accompanied by “red flag "symptoms. It provides information about the

Box 2 : Alarm signs and symptoms in constipation

- Constipation starting extremely early in life (<1 mo)
- Passage of meconium >48 h
- Failure to thrive
- Absence of withholding maneuvers
- Bladder dysfunction
- Empty rectal ampulla on digital rectal examination
- Abnormal neurological findings

calibre of the rectum and colon and may be useful if obstruction in the colon is suspected.

Further diagnostic tests when the clinician suspects HD depend on patient characteristics (age, health status) and test availability. Full-thickness rectal biopsy remains the gold standard for diagnosis and is performed under anaesthesia. Aganglionosis or hypertrophied nerves on rectal biopsy haematoxylin and eosin staining can indicate HD.

Anorectal manometry uses a small rectal balloon and anorectal pressure sensors to determine the presence or absence of the recto anal inhibitory reflex (RAIR -relaxation of the internal anal sphincter in response to rectal distension).Anorectal manometry may also have a role in determining rectal sensation threshold and the presence of anorectal dyssynergia, potentially directing therapy, including the addition of physiotherapy or biofeedback.

Spinal imaging, including magnetic resonance imaging, should be considered in the child with constipation and other neurologic signs or symptoms, including lower motor dysfunction, lower urinary tract symptoms, and lumbosacral spinal abnormalities.

Management

Most children with functional constipation with or without feacal incontinence benefit from a precise, well organized treatment plan. The treatment is comprehensive and has four phases:

1. Education
2. Disimpaction or clean out of stools
3. Prevention of re-accumulation of stools
4. Withdrawal of treatment

Education

Education and reassurance constitute the primary component in the management of functional constipation and faecal incontinence and should continue throughout all stages of management. Developmentally appropriate discussion of the anatomy and physiology of the lower gastrointestinal tract and defecation is important and visual diagrams can aid in this education. Parents need to be educated that faecal incontinence is often involuntary and the result of overflow from constipation, or altered function of the rectum and pelvic floor as well as learned withholding behaviours in some children. Counselling can be provided to parents to help them establish a positive and supportive attitude toward their child during treatment.

Disimpaction or cleanout

Removal of impacted feacal matter decompresses the rectum, allows for the normal passage of stool, and prevents liquid stool from leaking around the fecal mass. Among the approaches to disimpaction are high-dose oral laxatives, enemas, manual disimpaction, or admission to the hospital for nasogastric administration of a bowel cleansing agent. High-dose oral laxatives and enemas are equally efficacious, but the preferred method for evacuation of faecal impaction is via the oral route.

Current recommendations suggest the use of polyethylene glycol solution (PEG 3350) at doses of 1 to 1.5 g/kg per day for 3 consecutive days (up to 6 consecutive days if necessary) to achieve disimpaction. If PEG 3350 is unavailable, once-daily sodium phosphate, saline, or mineral oil enemas for 3 consecutive days are acceptable. Suppositories may be used in combination with high-dose oral laxatives to help promote evacuation of the fecal impaction.

Manual disimpaction is rarely necessary and generally not advised except in cases of severe impaction and obstipation. If manual disimpaction is required, general anesthesia should be used to decrease the trauma associated with this procedure.

Prevention of reaccumulation of stools

a. Dietary modification

Encourage breastfeeding during early infancy and cereal supplementation should be started after 4 months of life.

Diets rich in high fiber are bran based cereals, pulses, fruits, vegetables etc. The

dietary recommendation for children older than 2 years of age is to consume an amount of dietary fiber equivalent to age in years plus 5grams/day.

b. Maintenance therapy with laxatives

Laxatives used for maintenance therapy should be individualized for each patient. In practice, laxative doses should be titrated to

Medication	Age	Dose
Slow oral disimpaction		1.5gm/kg/day
PEG 3350 without electrolytes (for 3 days		52gm/day
PEG 3350 with electrolytes (for 6 days)	2 to 4 yrs old	78gm/day
	5 to 11yrs old	2ml/kg twice/day
Milk of magnesia (for 7 days)		3ml/kg twice/day
Liquid paraffin (for 7 days)		2ml/kg twice/day
Lactulose or sorbitol (7 days)		
Rapid rectal disimpaction	Infants & toddlers	
Glycerin suppositories	< 1 year	60ml
Phosphate enema	> 1 years	60ml/kg body weight upto 135ml twice daily

Table 2 – Suggested medications for faecal disimpaction

Dietary fibres are non-starch polysaccharides – can be water soluble like oat bran, barley, nuts, seeds, beans, lentils, peas and some fruits like pomegranate, apple, plantain, strawberry, guava, pear, peach, amla and water insoluble like wheat bran, vegetables like bitter gourd, beetroot, carrot, radish, cucumber and whole grains.

The dietary fibres contribute to increase bulk of stools by virtue of fermentation and bacterial overgrowth and mechanical water holding effect which lead onto faster colonic transit and lesser colonic absorption.

The dietary fiber content in flours can be increased by not sieving and by the addition of ragi/jowar/mung flour, til or flaxseeds powder, grinded dried skin of orange/musambi powder. Milk can be enriched with dietary fibres by adding dry fruit powder, corn flakes, wheat flakes or mussel.

Intake of plenty of fluids is encouraged. Excess of drinks in the form of milk, sugar, chocolates juices and cold drinks to be avoided. Bakery foods like biscuits, breads and junk foods like chips, kurkure, maggi, burgers and pizza to be discouraged.

achieve at least one or two bowel movements every day that are loose enough to ensure complete daily emptying of the lower bowel and to prevent faecal incontinence and abdominal pain.

Osmotic laxatives increase the osmotic load within the lumen of the intestine, allowing for fluid retention. The retained fluid is incorporated into the stool and distends the colon, promoting peristalsis. Children may experience bloating, but these laxatives are generally safe; the most common adverse effect is diarrhoea. The two main osmotic laxatives are polyethylene glycol (PEG) and lactulose/ lactitol. Based on the literature, and the experience of the group, the ISPGHAN recommendations are: (i) PEG is the first line of therapy and is more effective as compared to lactulose/lactitol. However in children <1 year of age, the only drug recommended is lactulose/lactitol. (ii) In case of nonresponse or intolerance due to non-palatability to PEG, the second line of treatment is lactulose/lactitol which is safe for all ages. (*iii*) Two osmotic agents like PEG and lactulose/lactitol should not be given simultaneously. Combinations therapy with two classes of laxatives is not

Medication	Age	Dose
For long term treatment (years)		
PEG 3350 without electrolytes	>1 month	0.4 to 0.8gm/kg/day
Lactulose or sorbitol	>1 month	1-3ml/kg/day in 2 doses
Milk of magnesia	>1 month	1-3ml/kg/day in 2 doses
Liquid paraffin	>12 months	1-3ml/kg/day in 2 doses
Isabgol		Age in years + 5 = gm/day
		Titrate upto 20gm/day
For short term treatment (months)		
Senna syrup/tablets	1-5 years	5ml(1 tab) with breakfast,max 15ml/day
	5-10years	2 tablets with breakfast,maximum 3 tablets/day
Glycerin enemas	>10yrs	20-30ml/day (1/2 glycerin and ½ normal saline
Bisacodyl suppository	> 10yrs	10mg daily

Table 3 – Suggested medications and dosages for maintenance therapy of constipation

recommended for children.

Stimulant laxatives such as bisacodyl or senna irritate smooth muscle of the colon and stimulate the myenteric plexus to produce peristaltic activity within the colon. Children may experience abdominal cramping with the peristaltic activity. The abdominal cramping is self-limited and can be reduced by decreasing the dose. Although stimulant laxatives are safe, no studies have assessed dependency with chronic daily use. Stimulant laxatives can generally be reserved for intermittent use and rescue therapy.

Liquid paraffin may ease the passage of stool by lubricating the intestine and decreasing water absorption. A common complaint with use of liquid paraffin is leaking of the oil from the rectum, which can be unpleasant. Palatability of mineral oil is also a challenge for many children. Oral mineral oil is contraindicated in children younger than age 1 year or with known or suspected aspiration.

c. Behaviour modification

This component should be started at the time of bowel disimpaction or cleanout and continue throughout maintenance treatment. An important part of the standard medical-behavioural treatment of constipation is improving toilet sitting behaviour. However, stool withholding and toileting refusal behaviours may interfere with progress toward toilet sitting goals and sometimes must be addressed before implementing a toilet sitting plan.

Stool withholding and toileting refusal are believed to be related to the history of difficult-to-pass or even painful bowel movements and are often conceptualized as an anxiety or phobia about passing bowel movements, especially into the toilet. The initial focus of stool withholding management should be to ensure soft and easy to-pass bowel movements so that the child can gain comfort in passing a bowel movement on a daily basis. In early stages of treatment, bowel movements in a pull-up or diaper may need to be reinforced for the child to gain confidence and voluntarily relax the pelvic floor to achieve a bowel movement.

Toilet refusal behaviour should also be treated with interventions that gradually desensitize children toward toileting. Desensitization to the toilet may include rewarded trips to the bathroom to look at the toilet, stand by the toilet, sit on a closed lid fully clothed, and eventually sit on the toilet with open lid and pants down. Once the child is having bowel movements comfortably in the diaper or a pull-up and able to sit on the toilet

without significant anxiety, parents can use a shaping procedure to encourage bowel movements closer to the toilet and eventually into the toilet. Reward systems or incentives are used to encourage children to take a next step toward successful toileting behaviour.

Once the child is comfortable and compliant with sitting on the toilet, the overall goal is to improve daily toileting habits and routines. Scheduled toilet sits can occur 20 to 30 minutes after meals to take advantage of the gastrocolic reflex. The time on the toilet should be unrushed and positive. It may include special activities that are only available while on the toilet (special books, toys). Parents can also be counselled to provide modelling and coaching during toilet sitting, which includes the parents showing the child when they sit on the toilet and that they are pushing to help get bowel movements out in the toilet. Toilet sits should generally last 5 minutes, but some children need to gradually work their way up to longer sits if there is initial resistance.

Scheduled, rewarded toilet sits should include small step stools to assist the children in getting on the toilet and to use as leverage for their feet. A wider stepstool or potty stool may allow the child to spread out the feet and knees for better posture to allow successful defecation and for them to feel more comfortable and balanced on the toilet. Once children are having more productive bowel movements in the toilet and soiling has stopped for a 1 month, the number of daily toilet sits can be reduced. As treatment progresses, children can start to earn incentives/rewards for independently going to the toilet when they feel the urge to have a bowel movement rather than strictly relying on the schedule.

Withdrawal of treatment and follow up

Start reducing the dose of laxatives only after stool pattern has become normal. A stool diary is helpful in this regard. No abrupt stoppage of medications and ensure that faecal impaction does not recur. High fiber diet and toilet training should continue for 2 to 3 years to avoid relapse.

A suggested follow up schedule would be initially weekly review for 2 to 3 weeks, then monthly till stooling is normal and finally bimonthly for 6 months to an year.

Successful outcome of treatment should be defined as (*a*) stool normalcy while on laxatives for a period of at least 4 weeks of initiation of therapy, and (*b*) achievement of stool normalcy for a minimum period of 6 months before tapering. Normalcy of stools should defined as daily, not hard, nor loose watery stools, with absence of pain, straining, bleeding, posturing or incontinence.

Outcome and prognosis

Approximately 60%of children with functional constipation are symptom-free between 6 and 12 months after beginning treatment regardless of laxative use, with the remaining 40% of children still experiencing symptoms. 25% of children with functional constipation continue to experience symptoms into adulthood. Older school-age children and adolescents who have ongoing constipation and faecal incontinence are even more difficult to treat. All these points highlight the need for aggressive treatment as early as possible as well as close follow-up evaluation and adjustments to the treatment plan. Nonetheless, most children with constipation and faecal incontinence can be managed effectively by the general paediatrician.

Indications for referral to a paediatric gastroenterologist include medical red flags, trouble with disimpaction, trouble establishing maintenance therapy, and lack of improvement after 3 months of therapy. Referral to a pediatric behavioral specialist should be considered if significant conditions are interfering with treatment, such as attention-deficit/hyperactivity disorder, oppositional behaviors, anxiety or mood disorders, family conflict or parent-child conflict, or problems with adherence to recommendations.

Prevention

Prevention of colonic dysfunction have received much less attention but attending paediatrician can play a pivotal role by providing anticipatory counselling in terms of appropriate feeding practices, high fiber diet, interpretation of normal bowel habits, counselling life issues of the child and early detection of defeacatory disorders in children.

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A three-month-old girl with liver failure: How far have we reached after autopsy?

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CLINICAL PROTOCOL

History: A three-month-old female child presented with jaundice for 15 days, progressive abdominal distension for 10 days, lethargy for 5 days, black tarry stool for 2 days. There was no history of acholic stools, skin bleeds, fever, rash, diarrhea, tachypnea or seizures.

She was born second by order of birth of a non-consanguinous union with a birth weight of 2 Kg. The antenatal and perinatal period was uneventful. Her elder 3-year-old brother was developmentally normal with no similar history. She was breast-fed, which was supplemented by diluted, sugared, cow's milk, since birth.

She was admitted elsewhere for a couple of days prior to admission where she had been given IV antibiotics and a received a blood transfusion.

Clinical examination: On admission the patient was afebrile. Vitals parameters were normal. Oral mucosal bleed was noted. Anterior fontanelle measured 1 × 1 cm and was not bulging; Weight: 3.0 kg (<−3 Z-score); Length: 49 cm. (<−3 Z-score); Occipital-frontal circumference: 33.5 cm (<−3 Z-score). She had pallor, edema and icterus. There was no cyanosis, lymphadenopathy, clubbing. There was no dysmorphism, coarse features, or specific odour. On systemic examination, abdomen was soft, non-tender, distended with central, everted umbilicus. Fluid thrill was present. On palpation, liver was irregular, firm, non-tender with smooth surface, 5 cm below the right costal margin, with a span of 8 cm; spleen was firm and 2 cm below left costal margin. On evaluation of central nervous system, she was conscious and alert, fixing, and following light. Examination of chest and cardiovascular system was normal.

Investigations: Her haematological and biochemical investigations during the hospital stay are summarised in *Table 1*.

- Lipid profile(mg/dL): Triglyceride—97.3; cholesterol—231; low-density lipoprotein—75; high-density lipoprotein—46.5
- Alpha-fetoprotein - 21,000 µg/mL
- Direct Coomb's test (DCT) and glucose 6 phosphate deficiency (G6PD): Negative
- Eye: Slit Lamp and Fundus: No cataract, choroidal-retinal synaechae, retinal abnormalities
- Ultrasonography abdomen: Liver 6.9 cm; normal outline and echotexture; hepatic vein and portal vein normal; spleen: 6.3 cm; pancreas: N size and increased echogenicity; moderate ascites
- Urine Reducing substance: Nil
- Blood/Urine/Ascitic C/S: Sterile
- Venous blood gas (at admission) pH – 7.30, HCO^{3-} 17 meq/L–: Metabolic acidosis; normal lactate
- TMS/GCMS: No abnormal metabolite for aminoacidurias, organic acidurias, fatty acid oxidation defects and urea cycle defects.

Course during hospital stay

After admission the child was started on cefotaxime (for spontaneous bacterial peritonitis), octreotide and pantoprazole. Additionally, was supported with albumin infusion, vitamin K along with other fat and water soluble vitamin supplements. Upper GI endoscopy was performed which showed a Grade I esophageal varix and diffuse gastritis. Octreotide was stopped. Milk was stopped presuming galactosemia on day 2; however, after an initial improvement there was progressive worsening in coagulopathy/ ascites. No hypoglycaemia was documented during the hospital stay. Hemoglobin dropped in absence of GI bleed, and packed red blood cells were repeated twice. On day 10 of admission, in view of fever, pneumonia and worsening counts, antibiotics were upgraded to vancomycin/imipenem. Ascitic fluid was tapped almost daily due to rapid refilling. The child continued to worsen and eventually died on day 14 of admission.

Unit's diagnosis: Metabolic liver disease ? Galactosemia ?Mitochondrial hepatopathy

Discussion on clinical protocol:

Based on data and investigations available, we were dealing with a young infant with cholestatic jaundice. Cholestasis can be classified into biliary (obstructive, large extrahepatic, or small intrahepatic bile ducts) or hepatocellular (defect in membrane transport, embryogenesis, or metabolic dysfunction) in origin. The approach to such a patient would be to first try and identify whether the cause is biliary or hepatocellular.

The presence of pigmented stools, delayed – onset of jaundice and ascites (suggestive of hepatocellular injury) in a sick child suggests more likely a hepatocellular/ intrahepatic cause. The clinical pointers that lead towards a diagnosis in infants with intrahepatic cholestasis are tabulated in **Table 2.**

The presence of uncorrectable coagulopathy (INR > 2) points towards the diagnosis of pediatric acute liver failure. (1) Liver failure in an infant with early – onset ascites are important clues to the diagnosis in this child. The common causes of liver failure in an infant and their common clinical presentation is listed in **Table 3**.

If we look at this list in context of our child, Tyrosinemia is less likely, as generally the bilirubin is well below 10 mg%, AST/ALT are only mildly elevated and alpha fetoprotein is markedly elevated.(mean level 160000 microgram/decilitre) (2) Gestational alloimmune liver disease, in which maternal immunoglobulin G causes complement-dependent severe fetal liver injury and dysregulated handling of iron by the fetal liver, causing abnormal iron distribution in the body is an important cause of neonatal liver failure in an IUGR baby, however they present earlier, AST/ALT are just mildly elevated and the liver is generally shrunken. (3) Galactosemia is a possibility, however lack of improvement in INR/albumin and ascites despite 2 weeks off milk is odd.(4)The baby was exposed to sucrose, so hereditary fructose intolerance (HFI) is possible but features that do not fit in with our case is the absence of diarrhea or vomiting and normal levels of serum phosphate and uric acid.(5) Primary mitochondrial hepatopathy unless looked for can be a missed as a cause for severe liver disease in early infancy.(6) Multisystem disease may not always occur at presentation due to heterogeneous expression of genetic defect in different tissues; IUGR and moderate to marked rise of AST/ALT as in this case is well described. HLH is unlikely because of the absence of fever and cytopenias, while Niemann Pick C seems unlikely because of the small spleen size. (7) The normal lipid profile makes Wolman's disease an unlikely possibility. One would not consider CMV and other TORCH infections in such a setting as elevated TORCH titres are often a red herring in the workup of a neonate with cholestasis. Except for acquired HSV infection which has rapid deterioration, the rest of the TORCH infections rarely cause jaundice. The delayed presentation and the absence of skin lesions and other stigmata makes HSV unlikely.

Hence to sum up, the clinical possibilities are - mitochondrial hepatopathy, galactosemia and HFI.

However, it is to be remembered that all these disorders discussed above have a varied spectrum of presentation and may at times not have a "classical" presentation as discussed above and hence it is prudent to keep an "open "mind when evaluating such a child.

PATHOLOGY PROTOCOL

Partial autopsy was done in this case; externally, prosecutor noted pallor with icterus. Serous cavities: Yielded 500 mL (icteric fluid) in peritoneal cavity, 50 mL of serous fluid in pleural cavities, 15 mL of serous fluid in pericardial cavity.

Liver- Weight: 105 gm gross. Capsular and cut surface smooth with tiny nodules (<3 mm), cut surface was bile stained. (Fig. 1) Microscopy revealed hepatocytes showing pseudo acinar transformation, with micro- and macrovesicular steatosis and prominent giant cell transformation (Fig. 2). There was distorted architecture with porto-portal and porto-central bridging. Portal tracts were replaced by fibrous bands which were extending to the peri-portal areas with fibrosis also noted in perivenular zones. Focal peri-portal cholangiolar proliferation was noted. Intrahepatocytic and cholangiolar cholestasis was noted. No macroregenerative nodules seen. Extrahepatic biliary tract is within normal limits. *Lungs*- Weight: 70 gm. On gross examination were subcrepitant with focal areas of congestion. Trachea and airways did not show inspissated secretions. Micro: Occasional secondary bronchiole showed secretions, foamy macrophages identified in most of the alveoli. Cytomegalovirus inclusions were identified in pneumocytes lining the alveoli (Fig. 3A) focally. Many pigment laden macrophages were noted as well. No fungal hyphae/abscesses were seen. *Heart*- Weight: 20 gm. All chambers and valves were within normal limits. A single 8 mm abscess noted in left ventricular wall , which microscopically is composed of central necrotic material admixed with neutrophils and giant cells and few Aspergillus hyphae (Fig. 3B). *Thymus* - Weight: 2 gm. Within normal limits. Microscopic examination showed stress-induced involution with excess of Hassall's corpuscles. Adequate representation of CD3 T lymphocytes. *Bone marrow* was within normal limits.

Discussion on pathology protocol

Histologic or ultrastructural feature is almost never specific in the diagnosis of inherited liver disorders hence pathologists must rely on integrating clinical information with the biopsy features to avoid diagnostic roadblocks.

Steatosis is a common histopathologic finding in several inherited disorders affecting liver. A perturbation of mitochondrial metabolism is associated with microvesicular steatosis. Our patient had micro and macrovesicular steatosis. Galactosemia and HFI, are classically associated with diffuse macrovesicular or mixed steatosis in the newborn or infant. In galactosemia, typical liver biopsy shows extensive periportal and intra lobular fibrosis, pseudo acinar transformation and distortion of periportal vasculature. (8) All these features were identified on the biopsy of our patient. The histopathologic features of HFI mimic those of galactosemia, except that cirrhosis is usually absent. Other causes of hepatic steatosis in an infant include Wolman's disease (hepatocyte vacuolation, foamy kupffer cells, macrophages with positive lipid stains), cystic fibrosis (inspissated material within bile ducts) and alpha 1 antitrypsin deficiency (macro nodular cirrhosis, PAS-positive, diastase-resistant

hepatocyte inclusions) features of which were not seen on histopathology. (9)

Evidence of CMV and aspiration pneumonia and aspergillus myocardial abcesses were found.

Final Diagnosis

Micronodular cirrhosis (Probably consistent with galactosemia) with portal hypertension

Myocardial abscess (fungal, aspergillus): Left ventricle

The CMV inclusions and foamy macrophages (milk globules) in lungs

Open Forum

Classic galactosemia is caused by deficient activity of galactose-1-phosphate uridylyltransferase the second enzyme of the main pathway of galactose metabolism (Figure 4) and its prevalence is 1:16,000-60,000 live-births. (10) It is an autosomal recessive disorder caused by mutations in the *GALT* gene and over 300 variations have thus far been described. Mutational analysis of the GALT gene from Indian subjects has revealed heterogeneity in the structure of the gene and the presence of novel mutations. (11) Infants with classic galactosemia generally appear asymptomatic at birth. However, after a few weeks of galactose ingestion through breast or formula feeding they start developing symptoms that, if undiagnosed and untreated, may lead to early decompensation and eventually death.

This case presented with a cirrhotic liver by the age of 3 months. The most likely cause of cirrhosis at this age with micro nodular cirrhosis and absence of iron would be galactosemia. Cataract is present at diagnosis in only 30-50% infants (4). A definite diagnosis could only have been established with red blood cell enzyme studies, which could not be performed as the child had received a blood transfusion just before admission. Screening for reducing substances in urine can be informative; however, it is not sensitive or specific. If the child is on intravenous fluids, galactosuria may no longer be present, thus leading to false negatives as seen in our child who was feeding poorly on admission. A genetic work – up could not be performed because of financial constraints.

No clinical improvement on withdrawal of lactose is odd in our case as the disease has a favourable prognosis by timely introduction of a lactose free diet. However, it is possible that the delay in diagnosis and overwhelming sepsis – bacterial, fungal (aspergillus) and CMV could have led to the worsening condition and eventual demise of the child. Depressed neutrophilic function by galactose or its metabolites and deficiency of IgM bactericidal opsonic antibodies may contribute to the high incidence of sepsis. Though, bacterial sepsis like *E. Coli* is commonest, other organisms like fungal and viral infections can rarely be the culprit in these children. (12) In the series by Sarma et al. 87.5% (21/24) of the children diagnosed with galactosemia survived, with uncontrollable sepsis and/or poor compliance leading to death in 3 children.

Long term outcomes in children who survive are associated with a few complications. One of the most frequent and well-established long-term complications is cognitive impairment with IQ standard scores in the low average (85–100) to borderline-low (<85) range. Girls and women with classic galactosemia may have primary ovarian insufficiency, with an incidence above 80%. Because of their galactose-restricted diet, patients are at risk for nutritional deficiencies, particularly calcium which should be supplemented. (10)

To conclude, a cholestatic infant with ascites, coagulopathy, and/or haemolysis should raise a suspicion for galactosemia. A lactose – free diet is lifesaving. Sepsis is a known cause of early morbidity and mortality and should be managed aggressively.

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Table 1 – Laboratory investigations during the hospital stay

	Day of admission	Day 4	Day 10	Day 13
Hb (mg/dL)	8.6	11.8	6.4	
TLC (cells/mm^3)	20,100	10,400	38,600	
DLC (N/L/M/E)	27,67,2,4	52,40,6,2		
Platelets (cells/mm^3)	4.35 L	1.22 L	2.19 L	
INR	7 (after IV vitamin K)	1.3	2.05	1.3
Fibrinogen			1.23	
Na/K/CI (mmol/L)	131/6.3/102			
Ur/Creat (IU/ml)	22/0.25		10/0.27	
Bil: T/D (mg/dL)	17.6/15	18.5/12.7	20.9/10	
AST (IU/ml)	893	1062	811	
ALT (IU/ml)	223	863	633	
ALP (IU/ml)			465	
TP: Albumin(mg/dL)	4/2.6	3.5/2	<3.5/2.1	
Ca/P/UricA (IU/ml)		9.1/3/3		
Ascitic protein	0.3 gm%		0.3 gm%	
Ascitic Fluid cells	1000 polys		Nil	
Serum Albumin Ascitic Gradient	2.6			
Ascitic Bilirubin	2 mg%			

Table 2 – Clinical clues of intrahepatic causes of neonatal cholestasis

Clinical Clues	Diagnosis
Onset of jaundice At birth: Few weeks after birth: Any point of time:	 GALD PFIC type II, galactosemia, tyrosinemia Mitochondrial Hepatopathy, HLH
Seizures	Hypoglycemia: Galactosemia, HFI Intracranial bleed: Cholestatic disorders (PFIC), advance liver failure with coagulopathy CNS infection: HSV
Pruritus	PFIC, Alagille's syndrome, Neonatal sclerosing cholangitis
Intrauterine growth restriction	GALD, MH
Maternal clues	Genital vesicles: HSV Oligohydramnios, megaplacenta: GALD Cholestasis of pregnancy or Pruritus on oral contraceptives: PFIC3 Acute fatty liver of pregnancy, hyperemesis: FAOD
Family history Consanguinity Repeated abortions or sib-loss Affected sib or sib death Gall stones	 Increased risk of autosomal recessive disorders GALD Galactosemia, tyrosinemia, MH, HLH, PFIC, Alagille PFIC-2 & 3

Clinical Clues	Diagnosis
Early-onset ascites	Galactosemia, tyrosinemia, GALD, MH, HLH, NPC
Delayed passage of meconium	Cystic Fibrosis
Presenting as acute liver failure	Galactosemia, tyrosinemia, GALD, MH, HLH, NPC, HSV, HFI
Findings on examination	
Scalp vesicles	HSV
Cataract	Galactosemia
Cherry red spot	NPC
Impaired vision	Septo-optic dysplasia
Hearing defects	PFIC1, Tight-junction protein (TJP2) mutations
Rickets (craniotabes)	Tyrosinemia
Hypotonia	MH, NPC, Zellweger's syndrome, Trisomy 21
Cardiac murmur	Alagille's syndrome
Facial Dysmorphism	Alagille's, Zellweger's syndrome, Trisomy 21
Skin rash	HLH, FAOD
Spleno-hepatomegaly	HLH, NPC
Shrunken liver	GALD
Hypoplastic (male) genitalia	Panhypopituitarism

GALD – Gestational Alloimmune Liver Disease, PFIC – Progressive Familial Intrahepatic Cholestasis, HLH – Hemophagocytic Lymphohistiocytosis, MH - Mitochondrial Hepatopathy, HFI – Hereditary Fructose Intolerance, HSV – Herpes Simplex Virus, FAOD – Fatty acid oxidation defect, NPC – Niemann Pick C

Table 3 – Clinical Features and diagnostic tests of common causes of cholestatic jaundice in infants associated with liver failure

	Clinical features	Supporting laboratory parameters	Diagnostic tests
Galactosemia	Feeding intolerance, vomiting, diarrhea, lethargy, developmental delay, hepatosplenomegaly, coagulopathy, hypoglycaemia, seizures, renal tubular dysfunction, cataract (bilateral), E.coli sepsis and rarely hemolysis.	Urine positive for non-glucose reducing substances (NGRS) while on lactose feeds	RBC Galactose-1 phosphatase uridyl transferase enzyme assay

	Clinical features	Supporting laboratory parameters	Diagnostic tests
Hereditary fructose intolerance	History of dietary exposure to fructose/sucrose, protracted vomiting, diarrhea, failure to thrive, hypoglycemia, seizures,	Positive urine NGRS, Fructose challenge test (obsolete nowadays), hypophosphatemia, hyperuricemia.	Pathogenic variants in ALDOB on genetic testing or deficient hepatic fructose 1-phosphate aldolase (aldolase B) activity on liver biopsy
Type 1 Tyrosinemia	Coagulopathy with or without cholestatic jaundice , hypoglycaemia, hepatomegaly, ascites	High alpha-fetoprotein (mean level: 160,000 µg/mL)	Increased urinary succinylacetone
Mitochondrial cytopathy	Onset in the first week of life or later, Multisystemic, neurological involvement in form of severe hypotonia, myoclonus or psychomotor retardation.	Plasma lactate >2.5 mmol/L, molar ratio of plasma lactate/pyruvate > 20:1,	Genetic mutational analysis for respiratory chain disorders and tandem mass spectrometry for fatty acid oxidation defects.
Gestational alloimmune liver disease	Presents usually few hours to days (sometimes weeks) after birth as hypoglycemia, coagulopathy, jaundice, anemia, ascites, anasarca, and splenomegaly with a shrunken liver.	High serum ferritin, low serum transferrin, high transferrin saturation (95 % to 100 %).	Lip or salivary gland biopsy shows iron deposition; MRI shows low signal intensity of pancreas and heart on T2 imaging.
Hemophagocytic Lymphohistiocytosis	Prolonged fever, hepatosplenomegaly, bleeding, skin rash, CNS abnormalities, jaundice.	Bicytopenia or pancytopenia, hyperferritinemia, hypofibrogenemia, hypertriglyceridemia	Molecular diagnosis or HLH-2004 (5 out of 8) diagnostic criteria
Niemann–Pick disease (type C)	Spleno – hepatomegaly, ascites, Hypotonia, ataxia, vertical supranuclear gaze palsy, developmental delay, seizures.	Positive filipin staining in cultured fibroblasts.	Molecular genetic testing of NPC1 and NPC2

	Clinical features	Supporting laboratory parameters	Diagnostic tests
Wolman's disease	Hepatosplenomegaly, ascites, vomiting, diarrhoea	High total serum cholesterol, low-density lipoprotein, and triglycerides; and low serum high-density lipoprotein, calcified adrenal glands	Deficient lysosomal acid lipase enzymatic activity in leucocytes (or fibroblasts)

E.coli - Escherichia coli, RBC – Red blood cell, CNS – Central nervous system, HLH – Hemophagocytic Lymphohistiocytosis, NPC – Niemann Pick C

Figures

Fig. 1 – Capsular and cut surface smooth with tiny nodules (<3 mm), cut surface is bile stained (gross photograph)

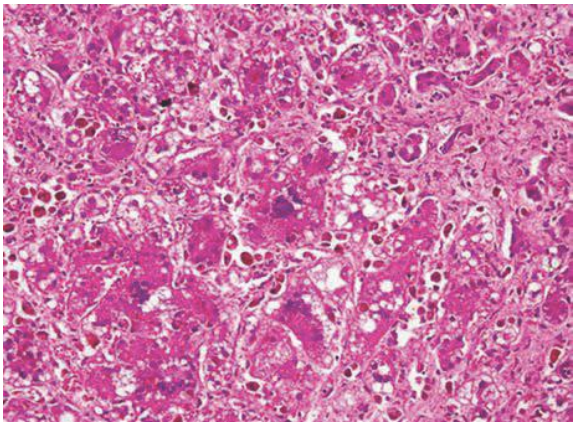

Fig. 2 – Hepatocytes show pseudo-acinar transformation, with micro- and macrovesicular steatosis and prominent giant cell transformation (H&E, 400×magnification)

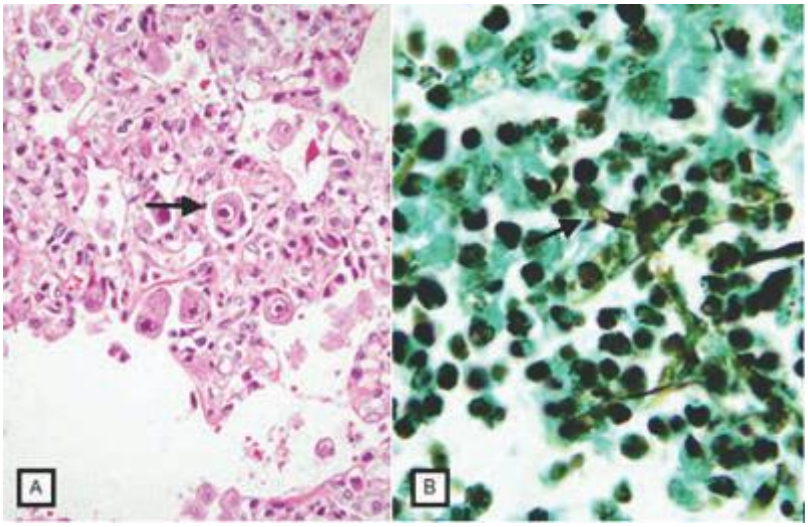

Fig. 3 – (A) CMV inclusions identified in pneumocytes lining the alveoli (H&E, 400×magnification) (B) Branching septate hyphae consistent with morphology of Aspergillus from the abscess in the left ventricular wall (D-Grocott stain 400×magnification)

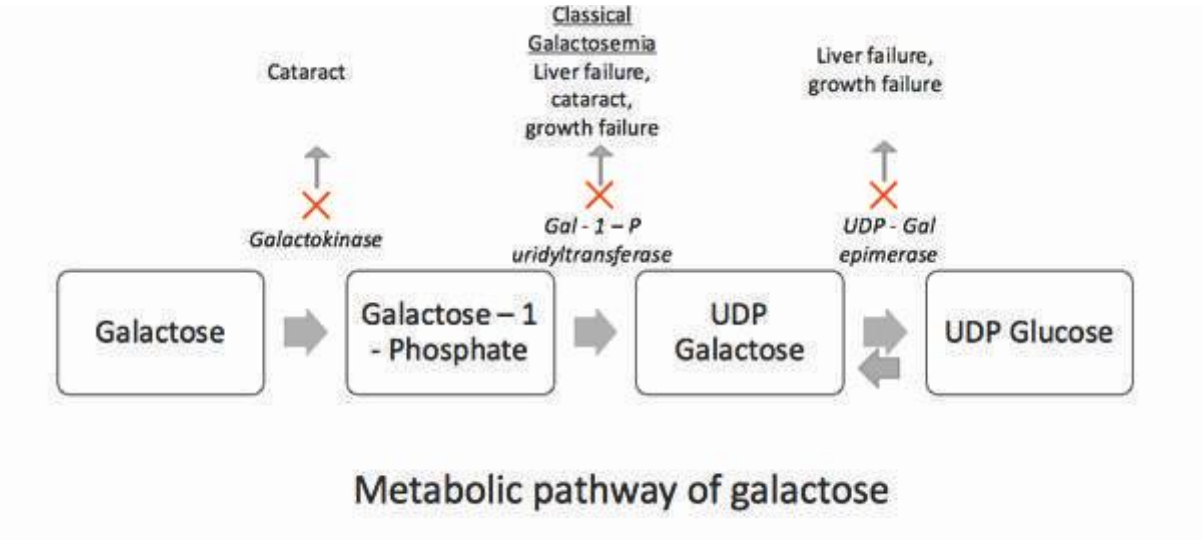

Fig. 4 – Galactose metabolism

Celiac disease presenting as acute unilateral blindness

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Abstract

Background: Celiac disease is known to present with extra gastrointestinal manifestations.

Case Characteristics: An eight years old male child presented with painless acute loss of vision in left eye.

Observation: MRI orbit was suggestive of demyelinating optic neuritis. Serology and duodenal biopsy confirmed celiac disease. Vision regained completely with steroids and gluten free diet.

Message: Acute loss of vision or blindness is an uncommon presentation of celiac disease.

Key words: Celiac disease, blindness, optic neuritis

Introduction: Celiac disease (CD) is an autoimmune condition affecting the small intestine, triggered by the ingestion of gluten, the protein fraction of wheat, barley, and rye. When patient with celiac disease ingest gluten, an immunologically mediated inflammatory response occurs that damages the mucosa of their intestines, resulting in malabsorption of food nutrients. Apart from gastrointestinal symptoms, celiac disease has extraintestinal symptoms like anemia, osteopenia, motor weakness, ataxia, seizures, peripheral neuropathy, dermatitis herpetiformis, bleeding diathesis and ophthalmic manifestations like uveitis, cataract, orbital myositis, retinopathy, occipital calcification and rarely optic neuropathy. We are reporting a case of celiac disease who presented as acute loss of vision of left eye.

Case report: An eight year old boy presented with painless acute loss of vision of left eye in July 2018 which was preceded by blurring of vision for few hours. There was no history of fever, rashes, vomiting, diarrhea, constipation, seizures or headache. On examination vitals were stable, weight: 18.1 Kg (5-10th centile), Height: 114 cm (5-10th centile). There was pallor on general examination. Systemic Examination was normal. He was referred to ophthalmologist and pediatric neurologist. Ophthalmologist's evaluation showed no abnormal finding. Paediatric neurologist advised MRI brain and Orbit. MRI showed Inflammatory changes in left preseptal orbital region extending into the post septal and retro bulbar region showing moderate contrast enhancement, left orbital optic nerve showed focal loss of perineural CSF signals, focal hyperintensity with focal acute neuritis changes (Fig. 1 A). CSF was advised but was refused by the parents. CRP was 1.2mg/L (0-5).

In view of anemia and poor growth following investigations were done: Hb 7.3 gm/dl, MCV: 55.5 fL, Total Leucocyte count 9100/µL; Platelets: 458000/µL, RDW: 23.3 %. Serum tissue transglutaminase IgA >300 unit/ml (Upper limit is 18unit/ml).UGI endoscopy was suggestive of scalloping of duodenal mucosal folds. Duodenal biopsy showed Marsh grade III b changes (Fig. 1 B)

He was put on strict gluten free diet. In view of acuity of symptoms and changes of demyelination he was given 3 doses of injection methyl prednisolone followed by oral prednisolone which was gradually tapered and stopped over next 4 weeks. The child regained

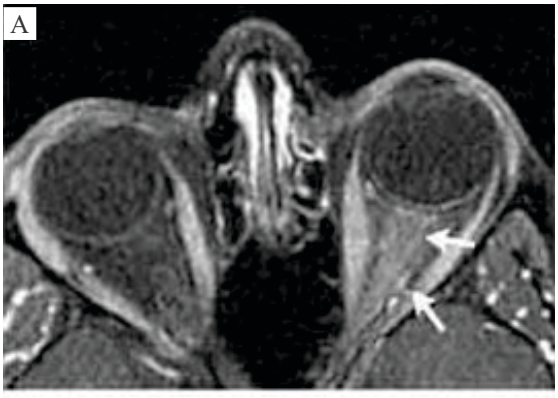
full vision in left eye after six days of treatment. On follow up till 6 months, his weight and height centiles have increased to 50%ile and there was no further episode of vision loss.

Discussion: Atypical forms of celiac disease without prominent gastrointestinal symptoms and with frequent extra-intestinal manifestations, are being increasingly recognized, especially over the past decade, both in adult and pediatric patients. The ophthalmic manifestations can be divided into autoimmune disorders and absorptive disabilities. The manifestations related to malnutrition are correlated to the low levels of vitamin A, Vitamin D, and calcium which could cause retinopathy, cataract, dry eye and pseudotumor cerebri. The manifestations related to autoimmune disorders are orbital myositis, uveitis, thyroiditis associated with orbitopathy and brain occipital calcification. [1]

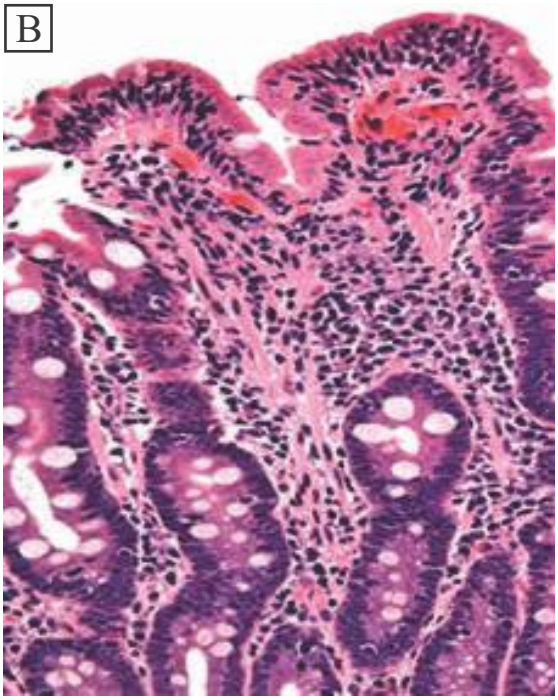
Similar presentations of celiac disease with acute loss of vision related optic neuropathy has been reported in literature. Boushehri et al. reported an adult who responded to immunosuppressive therapy and gluten free diet. [2] Another case of celiac disease with right sided optic neuritis was reported in which the neurological examination was unremarkable and brain MRI showed non specific white matter lesions. Vasculitis tests were normal and anti-aquaporin 4 antibody was negative. CSF was normal and oligoclonal band was negative. The optic neuritis improved with intravenous methylprednisolone pulse therapy for 5 days. [3] A pediatric case has also been reported with recurrent optic neuritis, celiac disease, partial IgA and IgG3 deficiency. Treatment with Tacrolimus was successful in preventing disease relapses. [4]

To conclude, we report the unusual association of optic neuritis and celiac disease. The fact that celiac is an autoimmune disease and one autoimmune disease predisposes to another, the optic neuritis in this case with response to immunosuppression appears to be linked to celiac disease.

Fig1 – (A) MRI orbit showed loss of perineural CSF signals, focal hyper intensity suggestive of demyelinating optic neuritis.



(B) Duodenal mucosal biopsy demonstrated crypt hyperplasia, lymphocytic proliferation and villous atrophy consistent with Marsh grade IIIb.



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A rare case of chronic diarrhoea in an infant

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Introduction:

Johanson-Blizzard syndrome (JBS) is a very rare autosomal recessive disorder first described in 1971 by Johanson and Blizzard [1]. It is characterized by exocrine pancreatic insufficiency, nasal wing hypoplasia, ectodermal scalp defect, growth retardation and other abnormalities. It is caused by mutations of the UBR1 gene, which is highly expressed in pancreatic tissue (2).

Less than 100 cases of JBS have been reported worldwide and very few from India. We here report a rare case of JBS who presented with steatorrhoea and failure to thrive.

Case report:

Two month old female baby presented with complains of chronic diarrhoea with greasy stools since birth. She was first child of her parents, born out of consanguineous marriage at full term. Her birth weight was 2 kg and was exclusively breastfed. She also had failure to thrive with weight at presentation of just 1.7 kg. She had peculiar dysmorphic facies with hypoplastic alae nasi, upslanting palpebral fissure and patchy loss of hair on scalp (Image 1)

Her routine investigations including complete blood count, liver function tests, serum electrolytes were normal. TSH was normal. Stool for fat globules showed 30 droplets/high power field. Ultrasound abdomen showed fatty infiltration of pancreas. Echocardiography was normal. BERA and fecal elastase were not done.

Her characteristic facies with evidence of exocrine pancreatic insufficiency (steatorrhoea & fatty infiltration of pancreas) led to syndromic diagnosis of Johanson Blizzard Syndrome. Her blood sample for genetic testing of JBS was sent. She was started on pancreatic enzyme supplementation (2000 IU lipase per feed, with estimated 20000 IU/day for 8-10 feeds/day) along with fat-soluble vitamin supplements.

Image : 1 : Characterstic facies of the baby

Outcome:

Baby was lost to follow up and later on enquiry found to have died at home at 3 months of age.

Later genetic testing confirmed the heterozygous missense mutation (c.1688C>A, p.Ala563Asp) in exon 44 in both alleles by Sanger sequencing and diagnosis of Johanson blizzard syndrome.

Discussion:

Classic cases of JBS present in early infancy with syndromic features and severe exocrine pancreatic insufficiency. The genetic defect of JBS is a homozygous loss-of-function mutation in the Ubiquitin-Protein Ligase E3 Component N-Recognin 1 (UBR1) gene, located on chromosome 15q15-21.UBR1 is essential in the development and maintenance of acinarcells and mutation in this gene results in in-utero destruction of acinar tissue followed by fatty

replacement (3). This defect leads to almost complete absence of pancreatic enzymes in duodenal secretions. Additional features include: short stature (>80%), dental abnormalities (>80%), sensorineural hearing loss (80%), mental retardation(77%), scalp defects including alopecia (76%), hypothyroidism (40%), imperforate anus (39%), and genitourinary malformations (38%)[2]. Abdominal imaging of affected patients shows replacement of the exocrine pancreas by lipomatous and connective tissues [1, 2].

An exocrine pancreatic defect is a constant feature of this condition. The diarrhoea caused by pancreatic enzyme deficiencies leads to hypoproteinaemia, edema, anaemia, and failure to thrive. Hence pancreatic enzyme replacement with fat-soluble vitamins supplementation is the mainstay of the treatment.

Pancreatic insufficiency and severe hypo-proteinaemia may lead to death in infancy or early childhood.

It is important to recognize this rare syndrome with characteristic facies in infants associated with severe exocrine pancreatic insufficiency. Early supplementation of pancreatic enzyme is required in neonatal period along with nutritional support. Prenatal counseling should be done for future pregnancies owing to autosomal recessive mode of inheritance of this condition.

References:

1. Johanson A, Blizzard R. A syndrome of congenital aplasiaof the alae nasi, deafness, hypothyroidism, dwarfism,absent permanent teeth and malabsorption. J Pediatr.1971;79: 982-7.

2. Zenker M, Mayerle J, Reis A, Lerch MM. Genetic basis and pancreatic biology of Johanson-Blizzard syndrome. Endocrinol Metab Clin North Am. 2006; 35: 243-53, vii-viii.

3. Schoner K, Fritz B, Huelskamp G, Louwen F, Zenker M, Moll R, Rehder H. Recurrent Johanson-Blizzard syndrome in a triplet pregnancy complicated by urethral obstruction sequence: a clinical, molecular, and immunohistochemical approach. Pediatr Dev Pathol. 2012; 15: 50-7.

GUESS THE DIAGNOSIS

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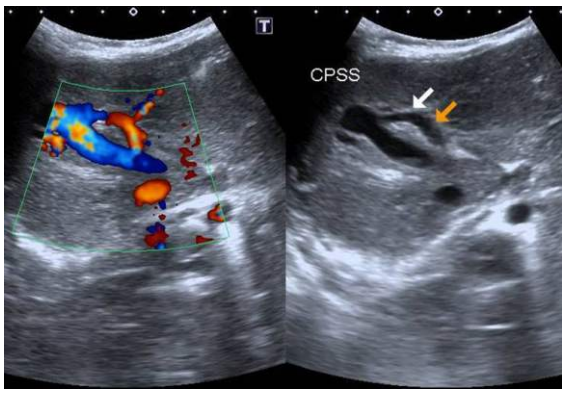
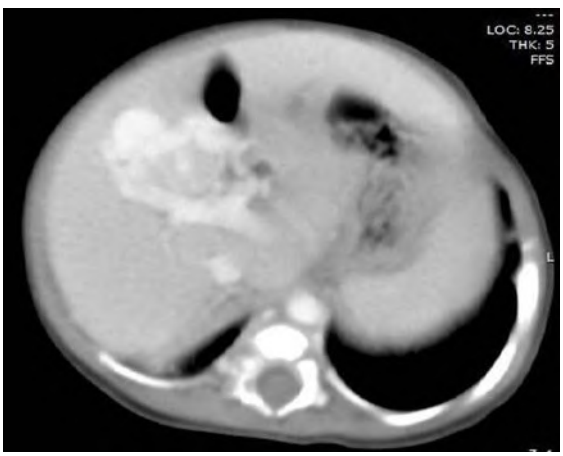
65 days old male infant, born full term small-for-gestational age (birth weight = 2.1 kg) of a non-consanguineous marriage, presented with conjugated hyperbilirubinemia since Day 15 of life. He had history of symptomatic hypoglycaemia within first hour of life which lasted for 2 days. His development was appropriate for age. Examination revealed a 3 cm soft palpable liver and grade III ejection systolic murmur at pulmonary area. Stools were well pigmented. Laboratory tests revealed conjugated hyperbilirubinemia (total bilirubin 4.1 mg/dL, direct fraction 2.4 mg/dL) and elevated transaminases (AST/ALT 439/154 IU/L), fasting hypoglycaemia (blood glucose <40 mg/dL after 4 hours fast) with positive urine non-glucose reducing substances. Ammonia level was 217 microgm/dL and alpha-fetoprotein level was 192,000 ng/mL. Galactose-1-phosphatase uridyl transferase (GALT) assay was normal. Echocardiography showed ostium secundum atrial septal defect (5 mm). His ultrasonography of abdomen (Picture 1) showed something characteristic for which he was taken up for computerized tomography (Picture 2). What is his diagnosis and how can we manage him?

Pictures 1 (A and B) and 2





Answer: **Congenital portosystemic shunt (CPSS).**

CPSS is a rare vascular anomaly of the liver with an incidence of 1:30,000 live births. This defect happens due to abnormal development of the liver vasculature. It has been postulated that incomplete involution of vitelline venous system during the development of hepatic sinusoids results in shunt formation. Around one-sixth of CPSS patients may have multiple anomalies, most commonly involving cardiovascular systems including atrial or ventricular septal defects, coarctation of aorta, tetrology of Fallot, patent ductus arteriosus, splenic artery aneurysm, coronary artery fistula or cutaneous hemangiomas. Other abnormalities seen are polysplenia syndrome, anomalies involving renal and biliary system, and genetic syndromes (trisomy 21, Leopard, Osler-Weber-Rendu). Patients with CPSS show wide spectrum of symptoms from incidental detection (22%) on colour-doppler to severe complications. Altered fetal hepatic perfusion leads to intrauterine growth retardation, neonatal cholestasis (9%), hypoglycemia and hypergalactosemia. Later presentations include unexplained neurocognitive dysfunction, behavioural issues and minimal hepatic encephalopathy due to elevated ammonia. One-fourth of these individuals develop hepatopulmonary syndrome or portopulmonary hypertension secondary to excessive vasoactive mediators bypassing the liver. Moreover due to abnormal vascular supply, tumours develop in 24% of such livers – focal nodular hyperplasia, nodular regenerative hyperplasia, adenomas and hepatocellular carcinoma [1].

Diagnosis is based on colour-Doppler which demonstrates abnormal communication between portal (PV) and hepatic veins (HV) or persistent ductus venosus. Intrahepatic PV branches may be non-visible or hypoplastic showing hyperechoic bands surrounded by hypoechoic stripes. PV flow may be slow or minimal. CPSS is classified as extrahepatic with complete (type I) or partial (type II) absence of intrahepatic PV flow; or intrahepatic (type 1 – right PV joins vena cava; type 2 – localized shunt from PV to HV in one lobe; type 3 – aneurysmal communication between PV and HV; type 4 – multiple communications between PV and HV; and type 5 – patent ductus venosus [2]. The infant in Pictures 1 and 2 has type 2 intrahepatic CPSS with dilated middle HV (solid arrows in Pictures 1B and 2) communicating with a branch of PV (arrows, Picture 1B). Main PV and vena cava is shown with black arrows and triangle, respectively (Picture 2). Treatment is based on shunt size and fraction, location, age, symptom severity and presence of tumours. All symptomatic shunts, asymptomatic extrahepatic shunts or asymptomatic large intrahepatic shunts need early intervention. Contrarily, small intrahepatic shunts can be left alone till 1 year of age to allow for spontaneous closure. Interventional closure can be performed either percutaneously using Amplatzer devices or coils, or surgically in one or two stages. Balloon occlusion test is performed prior to surgical closure to check PV pressure and tolerance of bowel. With the advancement in interventional radiology techniques, liver transplantation is rarely required for CPSS [1, 2].

References:

1. Bernard O, Franchi-Abella S, Branchereau S, Pariente D, Gauthier F, Jacquemin E. Congenital portosystemic shunts in children: recognition, evaluation, and management. Semin Liver Dis. 2012 Nov;32(4):273-87.

2. Sokollik C, Bandsma RH, Gana JC, van den Heuvel M, Ling SC. Congenital portosystemic shunt: characterization of a multisystem disease. J Pediatr Gastroenterol Nutr. 2013 Jun;56(6):675-81. Review.

SUGAR AND LIVER:

STUDY 1:

Schwimmer JB, Ugalde-Nicalo P, Welsh JA, et al. Effect of a Low Free Sugar Diet vs Usual Diet on Nonalcoholic Fatty Liver Disease in Adolescent Boys: A Randomized Clinical Trial. JAMA. 2019;321(3):256–265. doi: 10.1001/jama.2018.20579

The study concluded Adolescent boys with NAFLD, 8 weeks of provision of a diet low in free sugar content compared with usual diet resulted in significant improvement in hepatic steatosis. This is an open-label, 8-week randomized clinical trial of adolescent boys aged 11 to 16 years with histologically diagnosed NAFLD and evidence of active disease (hepatic steatosis >10% and alanine aminotransferase level ≥45 U/L) randomized 1:1 to an intervention diet group or usual diet group. The intervention diet consisted of individualized menu planning and provision of study meals for the entire household to restrict free sugar intake to less than 3% of daily calories for 8 weeks.

The mean decrease in hepatic steatosis from baseline to week 8 was significantly greater for the intervention diet group (25% to 17%) vs the usual diet group (21% to 20%). The geometric mean decrease in alanine aminotransferase level from baseline to 8 weeks was significantly greater for the intervention diet group (103 U/L to 61 U/L) vs the usual diet group (82 U/L to 75 U/L) and the adjusted ratio of the geometric means at week 8 was 0.65 U/L (95% CI, 0.53 to 0.81 U/L; $P < .001$).

STUDY 2:

Schwarz JM, Noworolski SM, Erkin-Cakmak A, et al. Effects of Dietary Fructose Restriction on Liver Fat, De Novo Lipogenesis, and Insulin Kinetics in Children With Obesity. Gastroenterology. 2017;153 (3):743-752. (doi: 10.1053/j.gastro.2017.05.043. Epub 2017 Jun 1.)

The effect of 9 days of isocaloric fructose restriction on de novo lipogenesis [DNL], liver fat, visceral fat (VAT), subcutaneous fat, and insulin kinetics in obese Latino and African American children with habitual high sugar consumption (fructose intake >50 g/d) in 9-18 years old; (n = 41), were studied. Starch was substituted for sugar, yielding a final fructose content of 4% of total kilocalories. Metabolic assessments were performed before and after fructose restriction. Liver fat, VAT, and subcutaneous fat were determined by magnetic resonance spectroscopy and imaging.

Compared with baseline, on day 10, liver fat decreased from a median of 7.2% (interquartile range [IQR], 2.5%-14.8%) to 3.8% (IQR, 1.7%-15.5%) ($P < .001$) and VAT, visceral fat decreased from 123 cm^3 (IQR, 85-145 cm^3) to 110 cm^3 (IQR, 84-134 cm^3) ($P < .001$). The DNL area under the curve decreased from 68% (IQR, 46%-83%) to 26% (IQR, 16%-37%) ($P < .001$). Insulin kinetics improved ($P < .001$). These changes occurred irrespective of baseline liver fat. The findings support efforts to reduce sugar consumption.

LEDIPASVIR-SOFOSBUVIR IN CHILDREN 6-12 YEARS:

STUDY 3:

Murray, K. F., Balistreri, W. F., Bansal, S. et al (2018), Safety and Efficacy of Ledipasvir–Sofosbuvir With or Without Ribavirin for Chronic Hepatitis C in Children Ages 6-11. Hepatology, 68: 2158-2166. doi:10.1002/hep.30123

It is an open-label study with 92 patients, 88

with genotype 1(maximum), 89 received treatment with ledipasvir-sofosbuvir without ribavirin for 12 weeks, 97% were perinatally-infected, and 78% were treatment naive. The median age was 9 years.(age : 6 – 12 years)

The doses of ledipasvir (45 mg) and sofosbuvir (200 mg) were half of those used in adults.

Patients were assigned to ledipasvir- sofosbuvir for 12 weeks, except for interferon-experienced cirrhotic patients with HCV genotype 1, who received ledipasvir-sofosbuvir for 24 weeks. HCV genotype 3 interferon-experienced patients with or without cirrhosis were assigned to ledipasvir-sofosbuvir plus ribavirin for 24 weeks. SVR12 was 99% (91/91).

Ledipasvir-sofosbuvir was well-tolerated; the common adverse events reported were headache ,pyrexia and abdominal pain. Consistent with observations in adolescents and adults, treatment with ledipasvir-sofosbuvir was well tolerated in children 6 to <12 years old.

ORAL ANTIBIOTICS & PEDIATRIC IBD.

STUDY 4:

Jessica Breton, Arthur Kastl, Natalie Hoffmann,et al. Efficacy of Combination Antibiotic Therapy for Refractory Pediatric Inflammatory Bowel Disease, Inflammatory Bowel Diseases, izz006, https://doi.org/10.1093/ibd/izz006

Oral combination antibiotics may improve disease course in refractory inflammatory bowel disease. Sixty-three patients with refractory UC, Crohn's colitis, and IBD-U. received a combination of 3 or 4 oral antibiotics (most commonly amoxicillin, metronidazole, and either doxycycline or ciprofloxacin) for a median (IQR) of 29 (21–58) days.

Children over the age of 7 years were prescribed triple therapy (orally prescribed) with amoxicillin 50 mg/kg divided by 3 (up to 500 mg three times a day), metronidazole 15 mg/kg divided by 3 (up to 250 mg three times a day), and doxycycline 4 mg/kg divided by 2 (up to 100 mg twice a day). Doxycycline was substituted for ciprofloxacin 20 mg/kg divided by 2 (up to 250 mg twice a day) in children 7 years and younger. Patients with a known allergy to 1 of the drugs were treated with oral gentamycin instead of the allergenic drug. Vancomycin could be added as the fourth medication (250 mg, or 125 mg in those younger than 8 years, four times a day) in those younger than 8 years) in hospitalized children. The antibiotic cocktail was typically prescribed for 3 ± 1 weeks.

Thirty-four patients (54%) were deemed corticosteroid-refractory or -dependent, with the majority (62/63) having a previous or present loss of response or primary nonresponse to anti–tumor necrosis factor alpha (anti-TNFα) therapy. Use of combination antibiotics led to a significant decrease in median Pediatric Ulcerative Colitis Activity Index (PUCAI) score (IQR) from 55 (40–65) to 10 (0–40; $P < 0.0001$) over 3 ± 1 weeks, with 25/63 (39.7%) patients achieving clinical remission(PUCAI <10 points). The clinical benefits of oral antibiotics were independent of anti-TNFα therapy optimization.

Compiled by: Dr. Yogesh Waikar

Publications (Citations and Author's conclusions) by ISPGHAN members on topics related to pediatric gastroenterology, hepatology and nutrition (Original articles and reviews published in indexed journals)

September

Shava U, Yachha SK, Srivastava A, Poddar U, Sen Sarma M. Assessment of stool frequency and colonic transit time in Indian children with functional constipation and healthy controls. Indian J Gastroenterol. 2018 Sep;37(5):410-415

Indian children have significantly higher stool frequency and shorter colonic transit time, which are different compared to the reported figures from the West. Most of the Indian children with functional constipation had normal colonic transit time.

October

Sen Sarma M, Yachha SK, Rai P, Neyaz Z, Srivastava A, Poddar U. Cholangiopathy in children with extrahepatic portal venous obstruction. J Hepatobiliary Pancreat Sci. 2018 Oct;25(10):440-447

A majority of children with extrahepatic portal venous obstruction have asymptomatic cholangiopathy and should be routinely evaluated for Portal cavernoma cholangiopathy at the time of first presentation by a combination of magnetic resonance cholangiography-portovenography (MRC - MRPV). Additionally, superior mesenteric vein block with portal cavernoma results in significantly higher changes of cholangiopathy on MRC and Endoscopic ultrasound.

Nabi Z, Shava U, Sekharan A, Nageshwar Reddy D. Diagnosis of Hirschsprung's disease in children: Preliminary evaluation of a novel endoscopic technique for rectal biopsy. JGH Open. 2018 Oct 4;2(6):322-326.

Rectal biopsy using endoscopic mucosal resection with a band ligation device is feasible, safe, and provides adequate sample for the evaluation of HD in children.

Yachha SK, Srivastava A, Mohan N, Bharadia L, Sarma MS; Management of Childhood Functional Constipation: Consensus Practice Guidelines of Indian Society of Pediatric Gastroenterology, Hepatology and Nutrition. Indian Pediatr. 2018 Oct 15;55(10):885-892

Functional constipation should be diagnosed only in the absence of red flags on history and examination. Those with impaction and/or retentive incontinence should be disimpacted with polyethylene glycol (hospital or home-based). Osmotic laxatives (polyethylene glycol more than 1 year of age and lactulose/lactitol less than 1 year of age) are the first line of maintenance therapy. Stimulant laxatives should be reserved only for rescue therapy. Combination therapies of two osmotics, two stimulants or two classes of laxatives are not recommended. Laxatives as maintenance therapy should be given for a prolonged period and should be tapered off gradually, only after a successful outcome. Essential components of therapy for a successful outcome include counselling, dietary changes, toilet-training and regular follow-up.

November

Lal BB, Sood V, Khanna R, Alam S. How to identify the need for liver transplantation in pediatric acute-on-chronic liver failure? Hepatol Int. 2018 Nov;12(6):552-559

APASL ACLF Research Consortium-Acute-on-chronic liver failure (AARC-ACLF) and chronic liver failure-sequential organ failure assessment (CLIF-SOFA) models are superior to other prognostic scores in pediatric ACLF. The scores are dynamic and a patient with either of these scores ≥ 11 at admission and/or a rising score at day 4 has high likelihood of death and needs to be urgently listed for liver transplantation.

Pradhan S, Jagadisan B. Yield and Examiner Dependence of Digital Rectal Examination in Detecting Impaction in Pediatric Functional Constipation. J Pediatr Gastroenterol Nutr. 2018 Nov;67(5): 570-575.

Digital Rectal Examination detects cases of impaction not discernible by other means. Such a finding may be comparable between examiners. These children may be identified by other clinical characteristics.

December

Kumari N, Kumar A, Thapa BR, Modi M, Pal A, Prasad R. Characterization of mutation spectrum and identification of novel mutations in ATP7B gene from a cohort of Wilson disease patients: Functional and therapeutic implications. Hum Mutat. 2018 Dec;39(12): 1926-1941.

After sequencing 21 exons of ATP7B gene from 50 WD patients we identified 28 variants comprising, eight variations affecting 23% alleles were first time reported in Indian cohort. Functional analysis of these novel variants in five different cell lines lacking inherent ATP7B expression demonstrated sensitivity to $CuCl_2$ - treatment, experiencing augmented cellular copper retention and decreased copper excretion as well as ceruloplasmin secretion to that of wildtype-ATP7B expressing cells. Interestingly, pharmacological chaperone 4-phenylbutyrate, a clinically approved compound, partially restored protein function of ATP7B mutants. These findings might enable novel treatment strategies in WD by clinically enhancing the protein expression of mutant ATP7B with residual copper export activity.

Bolia R, Rajanayagam J, Hardikar W. Lower 6-MMP/6-TG Ratio May Be a Therapeutic Target in Pediatric Autoimmune Hepatitis. J Pediatr Gastroenterol Nutr. 2018 Dec;67(6):695-700.

Thiopurine metabolite levels should be measured in patients with AIH who have experienced a loss of remission. A 6-Methymercaptopurine/6-Thioguanine ratio of < 4 with the addition of allopurinol could be considered in these patients.

Rathi N, Desai S, Kawade A, Venkatramanan P, Munshi R, Kang G, Babji S, Bavdekar A, et al. A Phase III open-label, randomized, active controlled clinical study to assess safety, immunogenicity and lot-to-lot consistency of a bovine-human reassortant pentavalent rotavirus vaccine in Indian infants. Vaccine. 2018 Dec 18;36(52):7943-7949.

Lot-to-lot consistency of bovine-human rotavirus reassortant pentavalent vaccine ROTASIIL® was demonstrated in terms of geometric mean concentration ratios of IgA antibodies. The vaccine safety and immunogenicity profiles were similar to those of Rotarix®.

January

Rammohan A, Reddy MS, Narasimhan G, Rajalingam R, Kaliamoorthy I, Shanmugam N, Rela M. Auxiliary Partial Orthotopic Liver Transplantation for Selected Noncirrhotic Metabolic Liver Disease. Liver Transpl. 2019 Jan;25(1):111-118

The largest series (n = 12) of Auxiliary Partial Orthotopic Liver Transplant (APOLT) for Non - Cirrhotic metabolic liver disease (NCMLD). APOLT is a safe and effective alternative to OLT and may even be better than OLT due to lesser physiological stress and the smoother postoperative period for selected patients with NCMLD.

Singh SK, Borkar V, Srivastava A, Mathias A, Yachha SK, Poddar U. Need for recognizing atypical manifestations of childhood sporadic acute viral hepatitis warranting differences in management. Eur J Pediatr. 2019 Jan;178(1):61-67

Twenty-two percent of children with sporadic acute viral hepatitis have atypical manifestations, more often with HAV infection, and prolonged cholestasis is most common. Recognition of these manifestations ensures correct diagnosis and treatment.

Nagral A, Sarma MS, Matthai J, Kukkle PL, Devarbhavi H, Sinha S, Alam S, Bavdekar A, Mohan N, Sathiyasekaran M,

Poddar U, Sibal A, Sankaranarayanan S, Srivastava A, Thapa BR, Wadia PM, Yachha SK, Dhawan A, et al. Wilson's Disease: Clinical Practice Guidelines of the Indian National Association for Study of the Liver, the Indian Society of Pediatric Gastroenterology, Hepatology and Nutrition, and the Movement Disorders Society of India. J Clin Exp Hepatol. 2019 Jan-Feb;9(1):74-98.

Experts from national societies from India representing 3 disciplines, hepatology (Indian National Association for Study of the Liver), pediatric hepatology (Indian Society of Pediatric Gastroenterology, Hepatology and Nutrition), and neurology (Movement Disorders Society of India) got together to evolve these guidelines.

While ceruloplasmin and 24-h urine copper continue to be important, there is little role of serum copper and penicillamine challenge test in the diagnostic algorithm. A new scoring system - Modified Leipzig score has been suggested with extra points being added for family history and serum ceruloplasmin lower than 5 mg/dl. Liver dry copper estimation and penicillamine challenge test have been removed from the scoring system. Rising bilirubin and worsening encephalopathy are suggested as indicators predicting need for liver transplant but need to be validated.The clinical practice guidelines provide recommendations for a comprehensive management of WD which will be of value to all specialties.

Puttaiah Kadyada S, Thapa BR, Kaushal K, Walia R, Rana SV, Dhaka N, Lal SB, Prasad R, Das S, Thakur R, Kamal K. Incomplete functional and morphological recovery after acute and acute recurrent pancreatitis in children. J Gastroenterol Hepatol. 2019 Jan;34(1):293-301

There was high frequency of biochemical evidence of exocrine insufficiency in Acute Pancreatitis (AP) and Acute Recurrent Pancreatitis (ARP). β-Cell function (2-h oral glucose tolerance test to calculate oral disposition index) was preserved among AP but was poor in ARP. Nearly one-third showed morphological changes in imaging.

February

Poddar U, Singh S, Pawaria A, Srivastava A, Yachha SK. Aetiological spectrum, clinical differentiation and efficacy of polyethylene glycol over lactulose in children with constipation: Experience of 316 cases. J Paediatr Child Health. 2019 Feb;55(2):162-167.

Functional Constipation is the most common cause of constipation in children. Presence of delayed passage of meconium, growth failure and absence of retentive posturing and absent faecal impaction raise the suspicion of an organic cause. Both lactulose and Polyethylene glycol (PEG) are equally effective. PEG has an edge over lactulose as the need for switch over was uncommon.

Shanmugam NP, Valamparampil JJ, Reddy MS, Al Said KJ, Al-Thihli K, Al-Hashmi N, Al-Jishi E, Isa HMA, Jalan AB, Rela M. Auxiliary Partial Orthotopic Liver Transplantation for Monogenic Metabolic Liver Diseases: Single-Centre Experience. JIMD Rep. 2019;45:29-36

A total of 13 APOLT procedures were performed for MLD during the study period. The underlying aetiologies being propionic academia-5, citrullinemia type 1-3 and Crigler-Najjar syndrome type 1-5 cases respectively. APOLT is a safe procedure, which provides good metabolic control and improves the neurodevelopment in children with selected MLD.

Nagral A, Jhaveri A, Sawant S, Parikh NS, Nagral N, Merchant R, Gandhi M. Treatment of Chronic Hepatitis C Infection with Direct Acting Antivirals in Adolescents with Thalassemia Major. Indian J Pediatr. 2019 Feb;86(2):148-153

Generic Direct Acting Antivirals are effective and safe in Thalassemia Major adolescents with Hepatitis C Virus.

Compiled by: Dr. Rishi Bolia

ISPGHAN 2018: 5th Annual conference, Mumbai

ISPGHAN 2018, 5th annual national conference of Indian Society of Pediatric Gastroenterology, Hepatology & Nutrition and 28th annual conference of Pediatric Gastroenterology chapter of IAP; was held at Mumbai from 26th to 28th October 2018. This 3-days program consisted of a half-day pre-conference workshop on 26th October and full days conference on the remaining 2 days. Dr Y K Amdekar was organising chairperson and Dr Abha Nagral was organising secretory. The conference had over 500 registered delegates comprising of post-graduates students, DM students, Paediatric Gastroenterologists, Paediatricians, Gastroenterologists, Geneticists and dieticians.

In the pre-conference workshop, a series of interesting case scenarios were presented by post-graduate students from various teaching institutes all over India. The cases included liver failure, neonatal cholestasis with pruritus, metabolic liver diseases, seizures disorder with liver disease, fatty liver disease and so on. This workshop was live telecasted to paediatricians all over the country. Active participation of delegates and in-depth discussion by expert panelists made the workshop memorable.

During the main conference, various national and international faculty delivered lectures on current trends in various topics on disease related to liver, luminal gastroenterology, pancreas and nutrition. Sessions of panel discussion made the conference very interactive. A review of recently published high impact research papers in gastroenterology and hepatology, highlighted current development in the field in preceding one year.

In 2018, the prestigious **"Mehta-Mittal-Sankarnarayan oration"** was delivered by Prof Seema Alam. The topic of the oration was " Pediatric liver matures into the adult liver. Specialty follows suit." Prof Alam narrated the journey of development of paediatric hepatology department at ILBS, New Delhi.

The most integral part of any scientific conference is the kind of research papers which are submitted and discussed. Day 1 of conference, 4 papers were presented for **Dr. CP Mittal award.** This award was won by Dr Durga Prasad, SGPGIMS, Lucknow. He represented his research work on "Early renal dysfunction in non-azotemic cirrhotic children by renal resistive index and to assess effect of paracentesis and albumin therapy: A prospective observational study." Second prize was won by Dr Nirzar Parikh from Jaslok Hospital, Mumbai for paper "Treatment of chronic hepatitis C infection with direct acting antivirals in adolescents with thalassemia major."

Five oral papers were presented in GI plenary session. First prize was one by paper titled "Gastrointestinal polyps and polyposis syndromes in children: lessons for precision and surveillance" presented by Dr Parijat Tripathi from SGPGIMS, Lucknow. Second prize was won by Dr Upender Shava from Asian Institute of Gastroenterology, Hyderabad, who presented paper titled "Diagnosis of Hirschsprung's disease in children – preliminary evaluation of a novel endoscopic technique for rectal biopsy."

On second day, six best papers in Hepatology were presented for liver plenary session. First prize was won by Dr Snehwardhan Pandey, from ILBS, New Delhi, who presented "Predictors of hepatitis A virus induced paediatric acute liver failure- an etiology-specific study." Second award was one by Dr Upender Shava, AIG, Hyderabad who presented " Aetiology of recurrent acute pancreatitis in children: a large single center study." And 3rd prize was won by Dr Nirubhan Barathy from Kanchi Kamoti Child Trust Hospital, Chennai for his paper "Prevalence of

genetic polymorphisms in paediatric acute recurrent and chronic pancreatitis: A single centre experience."

In this year, conference received 101 abstract which was the highest number of abstracts for ISPGHAN till date. The highlight of the session was e-posters which was first time in an ISPGHAN meeting. Three best posters in each categories were given prizes. In GI posters, 1st prize was won by Dr Amrit Gopan, SGPGIMS, Lucknow for abstract "endoscopic ultrasonography in children: Pivotal role in diagnostic utility, clinical impact and safety." 2nd prize was won by Dr Upender Shava, AIG, Hyderabad for "Outcome of Per Oral Endoscopic Myotomy in Children with Achalasia-Median Follow-up of 540 days." And 3rd prize was won by Dr Parijat Tripathi, SGPGIMS, Lucknow for "Rising burden of difficult-to-treat and multidrug-resistant abdominal tuberculosis in children." In hepatology posters, 1st prize was won by Dr Nikita Garg, Jaslok Hospital, Mumbai for "Hepatopulmonary syndrome following radiological interventions in Budd Chiari Syndrome." Second place was won by Dr Rajeev Khanna, ILBS, New Delhi for "HVPG relates to severity of liver disease and complications of portal hypertension in children with chronic liver disease." 3rd prize was won by Dr Amrit Dhungel, Medanta, The Medicity, New Delhi for "Successful outcome of ABO incompatible paediatric living related liver transplant using the standard immuno-suppression."

General body meeting was held on 27th October 2018. Prof S K Yachha was unanimously elected as the first fellow of ISPGHAN. A decision of launching online ISPGHAN bulletin on quarterly basis, was taken. For years 2019 and 2020, ISPGHAN conference would be conducted at Chennai and Jaipur, respectively.

ISPGHAN 2018 conference was a great success and reflected progressive growth of specialty of Paediatric Gastroenterology and Hepatology in India.

By Dr. Vibhor Borkar

1st ISPGHAN Literature Review Festival – Nagpur

ISPGHAN literature review festival was successfully held at Nagpur on 15th and 16th Decemeber 2018 .It was organized by Dr .Yogesh Waikar, Pediatric Gastroenterologist from Nagpur and was attended by 17 Pediatric Gastroenterologists from state of Maharashtra and other states of India. Dr. Malathi Sathiyasekaran President of ISPGHAN guided the meeting. International faculty from University of Cincinatti, Cincinatti Children's Hospital Dr Ajay kaul , Head Department Pediatric Neuro-gastroenterology has delivered Key note lecture on Tricks and Trades of Pediatric therapeutic Endoscopy.

Being closed door meeting for pediatric gastroenterologist only. literature review of topics like Complications of Pediatric Endoscopy, Refractory esophageal stricture, Immuno-suppression in Pediatric Liver transplant , vascular and biliary complications post liver transplant, post kasai Protocols ,Hepatitis B and C update, HLH, Autoimmune Hepatitis , Treatable Metabolic liver diseases other than Wilson, IBD, Variceal and non-variceal GI bleeding were discussed in details. Topics were given 6 months prior and were well prepared and scrutinized by distinguished Faculty members.

There was no inaugural ceremony, no thanks giving, no Introductory slides.

The concept being so liked and acknowledged that in 2019 Dr Rimzim Shrivastav from Raipur has agreed to do 2nd Literature review festival. Dr Somashekhar from Bangalore has agreed for 2020 slot making it an annual rotating Pediatric Gastroenterology event.

By Dr. Yogesh Waikar

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

Application Form for Membership

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).

1. Name (in full in capitals):.....
2. Qualifications:.....
3. Designation:.....
4. Address with pincode(for communication):.....
.....
Phone/Mobile No.....
Email id :.....
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
a) NEFT transfer to Account name: "ISPGHAN", Account No: 048201000027026,
IFSC: IOBA0000482, MICR: 600020032, India Overseas Bank, Mahalingapuram Branch, Chennai
NEFT Trans..... No:..... Date:..... Amount :.....
Bank Name:.....
OR
b) Multicity Cheque (In favor of "ISPGHAN")
Cheque No:.....Dated :.....Amount.....
Bank Name.....
Signature.....Date :.....

(**To be completed by the person(s) proposing and seconding the membership of the application**)

To the best of our knowledge and belief the overleaf particulars of
Dr..... Place.....are correct.
We consider him/ her fit and proper person to be admitted as a Life Member/ Associate Life Member/Affiliate Foreign Member of the Indian Society of Pediatric Gastroenterology, Hepatology and Nutrition.

Proposed by:	Seconded by:
Signature:	Signature:
Name:	Name:
Address:	Address:
Date:	Date:

Complete Registration form with Cheque/NEFT receipt should be sent by post to :
Dr Anshu Srivastava, Secretary, ISPGHAN
Additional Professor, Department of Pediatric Gastroenterology,
Sanjay Gandhi Post Graduate Institute of Medical Sciences, Rae Bareli road, Lucknow
Email: ispghansec@gmail.com

For Office Use			
To be completed by the Executive Committee of the Indian Society of Pediatric Gastroenterology, Hepatology and Nutrition (ISPGHAN) ISPGHAN Registration Number allotted:			
• Admitted as Life Member/ Associate Life Member/Affiliate Foreign member of the Society • Application rejected for the above reasons (Delete clause which is not applicable)			
Place : Date :		Signature Designation	
Membership Fee paid:			
Life Member (Indian) Associate Life Member Affiliate Foreign Member		Rs.3000.00 Rs.2000.00 US $ 100.00	

Approved

Membership Criteria

Membership Categories	*Eligibility criteria	Current Membership fee
***Life Member**	Fresh/New Life Membership of ISPGHAN shall be open to members of the medical profession, who are residents in India and who have a postgraduate degree in Pediatircs (MD, DNB), Gastroenterology or Pediatric gastroenterology from India or abroad, recognized by the Medical Council of India, and interested or involved in the practice of Pedaitric gastroenterology, hepatology and nutrition.	Indian rupees 3000
***Associate Life Member**	Associate Life Membership shall be open to members of the medical profession who are Diploma holders in Pedaitric, Postgraduate students in Pedaitric, gastroenterology or pediatric gastroenterology as well as to postgraduates in other medical disciplines (recognized by the competent authorities in India), who are interested or involved in the practice of pediatric gastroenterology, hepatology and nutrition.	Indian rupees 2000
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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INDIAN ACADEMY OF PEDIATRICS

ISPGHANcon - 2019

Indian Society of Pediatric Gastroenterology Hepatology and Nutrition

(Ped gastroenterology chapter of IAP)

Invites you to attend
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Date

18th-20th oct'19

Venue

ITC Grand Chola,Chennai

CONFERENCE SECRETARIAT

Dr. Rela Institute & Medical Centre,

Address : No.7, CLC Works Road, Chromepet, Chennai-600 044.

Phone : +91 8056122134

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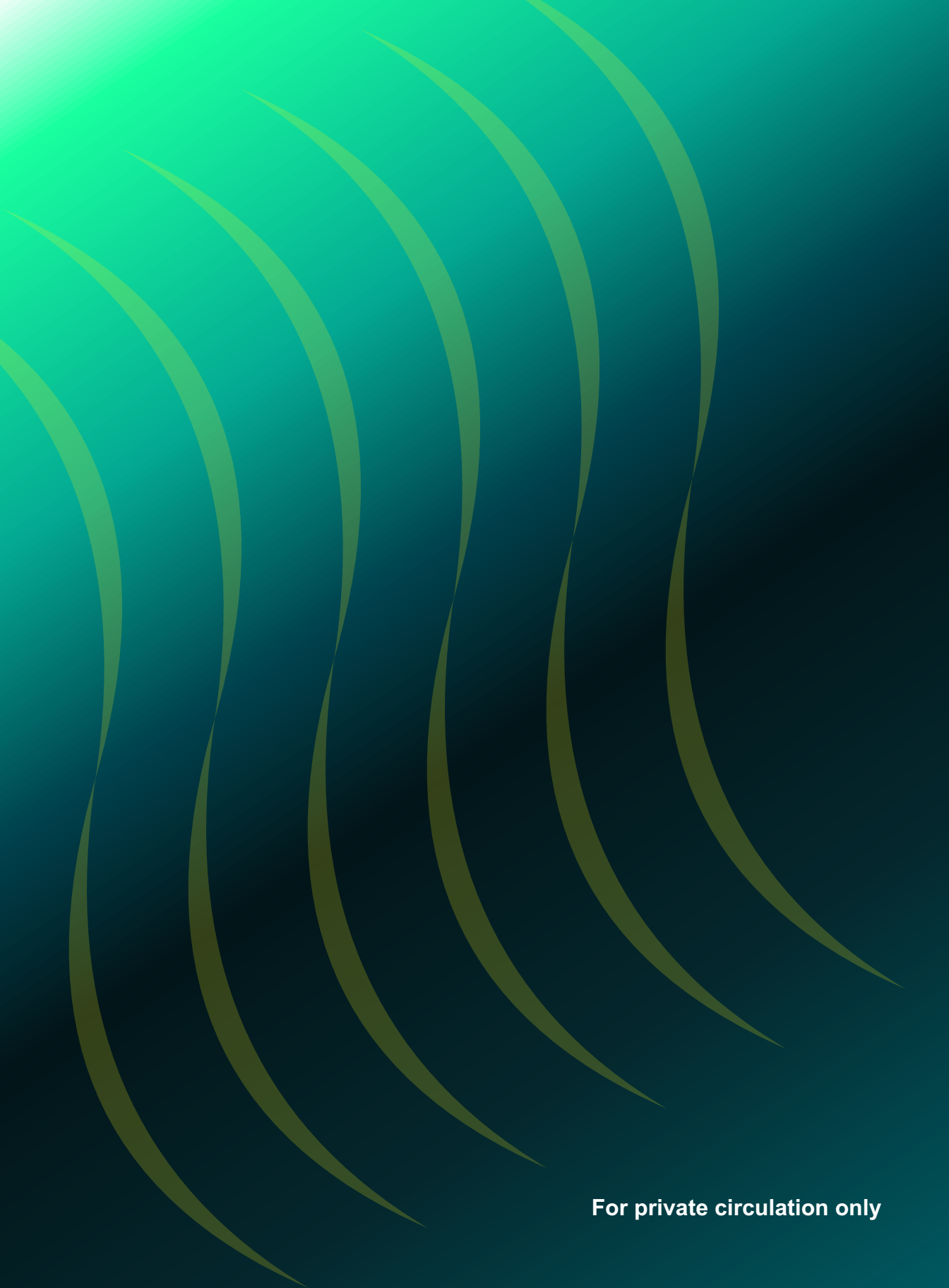
REGISTRATIONS OPENING SOON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