July 2020

Andhra Hospitals

The peoples pulse

E journal of Paediatrics

Issue.2

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Vol.1

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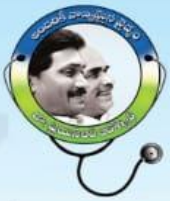

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DEPARTMENT OF PAEDIATRICS, ANDHRA HOSPITALS, VIJAYAWADA
E-JOURNAL

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Foreword

Greetings from the Andhra Hospitals!

For the past two decades, we are delivering excellence in terms of quality health care in the field of Paediatrics including Paediatric and Neonatal intensive care, Paediatric cardiac intensive care and other allied Paediatric sub-specialities.We take pride in introducing ECMO in pediatric specialty for the first time in the state of Andhra Pradesh. In this context, we convey our heartfelt thanks to you for your continued support and encouragement which played a pivotal role in our success.

As a token of our commitment to contribute to continuous medical education, we are introducing this monthly E-journal to showcase important clinical guidelines, recent advances in paediatric sub-specialties, interesting case reports, image quiz, OSCE scenarios etc, gathered from our patient database.
We hope this endeavor would prove to be useful to practicing paediatricians, intensivists, neonatologists and post-graduate students.

Please send your valuable feedback and suggestions to ***maramkp@gmail.com*****.**

Dr. P. V. Ramana Murthy M.S. FRCS (UK)

Managing Director & Chief Surgical Gastroenterologist

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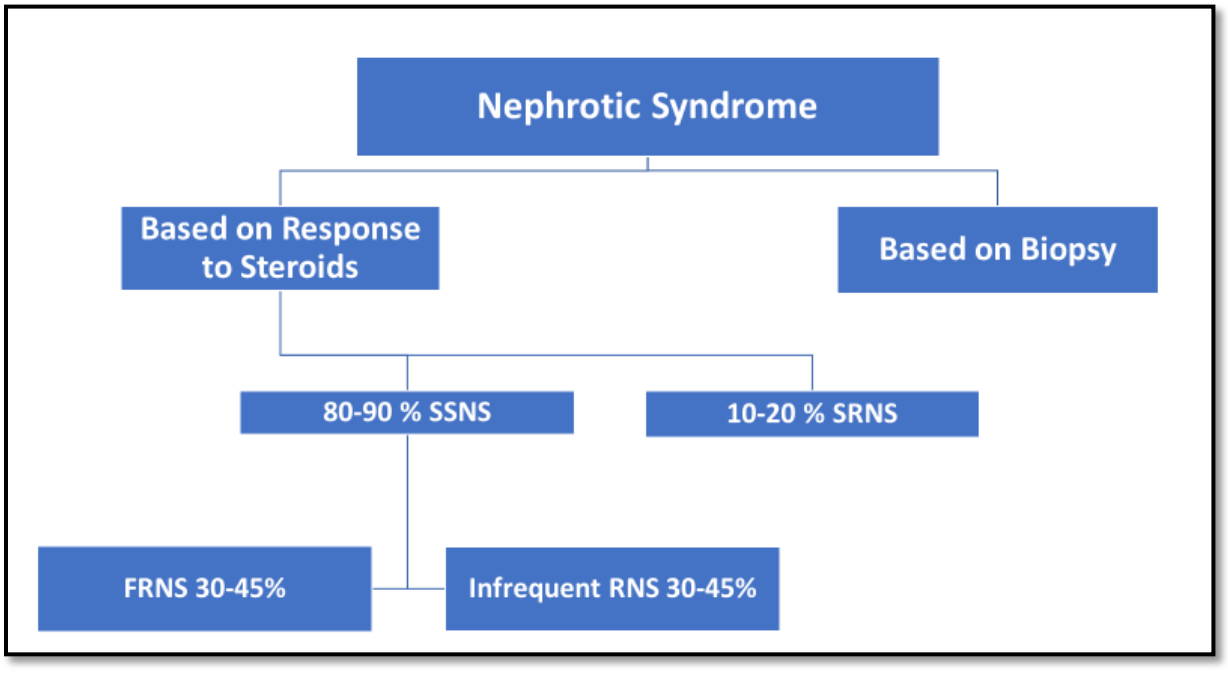
Introduction

Idiopathic Nephrotic syndrome presents with Proteinuria, Hypoalbuminemia and/or oedema. About 85% achieve complete remission with daily steroid treatment at standard dose of 2 mg/kg/day (60 mg/m^2/day, Max 60 mg/day). This is called Steroid Sensitive Nephrotic Syndrome. If a person fails to achieve remission by 8 wks of daily steroid, he/she is labelled as Steroid Resistant Nephrotic Syndrome.

Half of those who are steroid sensitive, will have infrequent relapses and the rest frequent relapses/Steroid Dependent.

This brief review is to look at Infrequent & Frequently Relapsing Nephrotic Syndrome and Steroid Dependent Nephrotic Syndrome, with focus on identification, investigations,and management options at our disposal.

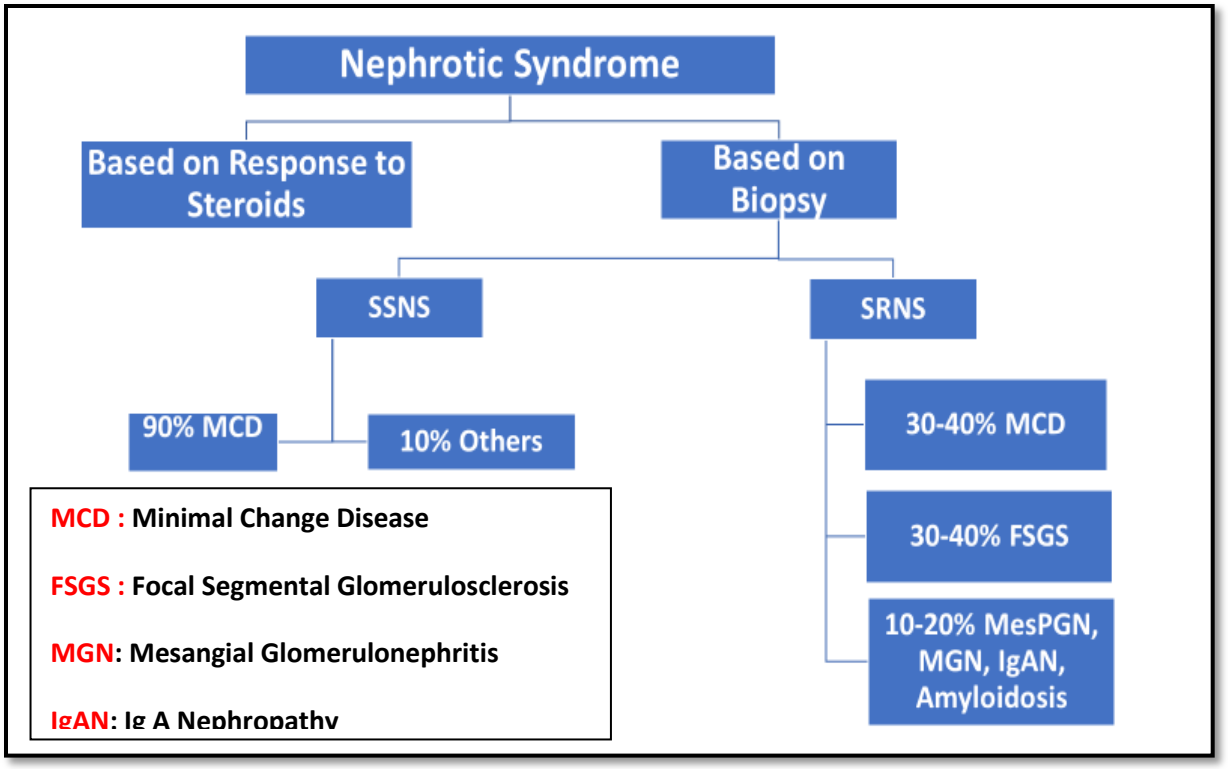
Classification



SSNS : **Steroid Sensitive Nephrotic Syndrome**

SRSN : **Steroid Resistant Nephrotic Syndrome**

FRNS : **Frequently Relapsing Nephrotic Syndrome**



Common terms used in Nephrotic Syndrome

Nephrotic Syndrome	UPCR: >2 gm/gm; 3+protein on urine dipstick 24 hrs Urine Protein- >1000 mg/m^2/day Edema or Low Albumin-2.5 g/dl
Frequent Relapses	2 or more relapses in 6 months of initial response/ 4 or more relapses in any 12 months period
Infrequent Relapses	1 relapse within 6 months of initial response/ 1 to 3 relapses in any 12 months period
Steroid Dependent	Two consecutive relapses during therapyor within 14 days of ceasing therapy
Initial Responder	Complete remission within 4 wks of steroid treatment
Steroid Resistant/Initial Non-responder	Failure of complete remission after 8 wks of steroid treatment
Relapse	UPCR 2 gm/gm or 3+ or more protein on urine dipstick for 3 consecutive days
Complete Remission	UPCR: <0.2 gm/gm; <1+ protein on urine dipstick for 3 consecutive days
Partial Remission	UPCR: 0.2-2 gm/gm; Reduction in Proteinuria by 50% or more from presenting value
No Remission	Failure to reduce urine protein excretion by

	50% from baseline or persistent excretion (UPCR : >2 gm/gm)
Late Non-responder	Persistent Proteinuria during 4 or more wks of steroid therapy following 1 or more remissions

Treatment options

Nephrotic Syndrome Initial episode	2 mg/kg/day or 60 mg/m^2/day (Max 60 mg) for 4-6 wks→ 40 mg/m^2/day or 1.5 mg/kg/day (Max 40 mg/day) on Alternate day(tapered over next 2-5 months)
Relapse in an Infrequent Relapser	2 mg/kg/day or 60 mg/m^2/day (Max 60 mg) till complete remission for 3 days→40 mg/m^2/day or 1.5 mg/kg/day (Max 40 mg/day) on Alternate day for at least 4 wks
Relapse in a Frequent Relapser	2 mg/kg/day or 60 mg/m^2/day (Max 60 mg) till complete remission for 3 days →40 mg/m^2/day or 1.5 mg/kg/day (Max 40 mg/day) on Alternate day for at least 3 months Lowest possible dose of Steroid on Alternate days to maintain remission
Relapse in a Steroid Dependent	2 mg/kg/day or 60 mg/m^2/day (Max 60 mg) till complete remission for 3 days →40 mg/m^2/day or 1.5 mg/kg/day (Max 40 mg/day) on Alternate day for at least 3 months Lowest possible dose of Steroid on Alternate days to maintain remission Lowest possible Daily Steroid dose to maintain remission for SD SSNS (If Alt.day dosing not effective)

Lowest dose: 0.1-0.5 mg/kg/Alt day for 3-6 months before tapering further (UK); 0.5-0.7 mg/kg/Alt day for 9-18 months before tapering further (India)

Steroid Sparing Agents

	Frequently Relapsing SSNS	**Steroid Dependant SSNS**
Alkylating Agents	Recommend	Suggest
Levamisole	Recommend	Recommend
Calcineurin Inhibitors	Recommend	Recommend
MMF	Suggest	Suggest
Rituximab	-	Suggest
Mizoribine	Not to be used	Not to be used
Azathioprine	Not to be used	Not to be used

Agent	Advantages	Disadvantages
Cyclophosphamide	Prolonged remission off therapy Inexpensive	Less effective in SD SSNS Monitoring of blood count during therapy Potential serious short- and long-term adverse effects Only one course should be given
Chlorambucil	Prolonged remission off therapy Inexpensive	Less effective in SD SSNS Monitoring of blood count during therapy Potential serious adverse effects Only one course should be given Not approved for SSNS in some countries
Levamisole	Few adverse effects Generally inexpensive	Continued treatment required to maintain remission Limited availability Not approved for SSNS in some countries
Cyclosporine	Prolonged remissions in some children with SD SSNS	Continued treatment often required to maintain remission Expensive Nephrotoxic Cosmetic side-effects
Tacrolimus	Prolonged remissions in some children with SD SSNS	Continued treatment often required to maintain remission Expensive Nephrotoxic Risk of diabetes mellitus Not approved for SSNS in some countries
Mycophenolate mofetil	Prolonged remissions in some children with FR and SD SSNS Few adverse effects	Continued treatment often required to maintain remission Probably less effective than CNIs Expensive Not approved for SSNS in some countries

FR, frequently relapsing; SD, steroid-dependent; SSNS, steroid-sensitive nephrotic syndrome.

Chapter 3: Steroid-Sensitive Nephrotic Syndrome in Children; KDIGO Clinical Practice Guideline for Glomerulonephritis; June 2012

Role of Renal Biopsy

Routine renal biopsy is not recommended forIdiopathic Nephrotic syndrome. It isto be considered for communities with high incidence of FSGS (African and Afro-American Population). In India, with high incidence of Minimal Change Disease, even in adolescents
(upto 50% by some accounts), renal biopsy is to be consideredfor late nonresponderto identify the renal pathology.

For children with SSNS on Calcineurin Inhibitors, especially if used for> 2 yrs, it is recommended to perform annual Renal Biopsies. Biopsy should be considered in children with deteriorating Renal function despite reduced CNI doses.

Indications for renal biopsy

1) Late nonresponderfollowing initial response to steroids
2) High index of suspicion for different underlying pathology
3) Deteoration in renal function while on Calcineurin Inhibitors
4)

Vaccination in SSNS

Live vaccines like Measles, Mumps, Rubella, Varicella, Rotavirus are contraindicated in children on Immunosuppressive or cytotoxic agents until:

1) Prednisolone dose is < 1 mg/kg/day (Below 20 mg/day)
2) Prednisolone < 2 mg/kg on Alternate day (< 40 mg on Alternate days)

3) Child has been off Cytotoxic agents (Cyclophosphamide, Chlorambucil) for > 3 months
4) Child has been off other immunosuppressive agents (Levamisole, MMF, CNI) for > 1 month

Pneumococcal and Influenza Vaccination:

1) Give Pneumococcal vaccine to children with Nephrotic syndrome on treatment, as per local recommendations
2) 2) Give Influenza vaccine to Children with Nephrotic Syndrome annually (Non-Live Vaccine)

Sibling and Household contacts

Healthy siblings and household contacts of children on immunosuppressive drugs should be vaccinated with Measles, Mumps, Rubella, Varicella and Rotavirus to prevent from cross infection

When Immunized, contacts should be separated from the immunocompromised child for up to 6 wks (to avoid exposure to shedding in Respiratory, GI and Urinary secretions)

Give Influenza vaccination annually to contacts (Non-Live vaccines)

Varicella Immunization in SSNS

It is a good practice to check status of Varicella Immunity (Varicella Ab Titres) at the time of diagnosis of Nephrotic Syndrome.

When child is exposed to Chickenpox or Zoster

Children with SSNS on low dose daily or alternate day steroid	Offer Varicella Immunization if not immune
Child with SSNS on immunosuppressive agents	Offer Zoster Immunoglobulins within 72 hrs of exposure Offer Acyclovir or Valacyclovir if chickenpox lesions appear

Summary

1) ***Steroid Sensitive Nephrotic Syndrome is most common among children***
2) ***Half of the SSNS are at risk of becoming frequent relapsers or steroid dependent***
3) ***Close monitoring and due diligence is needed for choosing steroid sparing agents***
4) ***Close monitoring is needed to identify and remedy adverse effects of steroids and steroid sparing agents***
5) ***Multi-disciplinary approach is crucial for long term care of these children***

References

1) Steroid-Sensitive Nephrotic Syndrome in Children; KDIGO Clinical Practice Guideline for Glomerulonephritis; June 2012
2) IPNA Clinical Practice Recommendations for the Diagnosis and Management of Children with Steroid-Resistant Nephrotic Syndrome.

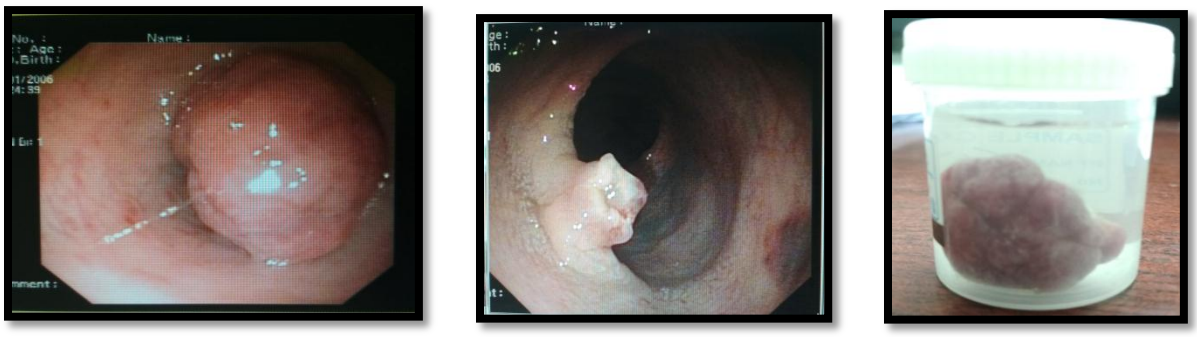
Approach to a child with bleeding per rectum

Dr. Upender Shava MD (Ped.), PDCC, DM (Ped. Gastro)
Consultant in Pediatric Gastroenterology, Hepatology and Nutrition
Pediatric Endoscopy Specialist.

CASE

Two-year-old girl child brought with complaints of intermittent blood in stools for last few months. Fresh blood found coating outside of stools, small amount and painless. No mucus in stools, loose stools.Occasionally mass prolapse per rectum, which requires manual reposition. No history of constipation.No fever,pain abdomen. No skin rash, joint swellings. No weight loss. On examination child had mild pallor, weight at 3rd centile, length normal.Per abdomen examination was normal. Perianal and per rectal examination are normal. In this young child with small fresh painless blood in stools clinical possibilities were colonic polyp, recurrent infections, inflammatory bowel disease/immunodeficiencies, bleeding diathesis, vascular malformations. Basic investigations showed microcytic and hypochromic anaemia (Hb 8.9gm/dL), platelets 4.3 lac/dL. USG abdomen was normal. Stool examination no ova and cyst, RBC present. Colonoscopy showed large single pedunculated polyp in rectum (Fig.1), remaining colon normal. Snare polypectomy of polyp was done. Histopathology of polyp is suggestive of Juvenile polyp. Child was started on iron and folic acid supplements.

Figure 1:



A B C

A) Colonoscopy showing large pedunculated polyp in rectum
B) Clean cut stalk after polypectomy
C) Resected polyp for histopathology.

DISCUSSION

Hematochezia is passage of bright red colour blood per rectum with or without mixed with stools, indicating source mostly from colon. Melena is black, tarry and foul smelling stools indicating a source of bleed above ileocaecal valve. Lower GI bleed is defined as bleeding originating below level of ligament of Treitz. Most common causes of LGI bleeding in children are anal fissure, acute infections, intussusception, juvenile polyps, Meckel's diverticulum, Inflammatory Bowel Disease (IBD) (table 1)

Profile of recurrent LGI in children from Indian studies show that, polyps are common cause (50%), others being infective colitis, SRUS, polyposis syndromes. Uncommon causes are Ulcerative colitis, Intestinal tuberculosis, allergic colitis.

Proper history taking and physical examination are most important to differentiate various causes of LGI bleeding children. Pediatrician should focus on primary factors like age of the child, location of bleeding in relation to characteristics of stool, amount of blood and presence of associated symptoms or signs.

History of allergies, IBD, polyposis and hemorrhagic diathesis in family are important. Umbilical sepsis, severe dehydration and umbilical cord catherization in newborn period are to be asked. Blood in stool starting after weaning and introduction of cow's milk strongly suggest milk protein allergy.

Analysis of blood pattern passed per rectum will help to localize the site of blood in LGI bleed. Blood coating outside of stools/toilet paper/hand used for washing/diaper or red drops tickling after passing stools mostly imply origin from anal canal or rectum. Blood mixed with mucus and loose stools suggest colitis. Maroon colored stools strongly suggestive of vigorous bleeding from distal small bowel. Current jelly stools indicative of bowel ischemia (intussusception or mid gut volvulus). Melena signifies bleeding from more proximal GIT (stomach/duodenum/proximal small bowel). Owing to quantity and cathartic action of blood through intestine, massive upper GI bleed may sometimes present as hematochezia. Red or purple color to stool from foods (tomato peal, beet roots…) or medicines (syrups, iron preparations…) may mimic hematochezia/melena in children. Stool for occult blood in this situation will be helpful test. Worms in stools should be asked for, as sometimes high load of worms infestation presents with GI bleeding.

Note should be made about associated symptoms like fever, vomiting, diarrhoea/constipation and important examination findings like growth, perianal area, per rectum, organomegaly, skin and mucus membranes.

Common causes of bleeding in children based on age shown in table 1

Table 1 Causes of LGI bleeding in children based on age			
Newborn (Birth to 1 month)	**Infant (1m - 2yr)**	**Pre-School Age (2 - 5yr)**	**School Age (> 5y)**
NEC	Anal fissure	Anal fissure	Anal fissure
HDN	Infectious colitis	Infectious colitis	Infectious colitis
HD enterocolitis	Allergic colitis	Polyp	Polyp
Malrotation with volvulus	Intussusception	Meckel's diverticulum	HSP
Allergic proctocolitis	Meckel's diverticulum	HSP	IBD
	LNH	HUS	LNH
	HD enterocolitis	LNH	
	Malrotation with volvulus		
	Intestinal duplication		

NEC: Necrotizing enterocolitis; HD:Hirschsprung's Disease; LNH: Lymphonodular hyperplasia; IBD- Inflammatory Bowel Disease

Combination of various clinical features helps us to point to specific etiology of LGI.Fever, loose stools, vomiting may suggest acute infective colitis. Eczema, recurrent wheeze, family history of asthma, food allergies points towards food protein allergy. Anal fissure, perianal fistulae/abscess, growth failure may suggest IBD. Fissure alone may be constipation related. Jaundice, palmar erythema, hepatosplenomegaly, ascites, dilated abdominal veins suggests portal hypertension related bleeding. Abdominal mass may be seen in intussusception, IBD. Skin rash (purpura), arthritis/arthralgia, hematuria may suggest vasculitis (HSP). Rectal polyps some felt on per rectal examination. In children with pigmentation of lips, buccal mucosa and face, recurrent pain abdomen Peutz Jeghers syndrome should be suspected. Bluish soft nodules over body (on soles and palms) with similar lesions in gastrointestinal tract are seen in blue rubber bled syndrome, similarly soft tissue swelling of lower limb associated with colonic/rectal vascular malformation in Klippel-Trenaunay Syndrome.

Investigations should be tailoredaccording to patient's history, symptoms and physical findings. Simple basic investigations like Hemogram, Acute phase reactants (Hemoglobin, platelets, ESR, CRP, Albumin) gives good information regarding severity of blood loss and evidence of inflammatory pathological. In suspected cases of infection stool cultures may be useful. Specific investigations like endoscopy (Gastroscopy, colonoscopy, enteroscopy, Capsule endoscopy), Meckel's scan, angiography CT scan and MRI are useful for localization of source of bleed. Endoscopy is also useful both as diagnostic (visualization of lesion and getting mucosal biopsies for histopathology) and therapeutic in case of polyp. Colonoscopy is not indicated acute onset bloody diarrhoea, as infection needs to be ruled out. It is contraindicated in toxic megacolon, obstruction, bowel ischemia, and peritonitis. Meckel's scan useful when Meckel's diverticulum or enteric duplication cysts are suspected. For angiography to detect the source of bleeding there should be at least 0.5ml/hr blood loss.

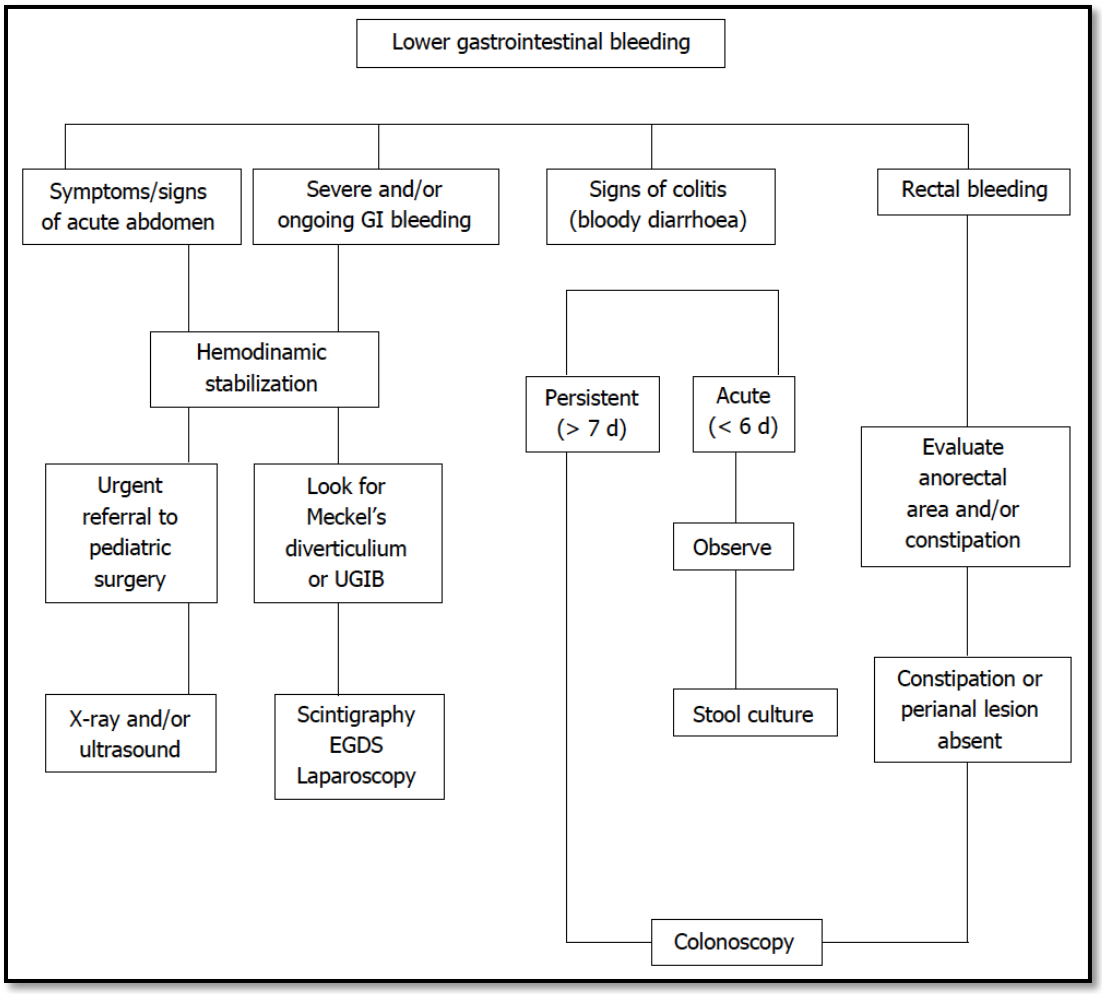
Initial focus should be on hemodynamic status. Tachycardia is import indicator of ongoing blood loss. Delayed capillary refill time and hypotension are obvious signs of hypotension, which when present should prompt to immediate resuscitation and shifting to ICU. If blood loss is minor and unquestionably stable hemodynamic child cane be managed on OPD basis.

Juvenile polyp: Intermittent painless rectal bleeding is the most common presentation. Rectal bleeding occurs during defecation. Major rectal bleeding responsible for acute anemia is a rare event, likely the result of autoamputation of pedunculated polyps. However, iron deficiency anemia is found in as many as one-third of cases.Rectal bleeding is recurrent, present for over three months in 55% of cases. Additional manifestations are unusual, including colicky abdominal pain, diarrhea with mucus, autoamputation with spontaneous extrusion, prolapse of rectal polyp, and prolapse of rectum.Colocolic intussusception rarely occurs. Colonoscopy is the procedure of choice for diagnosis of colorectal polyps of all sizes.It allows resection of most polyps. Although juvenile polyps may be distributed throughout the colorectum, they have a distal predominance within the rectosigmoid (70%). They are more often single (73%) than multiple.Recurrence was observed in 4%. The risk ofmalignant change for a solitary juvenile polyp is almost negligible.

Uncommon causes of LGI bleed I children include vascular malformation (rectal hemangiomas, hemorrhoids, Blue Rubber Bled Nevus Syndrome, Hereditary hemorrhagic telangiectasia, Klippel Trenaunay syndrome), Solitary Rectal Ulcer Syndrome, Diversion colitis, Anastomotic ulcers.

Management of individual causes of LGI bleed is out of this discussion.

Algorithm for Approach to a child with LGI bleeding



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2. Leung A, Wong AL. Lower gastrointestinal bleeding in children.PediatrEmerg Care. 2002;18:319–323.
3. Khurana AK, Saraya A, Jain N, et al. Profile of lower gastrointestinalbleeding in children from a tropical country. Trop Gastroenterol.1998;19:70–71.

VACCINATION PRIORITIES DURING COVID-19 PANDEMIC

1. Vaccinate newborns in maternity set up, before discharge. BCG, OPV and Hepatitis B vaccines are to be administered.

2. Prioritize primary vaccination series: DPT, Hep B, Hib, OPV/IPV, Rotavirus vaccines, PCV, Influenza, Varicella and MR/MMR. Avoid postponing these vaccines

3. Prioritize pneumococcal and Influenza vaccine to vulnerable groups. Healthcare personnel should be upto date in their age appropriate vaccinations.

4. Typhoid conjugate vaccines may be clubbed with the influenza vaccine at 6 months or MR/MMR at 9 months.

5. Inactivated JE vaccines (where applicable) should be administered at 1 year.

6. Hepatitis A vaccines and HPV vaccines may be postponed to a later date if logistic issues of transport, etc., exist. They may be administered after the priority vaccines have been given.

7. Multiple vaccines can be administered in the same session without fear of any increased adverse effects.

8. Boosters may be postponed to a later date, if logistic issues of transport, etc. exist.

9. If a child is in a healthcare facility for any reason, this opportunity should be utilized for administering any eligible vaccine.

Source: IAP-ACVIP

IMAGE QUIZ

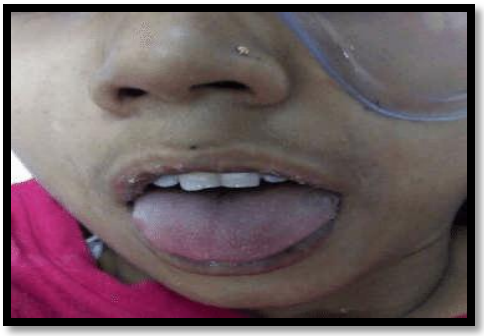
Dr Vinay Kumar Gadde

DNB Resident

A, 14-year-old, female was admitted with alleged history of consumption of an unknown quantity of Auxin (plant growth hormone). Half an hour later, she developed vomitings followed by altered sensorium, and was brought to the hospital in a gasping state. Physical examination revealed a pale cyanosed girl with poor respiratory effort, responding only to deep painful stimuli. Pulse was 100 per minute, blood pressure 120/70 mmHg. Pupils were bilaterally dilated with sluggish reaction. No other significant findings on physical examination. Her haemoglobin was 10.5g/dl on admission & blood sample looks dark chocolate coloured. Platelet count was normal, total leucocyte count showed persistent polymorphonuclear leucocytosis with reticulocyte count of 3%. Urine, E.C.G., X-ray chest and biochemical profiles were within normal limits except serum bilirubin of 2.0 mg/dl and an Arterial blood gas (ABG) analysis given below. However, her oxygen saturation on pulse-oximeter showed 70-75%. Methaemoglobin level was 55%.G6PD were normal. The patient was immediately intubated and put on mechanical ventilator. ABG analysis after intubation was given below. Inspite of increased Fio2 to 100% on ventilator her oxygen saturation on pulse-oximeter showed 70-75% but Pao2 increased to 280mHg.

Arterial blood gas

	Before intubation	After intubation
FiO2 (fraction of inspired oxygen)	21%	100%
pH	7.401	7.378
pCO2	30 mmHg	30mmHg
pO2	80 mmHg	280mmHg
SaO2 [%]	93.4	100
HCO3 [mmol/L]	25.5	22.1
Oximetry results		
Hb (hemoglobin [g/L])	13	12.5
FMetHb (fractional MetHb [%])	55 %	54.5%
Lactate [mmol/L]	3.0	3.4



Questions:

1). What is the diagnosis as per above information?

2). What is the pathophysiology of above condition?

3). What are the treatment of options for above condition?

Answer:

1). **Acquired Methaemoglobinemia** secondary to auxin (plan growth hormone) poisoning .

2). Normal oxyhemoglobin equilibrium

- Oxygen *binds* to HbFe2+ (ferrous) state.
- During oxygen transport, this transiently forms the HbFe3+ (ferric) state.
- The ferrous (HbFe2+) form of iron is needed to bind oxygen.

Formation of methemoglobin

- Various oxidizing substances convert the iron atom of hemoglobin into the Ferric(3+) state (forming methemoglobin). This is subsequently *incapable* of binding to oxygen (or transporting oxygen).
- Methaemoglobin is normally present as less that 1% of the total haemoglobin under physiologic conditions. Levels above it is defined as methaemoglobinaemia. (Disparity b/w Pao2 & pulse oximeter Spo2 is diagnostic clue)
- In normal individuals methaemoglobin level must be greater than 10% to be clinically recognized and only mild symptoms, headache, fatigue and nausea occur at level of 20-30%. Dyspnoea on exertion, lethargy and tachycardia at 30 to 45% levels, and at 50 to 70%, arrhythmias, coma, seizures, respiratory distress and lactate acidosis. Levels greater than 70% cause cardiovascular collapse and have a high degree of mortality if left untreated.

3) Treatment is with slow intravenous injection of **methylene blue** (the recommended dose is 2 mg/kg for infants, 1.5 mg/kg for older children) diluted in 1% sterile aqueous solution infused over 5 min. Relief is rapid and methemoglobin levels are generally brought below 10% within 30 min. The dose can be repeated after an interval of 1 h if the cyanosis has not cleared, till a maximum dose of 7 mg/kg over 24 h can even be repeated twice or thrice

Methylene blue exerts its reductive effects by activating the dormant but volatile hexose monophosphate (HMP) shunt to regenerate NADPH. Other options are Ascorbic acid(vitamin –C) may be useful in milder cases.

Sildenafil Pharmacology

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Consultant in PICU & Pediatric Cardiac ICU

Indication:

Persistent Pulmonary Hypertension of the Neonate (PPHN)

- refractory to inhaled nitric oxide (iNO) and other conventional therapies or
- those who are persistently unable to be weaned off inhaled nitric oxide or
- in situations where inhaled nitric oxide and high frequency ventilation are not available

Mechanism of action:

Selective phosphodiesterase type 5 (PDE5) inhibitor. PDE5 is found in the smooth muscle of the pulmonary vasculature, where it is responsible for the degradation of cyclic guanosine monophosphate (cGMP). cGMP produces smooth muscle relaxation. Sildenafil increases cGMP

Dosage:

Intravenous: Loading dose of **0.4mg/kg** over 3 hours followed by a continuous infusion of **70 micrograms/kg/hour** for upto 7 days

Oral: 0.5 mg to 1mg/kg/dose every 6 -8 hourly which can be titrated upto 2mg/kg/dose depending on clinical response.

Child 1 -11 months: Maximum dose 30 mg/day

Child 1 – 17 years (body weight upto 20 kg) : 10 mg 8 hourly

Child 1 -17 years 9 body weight > 20 kg) : 20 mg 8 hourly

Compatible Fluid for IV infusion: 5% Dextrose

Adverse Effects:

Hypotension, dyspepsia, flushing, headache, nasal congestion, worsening oxygenation

Monitoring:

Continuous monitoring of blood pressure and oxygen saturation

Practice Points:

- Pharmacokinetics of sildenafil in neonates is highly variable
- Drug interactions: CYP3A4 enzyme inhibitors such as rifampicin decrease levels of sildenafil.
- Concomitant administration with other antihypertensive agents may result in excessive hypotension.
- Consider reduced doses in the context of renal failure
- Care should be taken when stopping sildenafil. Weaning of the dose should be considered.