

RECOMMENDATIONS

Diagnosis and Management of Gastroesophageal Reflux Disease in Children: Recommendations of Pediatric Gastroenterology Chapter of Indian Academy of Pediatrics, Indian Society of Pediatric Gastroenterology, Hepatology and Nutrition (ISPGHAN)

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Justification: Gastroesophageal reflux (GER) related symptoms are a major cause of parental concern and referrals at all ages. These guidelines have been framed to inform pediatricians regarding current diagnosis and management of gastro-esophageal reflux disease (GERD). **Process:** A group of experts from the pediatric gastroenterology sub-specialty chapter of Indian Academy of Pediatrics (ISPGHAN) discussed various issues relating to the subject online on 25 October, 2020. A consensus was reached on most aspects and a writing committee was constituted. This committee had three meetings for a detailed discussion. The statement was sent to the entire group and their approval obtained. **Objective:** To formulate a consensus statement to enable proper diagnosis and management of GERD in children. **Recommendations:** GER is physiological in most infants and it improves as age advances. The pathological form, called GERD causes distressing symptoms that affect daily activities and may result in complications. The presentation would vary from regurgitation to severe symptoms due to esophageal or respiratory tract disease. In older children, esophagitis is the commonest manifestation of GERD. A careful history and clinical examination are adequate to make a diagnosis in most patients, but judicious investigations are necessary in a few. Upper gastro intestinal tract endoscopy may be required in those with esophageal manifestations, dysphagia and hematemesis. In children with extra-esophageal symptoms, MII-pH monitoring and scintigraphy are necessary. Empirical treatment with a Proton pump inhibitor (PPI) has not been proven useful in infants, but a four-week trial is recommended in older children without complications. While positioning and feed thickening have limited benefit in infants, life-style modifications are important in older children.

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Symptoms attributed to gastroesophageal reflux (GER) are a major reason for parental concern irrespective of the age of the child. GER is a physiological event in infants that improves with increasing age. While 50% infants reflux below 6 months, the prevalence reduces to 10 % by 2 years of age [1,2]. However, in 22 to 25% of infants, it is pathological termed Gastroesophageal reflux disease (GERD), and requires medical intervention [3]. In older children and adolescents, the overall prevalence of GERD is 5-8% and most of them will need some intervention [4]. A comprehensive history and clinical examination are adequate in most infants and children, but judicious investigations are necessary in some. In India, due to lack of clarity amongst pediatricians; there is a flawed approach, unnecessary investigations and inappropriate medications. These guidelines aim to improve awareness amongst pediatricians regarding management of gastroesophageal reflux disease.

PROCESS

A group of experts from the pediatric gastroenterology sub-specialty chapter of Indian Academy of Pediatrics (ISPGHAN) discussed various issues relating to the subject in an online meeting of select members on 25 October, 2020. A broad consensus was reached and a writing committee was formed. This committee had two meetings online on 21 November, 2020 and 1 December 2020 for a detailed discussion. The statement was sent to the entire group by e-mail and their approvals were obtained. A consensus statement was formulated after incorporating suggestions on 24 December, 2020.

GUIDELINES

Clinical Manifestations

In infants and children, GER has various manifestations with a range of severity. Symptoms may be mild, like random regurgitation, or severe symptoms due to esophageal or

respiratory tract disease (**Table I**). In some infants the symptoms can be non-specific and difficult to recognize. Amongst older children, about 60% of children present with epigastric pain, regurgitation and extra-esophageal symptoms [5,6]. Nausea and vomiting are seen in 21% of children [6]. The classic “reflux syndrome” or “reflux chest syndrome” consists of substernal, burning chest pain, with or without regurgitation, and cannot be expressed by most children below 8 years of age [4]. Only 6-8 % of children below eight years are able to give a classical description. Definitions used in this guideline are provided in **Box I**. Risk factors for GERD in **Web Box I** and features which suggest an alternate diagnosis than GERD are in **Web Box II**.

Diagnosis

GER is physiological in most infants and needs no tests for documentation. In GERD, investigations depend on the clinical manifestations. A thorough history and clinical examination has a reliability of 60-70% in adolescents and older children [7]. However, it is less reliable in infants and in those with extra-esophageal symptoms. Hence investigations are required in a small subset of patients. The choice of investigation is based on the clinical symptomatology of a given case. When typical symptoms (**Table I**) are present, upper gastro-intestinal endoscopy must be the first investigation. Tests like pH/MII (multichannel intraluminal impedance) may be the first choice in those with atypical symptoms or after failure of empirical therapy.

Infant GER Questionnaire

I-GERQ-R is an infant reflux symptom based assessment scale containing 12 items, completed by the caregiver. It has been validated in western settings as a screening tool to identify those with GERD and also to monitor outcome of therapy [8]. Data is not sufficient to recommend it in developing countries, where artificial feeding is much less prevalent than in the west.

Upper GI Endoscopy

Endoscopy helps direct visualization of esophageal mucosa, assess the function of the lower esophageal sphincter and obtain biopsies to rule out conditions like eosinophilic esophagitis. Endoscopically visible damage to the distal esophageal mucosa is the most reliable sign of reflux esophagitis. The typical features of GERD on esophageal histology are basal zone hyperplasia (>20% of total thickness) and elongation of papillae or rete pegs (>50% of total thickness). These may be useful in non-erosive reflux disease (NERD), but they lack sufficient sensitivity and specificity [9]. Endoscopy can also diagnose conditions like achalasia and hiatus hernia, as well complications like stricture and Barrett metaplasia. Indications for endoscopy are summarized in **Box II**.

Box I Definitions

Gastroesophageal reflux (GER): Physiological, involuntary passage of gastric contents into the esophagus with or without visible regurgitation.

Regurgitation: Bringing up of gastric contents into the oral cavity and sometimes out of the mouth. While regurgitation is the visible form of GER, absence of regurgitation, does not rule out reflux related disease.

Vomiting: Forceful expulsion of gastric contents through the mouth, which involves intense muscular activity of the respiratory and abdominal muscles and is a centrally mediated somatic reflex response, sometimes triggered by reflux.

Gastroesophageal reflux disease (GERD): Pathological form of GER resulting in symptoms that affect daily activities or complications that cause systemic disease. It occurs either from loss of calories or the consequence of the esophagus/respiratory tract being exposed to the gastric contents.

Table I Clinical Features of Gastroesophageal Reflux Disease

Typical features	Atypical features
<i>Infants</i>	
Regurgitation/vomiting	Apnea
Irritable during and after feedings	Chronic stridor
Refusal to feed /failure to thrive	Wheezing/recurrent pneumonia
Inconsolable crying	Hematemesis/Anemia
	Neurobehavioural changes
	Sandifer's syndrome
<i>Children</i>	
Nausea with or without vomiting	Chronic cough /recurrent pneumonia
Pain abdomen mostly epigastric	Recurrent stridor/bronchospasm
Heartburn/chest pain	Laryngitis/hoarseness of voice
Drooling/spitting/water brash	Sinusitis
Choking during feeding or night	Otitis media
Poor appetite/refusal to feed	Gastrointestinal bleeding/anemia
Nausea with or without vomiting	Dental erosion/halitosis
Pain abdomen mostly epigastric	Sleep disturbance
Heartburn/ chest pain	Chronic cough/recurrent pneumonia
Drooling/spitting/water brash	Recurrent stridor/bronchospasm
Choking during feeding or night	Laryngitis/hoarseness of voice
Poor appetite/refusal to feed	Sinusitis
	Otitis media
	Gastrointestinal bleeding / anemia
	Dental erosion /halitosis
	Sleep disturbance

Box II Indications for Endoscopy

Hematemesis
 Dysphagia
 Feeding aversion and a history of regurgitation
 Persistent faltering growth associated with overt regurgitation
 Back arching or features of Sandifer's syndrome.
 Persistent retrosternal or epigastric pain refractory to PPI trial
 Unexplained iron deficiency anemia
 A referral for fundoplication

24-hour Esophageal pH Monitoring

Esophageal pH monitoring is used to measure the magnitude of acidic reflux over 24 hours using a pH probe placed at the lower esophagus. It helps in establishing a temporal association between the patient's symptom episodes and acid reflux. Reflux index (percentage of time esophageal pH <4) of >10% in infants and >7% in children is considered significant. However sensitivity varies from 41% to 81% for diagnosis of GERD and currently it is not considered ideal for routine use after the advent of impedance pHmetry [7]. It may be used to correlate episodic symptoms like heartburn with reflux, confirm if acidic reflux is the cause of eosinophilic esophagitis and also assess if drug therapy is effective.

Combined esophageal multichannel intraluminal impedance and pH monitoring (MII-pH): At present, this is considered the best investigation for diagnosis of GERD. Multi-channel intra-luminal impedance measures electrical impedance changes as a bolus of solid, liquid or air passes between the sensors along the catheter (air>liquid). Here a pH electrode is incorporated into the impedance catheter. It monitors not only acid (pH<4) but also weakly acidic (pH 4-7) reflux episodes as well as non-acid/alkaline (pH>7). This is an important improvement, since 50% of children with GERD will be missed, if only acidic reflux is measured. MII-pH also provides details about the duration and degree of the reflux as well as the contents of the refluxate, whether liquid, gas or both together. It may also be of help to correlate extra-esophageal symptoms with reflux [10]. MII-pH study in a symptomatic patient with a normal endoscopy will reveal three patterns: *a*) Functional heart burn (normal acid exposure with no symptom correlation) *b*) Non-erosive reflux disease (abnormal acid exposure irrespective of symptom correlation) and *c*) Esophageal hypersensitivity (normal acid exposure but symptoms correspond to acidic/nonacidic reflux episodes). These findings provide important clues in deciding whether a given patient requires acid suppression, neuromodulators or anti-reflux surgery.

MII-pH study improves management decisions in children when compared to conventional 24-hour pH study [11]. However, it is still unclear if the treatment based on MII-pH study leads to long term reduction of symptoms. High

cost, non-availability of expertise and equipment, as well as paucity of reference values in children are constraints for recommending their routine use in India. Restricted availability of esophageal manometry equipment for the precise placement of MII-pH catheter is also a limiting factor. Indications for MII-pH study are given in **Box III**.

Trial of Proton Pump Inhibitor

Many randomized control trials (RCT) have supported the use of a 2-4 week trial of PPI administration in children with typical symptoms of GERD [12, 13]. Though there is no data from India, a trial of PPI may be judiciously used in older children when there are no alarm signs. However in infants, no study has shown any benefit irrespective of the duration of the therapy [14]. Hence empirical therapy with PPIs cannot be recommended in infants.

Esophageal Manometry

Manometry has poor specificity and sensitivity in the diagnosis of GERD. It is useful to rule out esophageal motility disorders during pre-operative evaluation of children undergoing fundoplication. It is also useful in the diagnosis of achalasia, wherein symptoms may sometimes mimic that of GERD [15].

Scintigraphy

Scintigraphy or milk-scan is a radionuclide based study for the diagnosis of pulmonary aspiration in GERD. It has low sensitivity, lacks standardized technique and there are no accepted normal values. In addition, it assesses only the immediate postprandial reflux. Hence it is not useful for documentation of esophageal reflux. It may be done to confirm pulmonary aspiration in patients with refractory respiratory symptoms or those with recurrent aspiration pneumonia, but normal esophageal pH monitoring study [16]. However a normal scan does not always rule out aspiration.

Upper GI Contrast Study

It is not useful for confirming GERD in infants and children. It has a role in evaluation for anatomic abnormalities like

Box III Indications for MII-pH Monitoring

Infants with extra-esophageal symptoms (non-epileptic seizure-like events or apneas)
 Feed refusal in infant with failure to thrive in the absence of other diagnosis
 Infants with unexplained crying, before considering acid-suppressive therapy
 Follow-up of esophageal surgical conditions (atresia, diaphragmatic hernia)
 Assess efficacy of antireflux therapy
 Evaluation of preadolescent children with unreliable GERD clinical picture

hiatal hernia, duodenal web, achalasia and malrotation of the gut, all of which may present with symptoms similar to GERD. In children with recurrent aspiration, video-fluoroscopic swallow studies are useful to differentiate oropharyngeal dysphagia from GERD, especially in neurologically impaired children [17].

Management

Treatment depends upon specific symptoms, disease severity, age of presentation, and associated comorbidity. The aim is to reduce the troublesome symptoms, avoid complications and maintain normal growth without any side effects of treatment. Management can be categorized as non-pharmacological, pharmacological and surgical

Non-pharmacological Measures

Feed thickeners: This is an option in non-breast fed infants. They increase the stickiness and weight of the feed so that it remains in the stomach for a longer time and decreases the risk of regurgitation [18]. Esophageal intraluminal impedance and pH studies in term healthy infants have demonstrated that feed thickeners decreased visible regurgitation by decreasing maximum height reached by the refluxate [19]. Various studies with use of different types of feed thickeners such as locust bean gum, cabor bean gum, xanthum gum, alginate with trials ranging from 1 to 8 weeks did not show superiority of any one over the other. Use of thickeners decreases reflux by 2 episodes/day and reduces anxiety of parents probably due to a placebo effect. It may be advised to term infants with mild disease [18]. However, thickeners can sometimes cause diarrhea due to increase in osmolality, and increased weight gain from high calorie density. In some babies, it may paradoxically increase symptoms of reflux by slowing down gastric emptying. Thickeners have not been found to be useful in preterm babies with some studies reporting an increased incidence of necrotizing enterocolitis [20,21]. In India, commercial infant feed thickeners are currently not available, but many use rice cereal as a cheap and acceptable alternative, even though there are no studies to support it.

Feed volume and position: It is necessary to assess for over-feeding when evaluating infants with GERD. There are no RCTs comparing volume of feed and its effect on GER [22]. Despite various intra-luminal impedance and pH studies showing that prone and left lateral positions decrease GER; only the supine position is still recommended due to increased risk of sudden infant death syndrome. Elevation of the head end of the crib and use of chairs can compromise respiration of infants by increasing pressure over the abdomen, and hence these are not advised [23]. Adolescents and older children with GERD

can use left lateral position and head end elevation to decrease reflux-related symptoms [4].

Life style modification: Avoiding modifiable external factors like chocolates, tobacco, passive smoking, high fat meals, alcohol, late dinner and weight loss help to decrease reflux in adults. It can be recommended in adolescents and older children, wherever applicable [4].

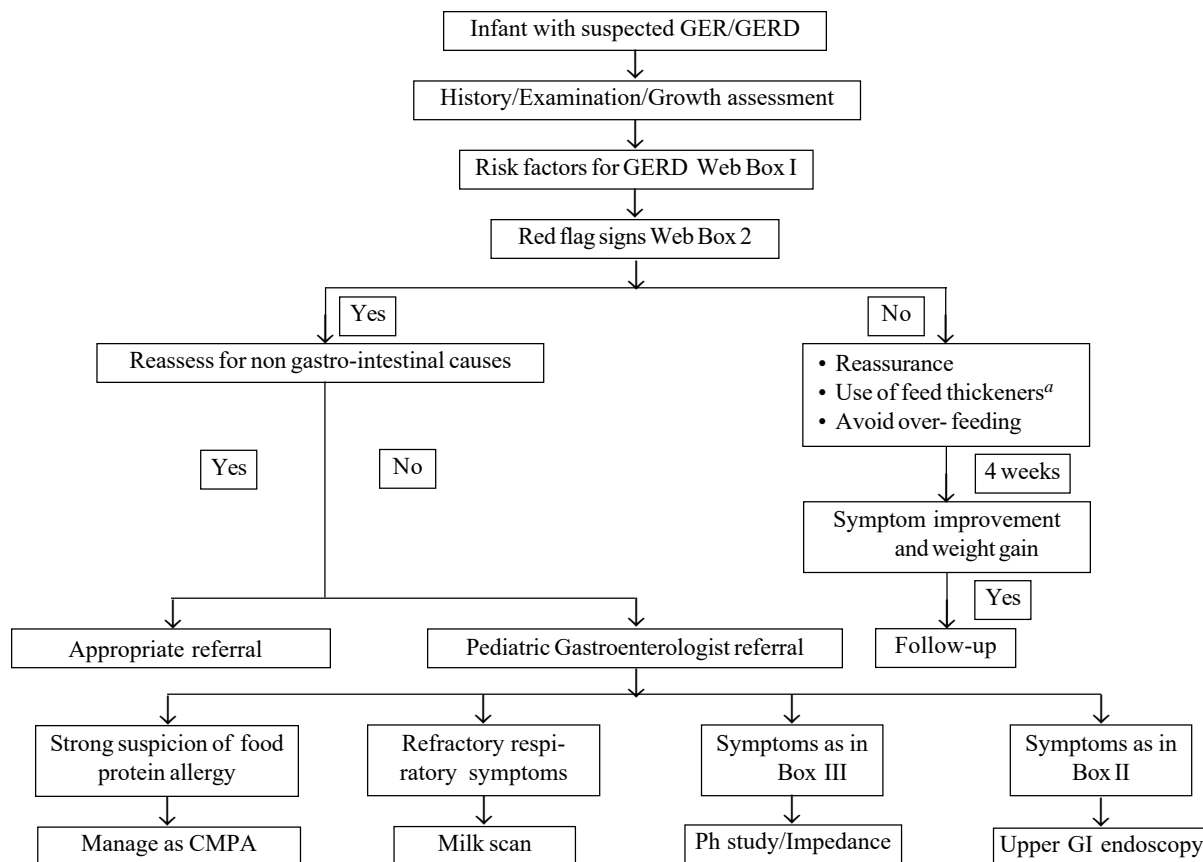
Hypo-allergenic formula: Symptoms of GERD and milk allergy in infants are non-specific and mimic each other. Since both the conditions are common in the West, some guidelines recommend a short trial of hypo-allergenic formula in babies who are not breast-fed. Since the prevalence of milk allergy in India is not known it is not scientific to support such a recommendation. It may be considered if there is a strong suspicion of milk allergy, after evaluation by a specialist.

Pharmacological Management

Proton pump inhibitors: Proton pump inhibitors (PPIs) are the anchor of medical treatment of GERD. They inhibit gastric acid secretion by noncompetitively inhibiting the active H^+K^+ -ATPase proton pumps in the gastric parietal cells. For optimal efficacy, PPI should be administered 30–60 minute before a meal so that it is absorbed before the proton pump is activated. They are the first-line therapy of erosive esophagitis in all age-groups and in the empirical treatment of typical symptoms of GERD i.e., epigastric or retrosternal pain in adolescents and older children. [11,24,25].

Evidence available so far does not support the use of PPIs for infants with unexplained crying or distress. In a recent study, where esophageal MII-pH monitoring tracings of 62 infants with unexplained distress were examined, it was found that the episodes of distress did not significantly correlate with GER [26]. Similarly, the role of PPIs in extra-esophageal symptoms like cough, wheezing or asthma is questionable [25]. A large randomized placebo controlled study of children with poorly controlled asthma showed no improvement in asthma control scores with the addition of a PPI to their asthma management plan [27].

The recommended duration of empirical PPI therapy for uninvestigated GERD symptoms is 2–4 weeks. In those in whom there is a complete resolution of symptoms, the PPI is tapered and stopped over 4–8 weeks. In partial responders, one may consider administering the same PPI twice daily rather than the conventional once daily dosing [28]. In those who do not show any response within 4 weeks, investigations (including an endoscopy) to rule out alternate causes for the symptoms should be performed (**Fig. 2**). Those with documented erosive esophagitis should receive 8 weeks of treatment [29]. Long term PPI at



^aFor babies on top feeding. CMPA-cow's milk protein allergy, GER-gastroesophageal reflux, GERD-gastroesophageal reflux disease.

Fig. 1 Algorithm for management of an infant with suspected gastroesophageal reflux disease.

the lowest effective dose should be advised for those who have a recurrence of symptoms after stoppage of the drug. It is important that such patients are periodically evaluated for its ongoing need with a specialist referral, when appropriate [30].

Available data does not support the use of PPIs in infants unless there is evidence of erosive esophagitis. In cases where a referral to a specialized center for an endoscopy is not possible, a trial of a PPI for up to 4 weeks may be acceptable, although not scientific.

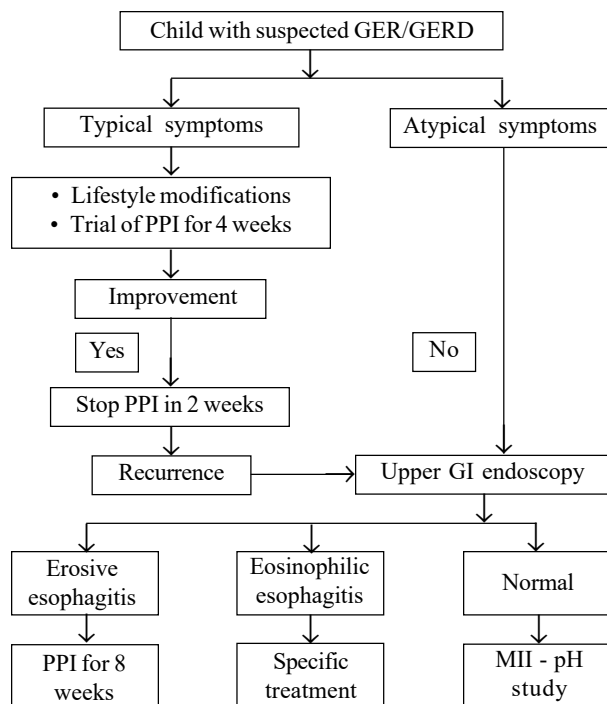
There is no difference in efficacy between the various available PPIs (omeprazole, lansoprazole, esomeprazole, rabeprazole, pantoprazole) [24]. As a result of differences in pharmacokinetics and pharmacodynamics children require higher doses on a per kilogram basis as compared to adults (**Table II**).

Long term PPI use may have potential adverse effects which may include gastrointestinal and respiratory infections, acute and chronic kidney disease and adverse

bone health [30,31]. However, the overall risk of these complications is low, with an absolute excess risk of 0.03-0.4% per patient/year, and it should not deter prescribers from using appropriate doses of PPIs for appropriate indications. It is important that PPIs are used appropriately and judiciously.

H₂-receptor antagonist: H₂-receptor antagonists (H₂RAs) act by inhibiting the histamine H₂ receptors of the gastric parietal cells. In a systematic review comprising 8 studies (276 children), H₂RAs were better than a placebo in GERD symptom relief and tissue healing [32]. However, they are less efficacious than PPIs in both rendering a patient symptom-free and the healing of esophagitis and are indicated only if PPIs are unavailable or contra-indicated [4, 33].

H₂RAs have a rapid onset of action and is therefore useful to provide immediate relief of symptoms. This is in contrast to PPIs, which are less efficacious for on-demand treatment. This is because a single dose of PPI does not inhibit all proton pumps immediately and takes almost 3



CMPA-cow's milk protein allergy, GER-gastroesophageal reflux, GERD-gastroesophageal reflux disease, PPI-proton pump inhibitors, MII-Multi channel intra luminal impedance.

Fig. 2 Algorithm for management of an older child with suspected gastroesophageal reflux disease.

days to reach a steady state. H2RAs are not suitable for long-term acid suppression, since they develop tachyphylaxis within a few weeks of use.

Ranitidine (dose: 5-10 mg/kg/day divided into two to three doses; Children > 30 Kg : 150 mg twice a day) is the most widely used. In view of the presence of N-nitrosodimethylamine (NDMA), a probable carcinogen, the Food and Drug Administration (FDA) and European Medicines Agency (EMA) have presently withdrawn the license of all ranitidine preparations.

Prokinetics: Prokinetics like domperidone and metoclopramide (cisapride, which is not available now) are used in treating GERD assuming that they would help in improving symptoms of GERD by increasing gastric emptying and consequently reducing the risk of reflux into the esophagus. However, there is little evidence supporting their use and individual meta-analyses for each of these prokinetics have found no benefit in the management of GERD [33,34]. Moreover, these drugs also have a potential for side-effects with metoclopramide associated with extrapyramidal symptoms and domperidone and cisapride having been implicated in cardiac arrhythmias. Prokinetics are therefore not recommended for routine use in GERD.

Baclofen: Baclofen is a GABA β receptors agonist that reduces the number of transient lower esophageal sphincter relaxations and accelerates gastric emptying. A meta-analysis of 9 RCTs in adults found baclofen to be useful in GERD. There are very few controlled trials in children. In addition, significant side effects such as lower seizure threshold, drowsiness and fatigue, have been reported and therefore it cannot be recommended for routine use in children [35].

Conventional antacids: Conventional antacids have no role for routine use in children because of low efficacy and potential side-effects such as aluminum toxicity with aluminum containing preparations and milk-alkali syndrome with calcium preparations.

Surface agents: Alginates are polysaccharides derived from brown seaweed and act as surface agents by forming a 'foam raft' on the top of gastric contents. A Cochrane review which included 5 RCTs in children concluded there is moderate evidence that alginates improve symptoms [24]. Currently it is available in India only in combination with conventional antacids (sodium bicarbonate 133.5 mg, sodium alginate 250 mg and calcium carbonate 80 mg per 5 mL) and the dose recommended is 10-20 mL/dose (after meals) in children ≥ 12 years old.

Table II Proton Pump Inhibitors Available in India

Drug	Pediatric dose (mg/kg/day)	Adult dose (mg)	Approved age	Available formulations
Omeprazole	1-4	20	1-17 y	Tablet, capsule, intravenous granules for oral suspension
Lansoprazole	0.7-1.44	30	1-17 y	Tablet, capsule, oral disintegrating tablet
Pantoprazole	1-2	40	5-17 y	Tablet, capsule, intravenous
Esomeprazole	3-5 kg-2.5 mg; >5-7.5 kg-5 mg; >7.5-<20 kg-10 mg; ≥ 20 kg-20 mg	40	1 mo to 17 y	Tablet, capsule, intravenous, granules for oral suspension
Rabeprazole	0.5-1	20	1-17 y	Tablet, capsule, intravenous granules for oral suspension

All drugs to be given once-a-day.

Sucralfate is a sucrose–sulfate–aluminum surface agent. It reacts with hydrochloric acid to form a cross-linking viscous material that attaches to the mucosal surface. There is limited data regarding its usefulness in children [33]. It is not indicated in the routine management of GERD in children.

Refractory GERD

It is defined as GERD unresponsive to eight weeks of optimal treatment. Refractory GERD is common in children who are neurologically impaired or have had esophageal atresia repair surgery. They usually have associated esophageal dysmotility, delayed gastric emptying and swallowing dysfunction. Such patients should be evaluated at a specialty center for anti-reflux surgery.

Since children with neurological impairment and recurrent aspiration often have swallowing dysfunction, the benefit of transpyloric feeding is difficult to establish. Presence of a nasogastric tube per se can sometimes increase reflux. However, a short trial of transpyloric feeding is justified prior to fundoplication [4].

Surgical Treatment

Surgical interventions are necessary only when medical management is unsuccessful. Surgery can be considered with GERD-related Acute life threatening events (ALTE) in infants, persisting troublesome symptoms despite adequate medical therapy, inability to withdraw medications and complications like recurrent peptic strictures and Barrett's esophagus [36].

Fundoplication: Nissen fundoplication (complete wrap), Thal fundoplication (anterior wrap) and Toupet fundoplication (posterior wrap) are done for management of GERD. Laparoscopic or open surgery can be considered based on the available surgical expertise, as both have similar short-term clinical outcome [37]. Before surgery, it is necessary to rule out associated comorbidities like esophageal dysmotility, and hiatal hernia. A meta-analysis of anti-reflux surgeries, which included 1280 children, demonstrated 86% median success rate for improvement of esophagitis related symptoms [38]. Neurologically impaired children had more postoperative complications (47%), higher mortality (13%) and failure rate (18%).

CONCLUSIONS

The recommendations are summarized in **Box IV**. Gastroesophageal reflux is an age-related phenomena in infancy, while in older children it may be related to life style. It is a clinical diagnosis and most need no investigations. When pathological, symptoms may be esophageal or extra-esophageal. Investigations like upper GI endoscopy, MII-pH are required in a select few, depending on the nature

Box IV Recommendations

- In most infants, GER is physiological and will improve with age. Investigations are required only if the reflux is pathological (GERD).
- In older children, esophagitis is the commonest manifestation of GERD.
- Upper GI endoscopy may be required in those with esophageal manifestations, dysphagia and hematemesis. MII-pH monitoring and scintigraphy may be recommended in those with extra-esophageal manifestations.
- Barium contrast studies should be done only if an underlying anatomical abnormality is suspected.
- Empirical PPI therapy in infants is not justified, but a four week trial may be undertaken in older children. While positioning and feed thickening have limited benefit in infants, life-style modifications are important in older children.
- Refractory GERD is most commonly seen after esophageal surgery and in neurologically impaired children, and hence needs specialist care.

and severity of symptoms. PPIs are the mainstay in treatment. Empirical therapy has no benefit in infants, while a 4-week trial can be given in older children with symptoms suggestive of esophagitis.

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Note: Additional material related to this study is available with the online version at www.indianpediatrics.net

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ANNEXURE

Participants in the Online Expert Group Meeting to Develop the Guidelines

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Web Box I Risk Factors for Development of GERD	
<i>Infants</i>	
Prematurity Medications as theophylline/caffeine for apnoea Congenital anomalies of respiratory tract Post-operative esophageal atresia/diaphragmatic hernia Neurological impairment Abdominal wall defects as gastroschisis and omphalocele Nasogastric tube placement	
<i>Children</i>	
Obesity Chronic respiratory disorders/wheezing/ asthma Neurological impairment Hiatus hernia Post-achalasia treatment Diet rich in drinking soda, spicy and fatty food	

Web Box II Red Flags in Gastro-esophageal Reflux Disease (GERD) and Differential Diagnosis
<i>Infants</i>
Symptoms < 1 week of age: Necrotising enterocolitis, Congenital G I tract anomalies
Vomiting: CMPA, Pyloric stenosis, Intestinal obstruction
Seizure / Hepatosplenomegaly: Metabolic disorders
Microcephaly/dysmorphic features: Genetic syndromes
Macrocephaly/bulging fontanelle: Raised intracranial pressure
Choking, coughing with feeds: Palato-pharyngeal incompetence, Tracheo-esophageal fistula
Fever/ lethargy: CNS infections, Urosepsis
Constipation/abdominal distension: Hirschsprung's disease
<i>Children</i>
Abdominal pain/ GI bleeding: Acid peptic disease
Stereotypical/ cyclical episodes: Cyclical vomiting syndrome
Behavioural changes: Rumination; unchausen syndrome