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Prevalence of Gastroesophageal Reflux in Children

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Abstract

Gastroesophageal reflux disease (GERD) is a digestive disorder that is caused by gastric acid flowing from the stomach into the esophagus. As per definition we can understand gastroesophageal refers to stomach and esophagus, and the reflex means flow back. It is very common in infants and most common cause is vomiting during infancy. Up to 67% of healthy infants manifest more than one regurgitant episode daily.[4] The peak incidence of symptomatic infantile reflux weather pathological (GERD) or not, is 4 months of age. This resolves in most infants by 1-2 years of age, unlike the pattern in children who are older than 3 years, less than 50% of who have spontaneous resolution of symptoms [5]

Introduction

Gastroesophageal reflux (GER) is characterized by the effortless passage of gastric content into lower esophagus. Reflux can be physiological, in which the infant remains free of clinical sequelae and pathological reflux or gastro esophageal reflux disease (GERD) in which symptoms and complications are associated with pathological GER[1]GER or regurgitation is very common in infancy. A classification that is particularly useful to clinicians categorizes reflux by its expected natural history[2].Thus infantile reflux, which results from a delay in the acquisition of normal upper gastrointestinal motility, is likely to resolve by the first birthday. In contrast childhood GER, although may begin in infancy appears to be a chronic disorder similar to reflux encountered in adults [3]

Prevalence

Up to 67% of healthy infants manifest more than one regurgitant episode daily.[4] The peak incidence of symptomatic infantile reflux weather pathological (GERD) or not, is 4 months of age.

This resolves in most infants by 1-2 years of age, unlike the pattern in children who are older than 3 years, less than 50% of who have spontaneous resolution of symptoms[5]

In a study on 948 infants < 13 months of age, at least one bout of regurgitation per day was present in 50% of babies between 0-3 months of age which increased to 67% at 4-6 months ,however a decline to 21% was seen at 7-8 months of age and by 10-12 months only 5% babies continued to regurgitation .The prevalence of more significant regurgitation (>4times/day) was much lesser but had a similar trend 20% at 0-3 months,23% at 4-6 months 3 % at 7-9 months and by 12 months only 2% had significant regurgitation.[6] In a similar study from Australia GER was 41% at 3-4 months of age and became <5 % at 13-14 months[7]

In a study from India on 602 children of 1-24 months of age, regurgitation was seen in 55% at 1-6 months of age, which dropped to 15% at 7-12 months and only 10% at 12-24 months of age [8]The above studies suggest GER is frequently seen in early infancy and almost completely disappears by one year of age. The prevalence of GERD in infancy is just 5-9% of all infants with regurgitations.[6,7] Persistence or appearance of regurgitation beyond 18 months of age suggests a pathological condition.

The prevalence of GERD in the general population is about 20% in the western world; however there is paucity of such data from the Indian subcontinent. A study from USA involving 566 children between 3-9 years of age and 615 between 10-17 years, pyrosis and heart burn was reported in 1.8% and 3.5% in the two groups respectively compared to 22% in adults. Indicating that prevalence of GERD slowly increases with age in children and becomes quite frequent among adults.[9]

Pathophysiology

There are three mechanisms for reflux (i) Transient lower esophageal sphincter relaxation ;(ii) transient increase in intra abdominal pressure, which overcomes the resistance of the anti-reflux barrier and (iii) spontaneous reflux through a permanently hypotonic sphincter. Transient lower esophageal sphincter relaxation, unassociated with swallowing, is the major mechanism allowing reflux to occur. Transient lower esophageal sphincter relaxations are associated with the majority of reflux episodes in children [10.]Contraction of the crural diaphragm around the gastro esophageal junction helps prevent reflux during episodes of increased intra-abdominal pressure. Low lower esophageal sphincter tone is an uncommon primary cause of reflux disease. However there are a number of hormones, neurotransmitters and medications that affect lower esophageal sphincter [11] Esophageal and gastric motor function also influence the pathogenesis of reflux. Clearance of refluxate from the esophagus is important in preventing reflux related complications. Primary motor abnormalities of the upper gastrointestinal tract may impair esophageal clearance, and thus worsen reflux disease. Peristaltic abnormalities due to esophagitis can also delay esophageal clearance, and make the esophagitis worse. [12] Delayed gastric

emptying contributes to GERD in children to a greater extent than in adults

Clinical Presentation

In infants with regurgitation it is important to differentiate physiological GER from other causes of vomiting and pathological GERD, Majority of infants with physiological GER present with regurgitation or vomiting without associated symptoms or failure to thrive. Infants with GERD may present with symptoms like vomiting, poor weight gain, irritability, feeding refusal sleep disturbance, recurrent pneumonia, asthma and apnea. In older children symptoms may differ and they may present with regurgitation, heart burn or retrosternal chest pain, dysphagia, asthma, chronic cough or recurrent pneumonia. Chronic respiratory conditions like sinusitis, laryngitis, otitis media and dental erosions are seen in children with GERD however no association as been established [13]

Conditions in children which predispose to GERD include obesity, cerebral palsy, neuromuscular disorders, cystic fibrosis, down's syndrome, tracheoesophageal fistulas, congenital diaphragmatic hernia, bronchopulmonary dysphasia, bronchiectasis, asthama, and strong family history of GERD.[14]

Esophagitis occurs in up to 83% infants with dysphagia; however symptoms like heart burn or dysphagia are less common manifestations in children than in adults with GERD.[15]

Respiratory sequelae are among the most important manifestations of reflux in children, yet may be unassociated with typical reflux symptoms. These include chronic chough, wheezing, apnea, hoarseness, stridor and recurrent pneumonia caused by aspiration, pulmonary disease and its consequent therapy can also exacerbate pre-existing reflux[16] hus it is often difficult to determine whether reflux or pulmonary disease is the primary disorder

Aspiration

The brain stem coordinates activities of the mouth, pharynx, larynx, esophagus and stomach to protect aspiration and reflux mediated respiratory disease. Respiratory diseases occurs through various mechanisms when this elaborate system is disrupted and may occur even in absence of aspiration, via esophageal respiratory neural reflexes[17] .The upper esophageal sphincter is the major barrier preventing material from the esophagus to be aspirated .Even minute aspirations of the esophagus or gastric fluid may be sufficient to stimulate airway neural element or release of inflammatory mediators resulting in laryngospasm[18] .Bronchospasm can result from alteration of the bronchi's baseline state of reactivity in response to reflux[19]

Asthma

The estimated prevalence of GERD among asthmatic patients is approximately 44%[20.] Reflux maybe responsible for episodes of nocturnal cough in asthmatics. In some cases of severe steroid dependent asthma medical and surgical anti reflux therapy has shown improvement of symptoms. [21] The association between reflux and persistent wheezing in infans is not well

estabilished. However one study of 12 infants with persistent wheeze refractory to bronchodilators and anti inflammatory medications demonstrated clinical improvement in 50% of the infants after anti reflux therapy consisting of a prokinetic agent and a histamine antagonist was instituted.[22]

Apnea

Apnea triggered by reflux, is often an obstructive phenomena, resulting from laryngospam caused by laryngeal aspiration of gastric material or stimulation of vagal afferents. Another proposed mechanism for reflux induced apnea is β-endorphin release triggerd by esophageal pain from reflux, resulting in a decrease respiratory drive and modification of the chemo laryngeal reflex [23]

Hoarse voice

Hoarseness may occur because of chronic reflux of gastric acid onto the vocal cords, resulting in inflammation and development of vocal cord nodules [24].Laryngospam secondary to aspiration of refluxate may result in stridor. Aspiration of gastric refluxate may also cause recurrent bronchitis or pneumonia. Children with neurological impairment and inadequate protective mechanisms are particularly at risk of reflux induced aspiration [25, 26]

Evaluation of GERD

GER being physiological, selection of cases for further evaluation should be carefully done. Routine diagnostic tests merely document the presence of reflux giving only inadequate information from management point of view.

In infants Orenstein's infant GER questionnaire (i-GERQ) may help in distinguishing GER from GERD. It is a symptom based questionnaire with maximum score of25.It has shown that a score of > 7 has 74% sensitivity and 94% specificity in diagnosing GERD in infants [27].The score when applied to the Indian population has shown a sensitivity of 43% and specificity of 79% [28]

I-GER Q score because of its simplicity and reproducibility can be used to segregate those infants who need further workup. Tables: I

Orenstein's infant GER Questionnaire

S.No	Questions	Points
1.	How often does the baby usually split up? • 1to 3 times per day • 3to 5 times per day • >5 times per day	 1 2 3
2	How much does the baby usually split up?	

	• 1 teaspoonful to 1 tablespoonful • 1 tablespoonful to 1 ounce • >1 ounce day	1 2 3
3	Does the spiting up seem to b uncomfortable for the baby?	2
4.	Does the baby refuse feeding even when hungry?	1
5	Does the baby have trouble gaining enough weight	1
6	Does the baby cry a lot during or after feeding	3
7.	Do you think the baby cries or fusses more than normal?	1
8.	How many hours does the baby cry or fuss each day • 1to3 hours • > 3 hours	1 2
9	Do you think the baby hiccups more than most babies?	1
10	Does the baby have spells of arching back?	2
11	Has the baby ever stopped breathing while awake and struggling to breath or turn purple or blue	6
	Maximum total score	25

Also Rome III criteria can be used to diagnose GER in infants. (Table II)

Table II: Diagnostic criteria of Infant Regurgitation according To Rome III Classification:

Must include all of the following in otherwise healthy infants 3 weeks to 12 months of age

- Regurgitation 2 or more times per day for 3 or more weeks
- No retching, hemetemesis, aspiration, apnea, failure to thrive, feeding or swallowing difficulties, or abnormal posturing.

pH Probe study

pediatric ambulatory pH probes permit 24 hours monitoring while the infant carries out normal activities.24hour pH monitoring is able to determine how frequently acid reflux occurs over

a given period, how long it takes to be cleared and the effect of feeding, body position and state of consciousness on GER. The advantage of this study is that it can be done in any age group, also can be useful in relating wpisodic events like apnea or behavioral disturbances with reflux in the evaluation of the success of medical and surgical therapy.[29,30]The main disadvantage is that it cannot measure non-acid or weekly acid reflux(pH>4).The parameter in pH study is the Reflux Index(RI). RI is the percentage of times esophageal pH is <4...A RI >5% in infants and >10% in children is suggestive of GER. [31, 32]

Multichannel Intraluminal- impedence measurement (MII)

This technique is based on the principle of change in electrical resistance that occurs during the passage of a bolus of gas or liquid across a measuring segment placed in the esophagus. Impedance is inversely proportional to electrical conductivity as the conductivity of liquid and gas is different this helps in differentiating liquid from gas reflux. It can detect both acid and non-acid reflux and direction of reflux. The combination of impedance study with pH study is superior to pH study alone in diagnosing GERD. The disadvantage of this study is high cost less availability and lack of evidence based parameters. [31, 33]

Endoscopy

It enables direct visualization of esophageal mucosa as well as study the dynamics of LES.[34] It is the best method for diagnosing esophagitis due to GERD. Macroscopic evidence of esophageal ulceration strongly suggests esophagitis, mucosal biopsy is required to diagnose less severe lesions and rule out other causes of esophagitis (eosinophillicesophagitis, crohns disease etc).The severity of endoscopic esophagitis in adults graded by the Savary and Millers classification is less applicable in pediatrics as esophagitis in children is restricted to grades 1 & 2.A modified classification with subdivision of the milder grades which would be more appropriate for pediatric use needs to be developed. [35] Indications of endoscopy are; persistence of symptoms in spite of therapy, dysphagia or odynophagia, evidence of GI bleed or iron deficiency anemia, strictures or ulcers on barium study and to rule out Barretts esophagus. Histological criteria for diagnosis of esophgitis have been graded. Basal cell zone hyperplasia (>20% of total thickness) and increased stromal papillary length (>50% of total thickness) are the most commonly used criteria [36.] Other features include infiltration with neutrophils or eosinophils, growing of blood vessels in hyperplasia etc [37, 38]

Barium studies

Contrast radiographic studies of the esophagus and stomach using Barium are not specific enough for evaluating severity of GERD but are useful in detecting anatomical defects like hiatus hernia, esophageal strictures, duodenal web or an atypical pyloric stenosis.[23] The sensitivity and specificity of barium study to diagnose GERD is less than 50%[39,40].The mere demonstration of GER on a

Barium study is of little significance, since many healthy asymptomatic infants also reflux barium into the esophagus [41]

Scintigraphy

Technetium labeled infant feeds can be used to measure the amount of radionuclide refluxed into the esophagus or lungs as well as gastric emptying time. The technique has a low sensitivity and specificity and the only situation where it is useful is recurrent pneumonias due to gastric content aspirations. Scintigraphy is not used in the routine evaluation of patients with suspected GERD[31]

Management

Management in GER can be divided into those who have physiological reflux during infancy and pathological GERD.

The important part of management of infants with physiological GER is counseling of the parents and explain the natural history of the above to them .The management in these children is mainly conservative and involves feeding advice, feed thickening and positioning of these infants. Mothers should be advised to avoid forceful feeding, overfeeding and to give small frequent feeds. Though it is known that reflux is minimal in prone position however it is not advocated due to increased risk of SIDS in this age group. Beyond infancy left lateral position is good to prevent reflux[42] Use of rice cereal to thicken formula is recommended for infants because of its increase of dietary caloric density and significant decrease in regurgitant frequency [43]

PPI are not recommended in infants with physiological GER as only few of them have symptoms due to acid reflux. A study conducted in infancy showed that there was no significant difference in the effect of placebo and PPI[44]

In older children avoidance of foods that have negative effects on lower esophageal sphincter tone (peppermint, caffeinated beverages, fatty food), gastric volume (carbonated beverages), or acidity (acidic beverages or food) decrease reflux activity. Also abstinence from alcohol and tobacco can be beneficial.

Pharmacological treatment

Treatment of GERD in children requires acid suppression with potent proton pump inhibitors (PPI) or Histamine 2 receptor blockers. Studies have shown that PPIs (omeprazole) are more potent that H2 receptor blockers(ranitidine/ famotidine) in healing esophagitis secondary to reflux in children [45] PPIs act best on activated parietal cells thus should be take half hour prior to breakfast as parietal cells get activated by meals. Once daily dose is sufficient but children require a higher per kg dose due to higher metabolism [44, 46] PPIs are given for a long period and empirical therapy in older children and adolescents having typical symptoms of GERD can be given for 4 weeks as in adults. [31]Out of all PPIs omeprazole, lansoprazole and esmoprazole are approved by FDA for pediatric use.

Histamine-2 receptor antagonist like ranitidine and famotidine are short acting and have a rapid onset of action with development of

tachyphalaxsis on use >6 weeks. Thus can be used for short therapy [47]

Prolong acid suppression is needed in GERD.PPI theray for atleat 12 weeks with tapering over 2-3 months is recommended. [48] If there is no improvement on treatment for 4 week dose shoud be increased. If on stopping there is recurrence of symptoms PPIs are restarted and given for prolonged periods. In a study on long term follow up in children prolonged treatment with PPI (median period 3-12 yrs) has been found to be safe.[49]

Antacids are not recommended for prolong use in children due to their side effects (osteopenia, rickets, microcytic anemia) in aluminium containing antacids and (hypocalcaemia, alkalosis and renal failure) in calcium containing antacids however can be used for symptomatic relief for brief periods.[50]

Prokinetics

There is not enough evidence to recommend the use of these drugs (matclopramide/cisapride) in management of GERD [31] They can be used in situations where there is associated gastroperesis.

Surgery

Nissens Fundoplication may be indicated in children with confirmed GERD who do not respond to optimal medical management or are dependent on the same or have associated life threatening complications. Despite its high success rate, post fundoplication complications are frequent. These include hiatal herniation, bowel obstruction, bloating, gastric dysmotility etc[51] Fundoplication in early infancy has higher failure rates than in late childhood [52, 31]

Conclusion

GER is common in infants but not GERD. Symptoms persisting beyond infancy result in GERD. Esophagitis is common feature of GERD in older children. There is no specific diagnostic test for GERD pHmetry; impedance studies and endoscopy are indicated for extra esophageal manifestations .Medical therapy with PPIs is safe and effective in the management. Surgery is indicated in children who have failed medical therapy however failure rates are high.

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