Introduction

GER is the passage of gastric contents into the esophagus and is referred to as GER disease (GERD) when GER causes troublesome symptoms and / or complications. GERD in infants and children is sometimes difficult to diagnose and even more difficult to treat ***(Loots et al., 2012).***

It is a physiologic process and is common in term and preterm ***(Tipnis and Tipnis, 2009).***

Many clinical signs and symptoms in preterm infants have been attributed to GER, including apnea, chronic lung disease, poor weight gain and behavioural symptoms such as irritability, grimacing, head arching, and frequent swallowing ***(Tipnis and Tipnis, 2009).***

In neonates relatively few GER episodes causes esoghageal acidification to PH <4. Premature infants receive frequent feeds which can induce a weaker acid secretory response than that observed in older infants and adults. As a consequence, gastric PH maybe >4 for prolonged periods, and reflux of gastric contents might be less acidic or even alkaline ***(Lopez-Alonso et al., 2006).***

Studies have found that the use of acid suppression therapy for GERD in infants younger than one year of age is increasing ***(Barron et al., 2007)*** and that nearly 25%of very low birth weight infants are treated with reflux medication at discharge ***(Malcom et al., 2008).***

Combined PH multichannel intraluminal impedance (PH impedance)monitoring is a method to measure bolus flow in a lumen in addition to recording PH in the distal esophagus and was first described in children by ***(Skopnik et al. (1996).***

Impedance is defined as the resistance against an alternating current between two electrode pairs ***(Pilio et al., 2011).***

It is now recommended to use PH impedance monitoring in neonates and children rather than PH monitoring alone for the detection of GERD by the north American society for pediatric gastroenterology, hepatology and nutrition (NASPGHAN) and the European society for pediatric gastroenterology, hepatology and nutrition (ESPGHAN) ***(Vandenplas et al., 2009).***

Aim of the Work

To study gastroesophageal reflux disease in neonates using combined multichannel esophageal impedance and PH metry pre and post proton pump inhibitor therapy.

Gastro-Oesophageal Reflux Disease in Neonates

Gastroesophageal reflux (GER), is the passage of gastric contents into the oesophagus, and is common and normal in neonates and infants. Regurgitation with clinically significant sequelae constitutes a diagnosis of gastroesophageal reflux disease (GERD). Therefore, it is essential that trials of therapies for GERD assess GERD-defining symptoms, not only physiologic measures of GER. The North American Society for Paediatric Gastroenterology, Hepatology, and Nutrition and the European Society for Paediatric Gastroenterology, Hepatology, and Nutrition jointly recommend nonpharmacological treatment approaches for GERD in neonates ***(Vandenplas et al., 2009).***

Gastroesophageal reflux occurs when stomach contents flow back up into the oesophagus-the muscular tube that carries food and liquids from the mouth to the stomach ***(Vandenplas et al., 2009).***

GER is also called acid reflux or acid regurgitation because the stomach's digestive juices contain acid. Infants with GER spit up liquid mostly made of saliva and stomach

acids. GER is common in infants under 2 years of age. About half of all infants spit up, or regurgitate, many times a day in the first 3 months of life. Most healthy infants experience few to no symptoms and stop spitting up between the ages of 12 and 14 months ***(Vandenplas et al., 2009).***

GERD is a more serious, chronic-or long lasting-form of GER. According to studies, health care providers may often overlook GERD or mistake GERD for GER. If an infant's GER progresses to GERD, additional symptoms- such as vomiting and poor feeding-occur and can adversely affect the child's overall health and temperament. Infants with severe symptoms or with GER that lasts beyond 12 to 14 months may actually have GERD and should see a paediatrician ***(Vandenplas et al., 2009).***

Pathogenesis of GER and GERD in infants:

The lower oesophageal sphincter is not fully developed in infants and therefore this results in GER. While the sphincter muscle is still developing, it may push stomach contents back up, resulting in regurgitation. Once the sphincter muscle more fully develops, regurgitation should stop ***(Vandenplas et al., 2009).***

In contrast, GERD most often occurs when the sphincter muscle becomes weak or relaxes when it should not, causing stomach contents to rise up into the oesophagus ***(Vandenplas et al., 2009).***

Several anatomical and physiological features make infants younger than 1 year of age, more prone to GER than older children and adults:

- Short, narrow oesophagus.
- Delayed gastric emptying.
- Shorter, lower oesophageal sphincter that is slightly above, rather than below, the diaphragm.
- Liquid diet and high caloric requirement, putting a strain on gastric capacity.
- Larger ratio of gastric volume to oesophageal volume.

Other possible contributing factors may be the consumption of relatively large quantities of liquid feeds and the fact that infants are frequently recumbent ***(National Collaborating Centre for Women's and Children's Health, 2015).***

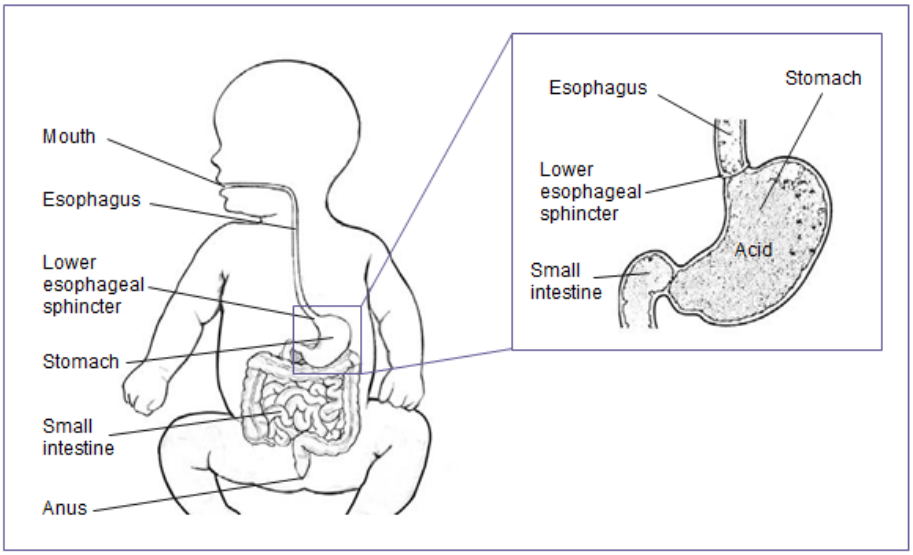

Fig. (1): Anatomy of lower oesophageal sphincter ***(National Collaborating Centre for Women's and Children's Health, 2015).***

Prevalence:

- Regurgitation of feeds is very common and occurs in at least 40% of infants ***(National Collaborating Centre for Women's and Children's Health, 2015).***
- GERD, because studies have used different definitions of GERD, estimates of prevalence in children younger than 2 years of age are imprecise ***(Gold, 2003).*** However, the number of children affected by GERD is thought to be small ***(Davies et al., 2015).***

Risk factors:

- Risk factors for developing GERD include**:**

- Premature birth.
- Parental history of heartburn or acid regurgitation.
- Obesity.
- Hiatus hernia.
- History of congenital diaphragmatic hernia (repaired).
- History of congenital oesophageal atresia (repaired).
- Neurodisability (such as cerebral palsy).

(Davies et al., 2015)

Symptoms of GERD in infants:

Infants with GERD spit up and have some or all of the following recurrent symptoms:

- Vomiting.
- Coughing.
- Gagging or trouble swallowing.
- Pneumonia or trouble breathing.
- Wheezing.
- Irritability, particularly after feedings.
- Arching of the back-often during or immediately after feedings.

- Poor feeding or refusal to feed.
- Poor weight gain or weight loss.
- Poor growth and malnutrition.
- Colic.

Other disorders can cause these symptoms, so a health care provider needs to confirm a GERD diagnosis.

Caregivers should call their infant's pediatrician right away if their infant:

- Vomits large amounts or has persistent projectile, or forceful, vomiting, particularly in infants younger than 2 months.
- Vomits fluid that is green or yellow, looks like coffee grounds, or contains blood
  - Has difficulty breathing after vomiting or spitting up
  - Refuses feedings repeatedly, resulting in poor weight gain or weight loss
  - Cries excessively and is extremely irritable
  - Shows signs of dehydration, such as dry diapers or no tears when crying.

(National institute for health, 2013)

Complication:

- Most children with regurgitation do not develop complications, but the following may occur in children with gastro-oesophageal reflux disease (GERD):
  - Reflux oesophagitis.
  - Recurrent aspiration pneumonia.
  - Recurrent acute otitis media (more than three episodes in 6 months).
  - Dental erosion in a child with neurodisability (for example cerebral palsy).
  - Rare complications include:
    - Apnoea.
    - Apparent life-threatening events (episodes of combinations of apnoea, colour change, change in muscle tone, choking, and gagging that are sometimes considered 'missed' sudden infant death syndrome).

(National Collaborating Centre for Women's and Children's Health, 2015)

Prognosis:

- Regurgitation and gastro-oesophageal reflux disease usually begin before the age of 8 weeks and resolve in 90% of infants (90%) before 1 year of age ***(National***

Collaborating Centre for Women's and Children's Health, 2015).

- Improvement in regurgitation and GERD is thought to occur because of ***(Tighe et al., 2014):***
  - An increase in length of the oesophagus.
  - An increase in tone of the lower oesophageal sphincter.
  - A more upright posture.
  - A more solid diet.

Diagnosis:

- Frequent effortless regurgitation of feeds is common and normal in infants less than 1 year of age. It may be difficult to differentiate between gastro-oesophageal reflux (GER) and gastro-oesophageal reflux disease (GERD) as there is no reliable diagnostic test.
- Suspect GERD in any infant (up to 1 year of age) or child if they present with regurgitation and one or more of the following:
  - Distressed behaviour shown, for example, by excessive crying, crying while feeding, and adopting unusual neck postures).
  - Hoarseness and/or chronic cough.

- A single episode of pneumonia.
- Unexplained feeding difficulties (for example refusing to feed, gagging, or choking).
- Faltering growth.
    - Note: additional features such as episodic torticollis with neck extension and rotation may indicate the presence of Sandifer's syndrome.

(National Collaborating Centre for Women's and Children's Health, 2015)

Assessment:

- Most cases of infant gastroesophageal reflux are diagnosed based on the clinical presentation (symptoms and signs of GERD).
- Conservative measures can be started empirically. However, if the presentation is atypical or if therapeutic response is minimal, further evaluation via imaging is warranted. ***(Bhatia et al., 2009)***
- There are no recognized classic physical signs of gastroesophageal reflux in the infant population.
- Some findings may include the following: Crying and irritability, failure to thrive, hiccups, sleep

disturbances, Sandifer syndrome (arching) ***(Tolia et al., 2015).***

- Physiologic (or functional) gastroesophageal reflux: These patients have no underlying predisposing factors or conditions; growth and development are normal, and pharmacologic treatment is typically not necessary.
- Pathologic gastroesophageal reflux or gastroesophageal reflux disease (GERD) - Patients frequently experience complications, requiring careful evaluation and treatment

(Bhatia et al., 2009)

- Secondary gastroesophageal reflux - This refers to a case in which an underlying condition may predispose to gastroesophageal reflux; examples include asthma (a condition which may also be, in part, caused by or exacerbated by reflux) and gastric outlet obstruction).
- Assess growth using centile charts to look for faltering growth.

(National Collaborating Centre for Women's and Children's Health, 2015, Henry, 2004)

Differential diagnosis:

Vomiting is a symptom associated with many disorders. Accordingly, gastroesophageal reflux cannot be assumed to be the primary problem in infants and children who present with a history of emesis. Warning signals that herald the requirement for additional evaluation include the following:

- Bilious or forceful vomiting.
- Hematemesis or hematochezia.
- Vomiting with diarrhea.
- Abdominal tenderness or distention.
- Onset of vomiting after 6 months of life.
- Fever, lethargy, hepatosplenomegaly.
- Macrocephaly, microcephaly, seizures.

(Orenstein et al., 2004)

The occurrence of any of these signs and symptoms indicates the need to consider a comprehensive metabolic, neurologic, and/or surgical evaluation, in addition to a gastroenterologic workup. Conditions to consider in the differential diagnosis of gastroesophageal reflux include the following:

Gastrointestinal disorders:

- Pyloric stenosis.
- Malrotation with intermittent volvulus.

- Intestinal duplication.
- Hirschsprung disease.
- Antral/duodenal web.
- Foreign body.
- Incarcerated hernia.

Other gastrointestinal disorders:

- Achalasia.
- Gastroparesis.
- Gastroenteritis.
- Peptic ulcer.
- Eosinophilic esophagitis/gastroenteritis.
- Food allergy.
- Inflammatory bowel disease.
- Pancreatitis Appendicitis.

Neurologic:

- Hydrocephalus.
- Subdural hematoma.
- Intracranial haemorrhage.
- Intracranial mass.
- Infant migraine.
- Chiari malformation.

(Orenstein et al., 2004)