

## Introduction of Gastro Esophageal Reflux Disease and Unani Concepts

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### INTRODUCTION

The gastrointestinal tract is responsible for the digestion of the food that attributed through chemical and mechanical processes. It provides nutrients, fluids and electrolytes to the body and excretes out waste products. It consists of a group of organs that includes liver, pancreas and GI tract which metabolize nutrients, medicine and other exogenous materials (Proctor, 2008). Gastro esophageal reflux is a physiological action that consists of unwilling expulsion of stomach contents in the esophagus that causes heart burn. It is a common practice characterized by heart burn, acid regurgitation and with or without mucosal damage (Kahrilas, 2003). Usually it may not produce any damage to the mucosa. If there is any pathology involved, mucosal damage is sure. In 40% of the patients, the endoscopic findings are observed while 60% patients have no endoscopic results of heart burn (Orlando, 2008). When there all the symptoms of the gastro esophageal reflux disease are present but the upper endoscopic results shows that there is no erosion or mucosal damage the condition is called non-erosive reflux disease (NERD) (Dent *et al.*, 1999; Richter and Castell, 1982; Waring, 2001).

### ANATOMY OF ESOPHAGUS

Normally esophagus consists of 22cm to 25cm long tunnel and that its upper one third parts consists of skeletal muscles and lower two third part is smooth muscle. It initiates from the pharynx and ends at the stomach. It passes from behind the trachea and heart, right in front of the spine and passes through the diaphragm at the point of entrance in the stomach as shown in the Figure 1.

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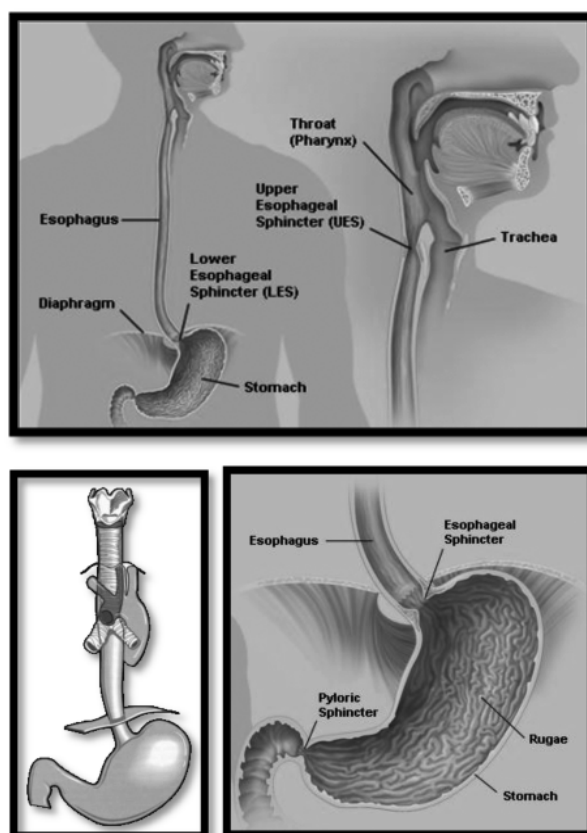


Figure 1: Anatomy of the Esophagus

### PHYSIOLOGY OF ESOPHAGUS

Esophagus is an initial part of the digestive system that delivers food from oral cavity to stomach. It consists of two high pressure zones called lower esophageal sphincter and upper esophageal sphincter. The upper esophageal sphincter is controlled by the cricopharyngeus muscle and remains close all the times to prevent inspired air to esophagus and esophageal contents to oropharynx. During the swallowing process, the swallowing center in the

brain located in the medulla oblongata passes impulses towards upper esophageal sphincter and lower esophageal sphincter's skeletal muscles and smooth muscles through vagus nerve are carried by vagal postganglionic or pre-ganglionic cholinergic fibers, respectively, to pass the food. The acetylcholine contracts the skeletal muscles of the esophagus and smooth muscles are contracted by the vasoactive intestinal peptide and nitric oxide. There are three type of protecting mechanism systems

are also involved during the process of swallowing to protect esophagus from the gastric acid reflux injury (Orlando, 2008). These are;

- Antireflux barriers – frequency limitation of the reflux
- Luminal clearance mechanism –fasten the passing through the esophagus
- Tissue resistance – minimize epithelial contact to avoid damage

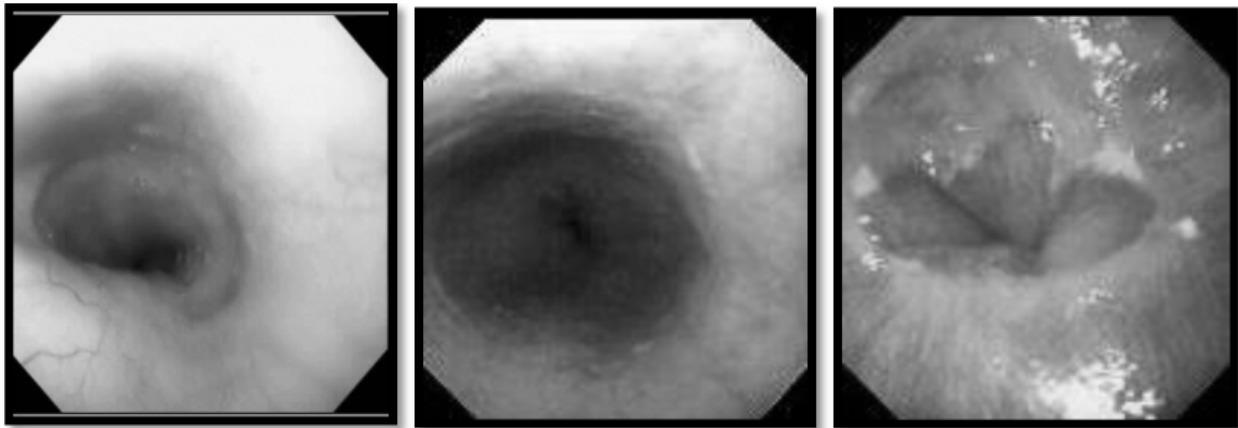


Figure 2: Normal Endoscopic View of Esophagus

### PHYSIOLOGY IN UNANI PERSPECTIVE

Al-Tibri in his book *Firdos-al-Hikmat fit Tib* state that the temperament of the esophagus is “*Cold and Dry*”. The stomach is the most sensitive internal organ of the body even from heart and liver therefore the stomach pain cause mental pressure that ultimately cause insanity. The lack of appetite is the result of if increased level of hotness in the stomach and increased appetite with slow digestive process refers that the temperament of the stomach goes towards the coldness. He also prescribed gastro esophageal reflux disease as “*it is muscular disorders of the esophagus in which the tonicity of the muscles that controls the esophageal sphincter decreases and they remain relax, as a result the sphincter remains open*” (Tibri *et al.*, 1994)

### GASTRO ESOPHAGEAL REFLUX DISEASE MECHANISM

Gastro esophageal reflux is a physiological action

that consists of unwilling expulsion of stomach contents in the esophagus that causes heart burn. It is a common practice characterized by heart burn, acid regurgitation and with or without mucosaldamage. The mechanism of acid reflux has prescribed in Figure 3 (Sperber *et al.*, 2007)

When food particles along with gastric juice having acidic pH reflux into the esophagus heart burn is developed. It happened due to the epithelial tissue lining that differs in esophagus than stomach, not suitable for the acidic environment (Gerd, 2011). Endoscopically it can be defined that which type of the material is present in the esophagus. The presence of the bilious material in esophagus is defined in the Figure 4.

Jhonsson *et al* prescribed, usually it considered that gastro esophageal reflux disease related heart burn is caused by the acid reflux but studies shows that the cause of the intra-esophageal stimulus is not only acid reflux. It may be developed by the non-

acidic stimuli that consist of increased volume due to over eating, non-acidic reflux or esophageal motor dysfunction etc. Hence the myth “no acid, no heart burn” should be discarded, because acid reflux is not the only cause but one of the causes (Johnsson *et al.*, 1998).

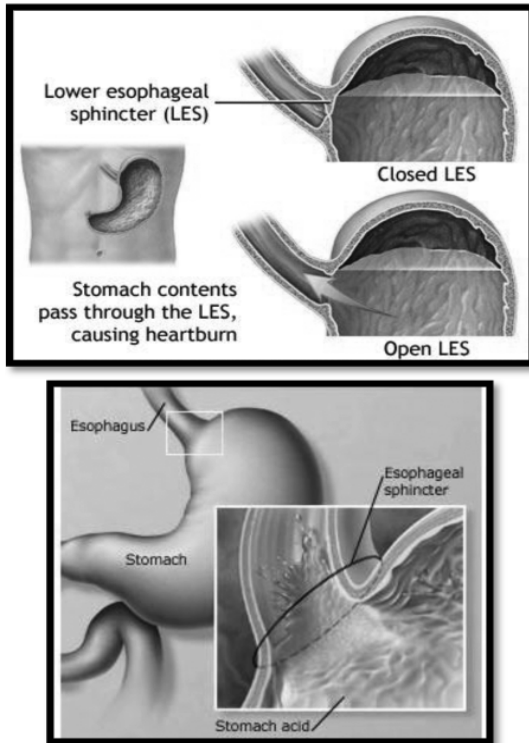


Figure 3: Function of the Lower Esophageal Sphincter

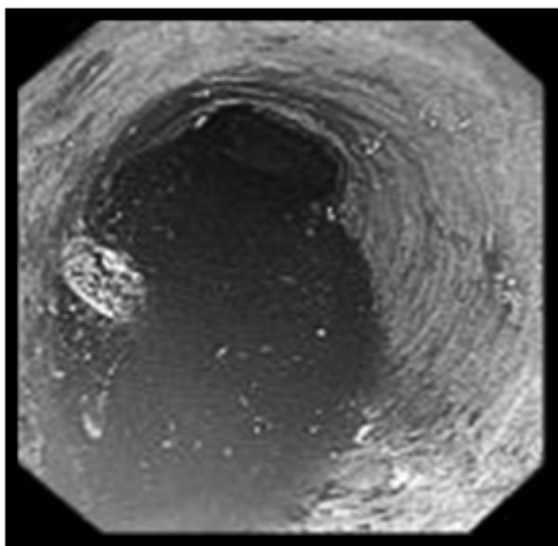


Figure 4. Presence of Bilious Stomach Material in the Esophagus

## GASTRO ESOPHAGEAL REFLUX DISEASE MANIFESTATIONS

The different manifestations of gastro esophageal reflux disease are shown in the Figure 5. Initially the lower esophageal sphincter starts relaxing (a), in the case when the esophageal sphincter closes strictly instead of relaxing (b). Patches developed in the esophageal walls (c). The indication of the mucosal damage of esophageal sphincter (d). Relax sphincter along with the patches of esophageal wall (e). A big ulcerative patch in the wall of esophagus (f). Relaxed sphincter with carcinoma (g, h). Carcinoma causing complete contraction of the sphincter (i). The complete gastro esophageal reflux disease along with carcinoma and severe mucosal damage (Figure-5j, k, l);

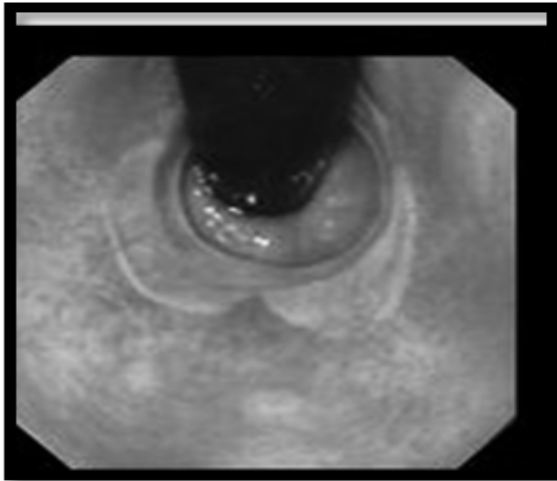
In the world over both developed and developing countries, esophageal reflux is a common condition with different sign and symptoms but increasing rapidly around the globe (Edwin, 1998). Gastro esophageal reflux disease is not only the disease of the adults but it is also common in children. Pediatric gastro esophageal reflux clinical practice guidelines have been issued by Vendenplas Y. A. compromise on the gastro esophageal reflux and gastro esophageal reflux disease’s diagnosis and treatment in the children are suggested that could be gainfully utilized for the diagnosis and treatment. These guidelines based on the literature search available evidence and bibliographies. This study reviews 600 plus articles. The evidence-based information provides guidelines for diagnosis and treatment of gastro esophageal reflux and gastro esophageal reflux disease in the children (Vindelplas and Rudolph, 2009). The patients having gastro esophageal reflux disease under the age of 12 years do not have heart bun while they have the symptoms of swallow difficulty, asthma and dry cough (NDDIC, 2007). Jiang and co-workers reported an analysis on the role of proximal gastric acid reflux in causation of respiratory symptoms in children with gastro esophageal reflux. The correlation of gastric reflux and respiratory diseases is known but the mechanism of the two bringing the reflux activity is not clear. A 24-hour esophageal pH monitoring of proximal and distal esophagus was



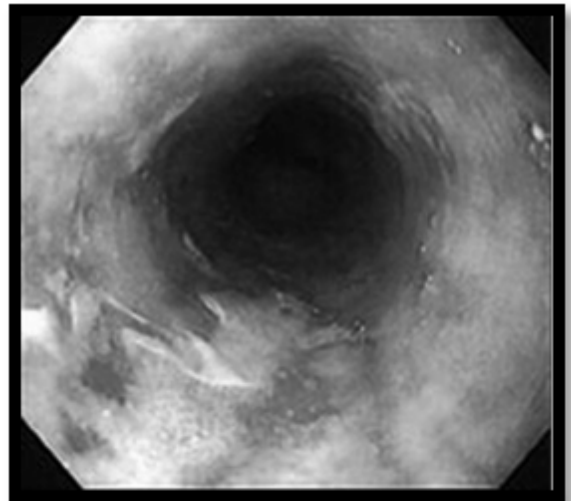
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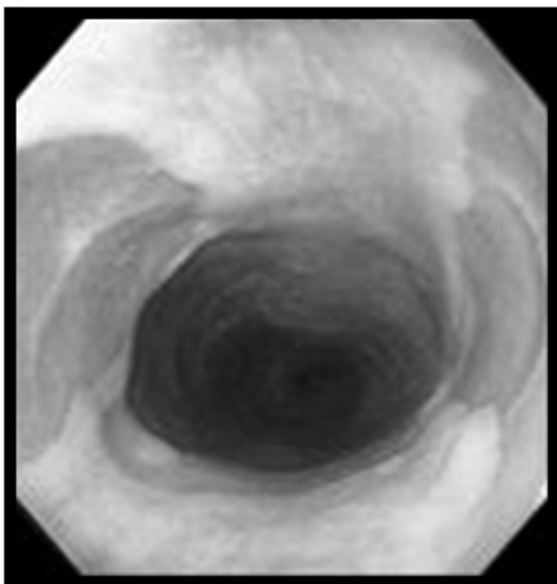
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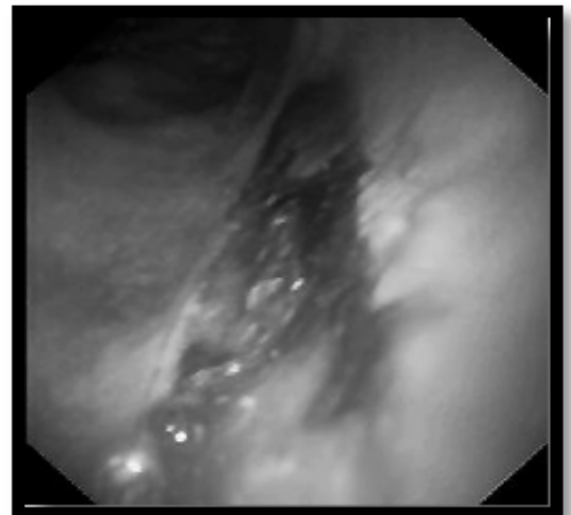
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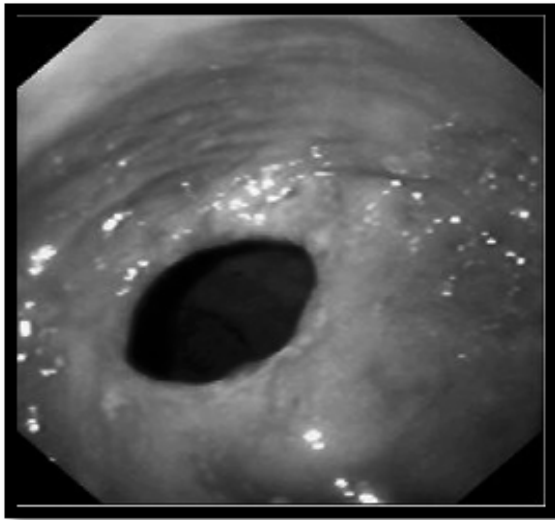


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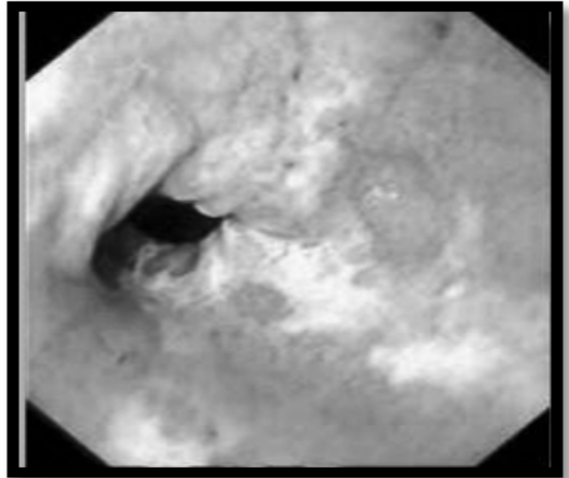


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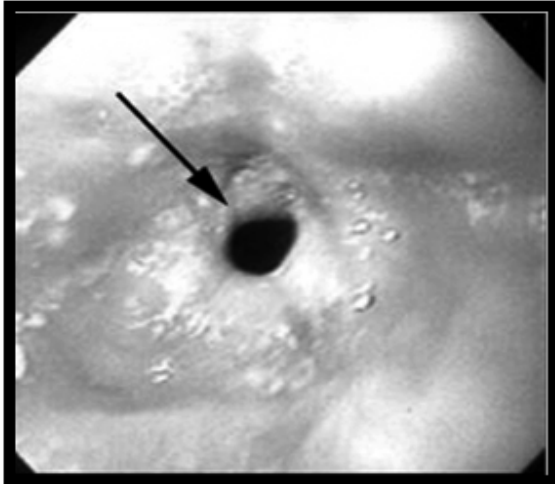




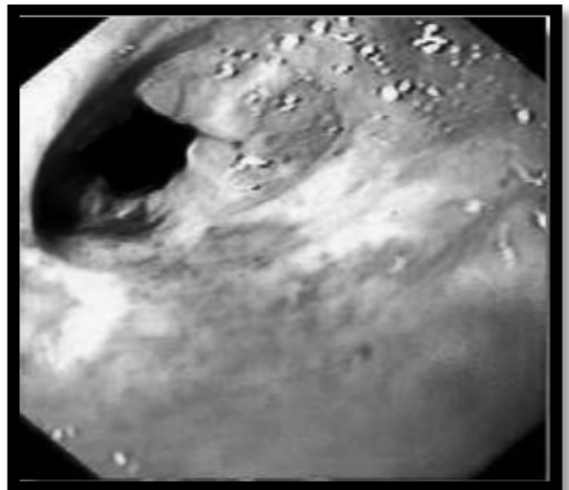
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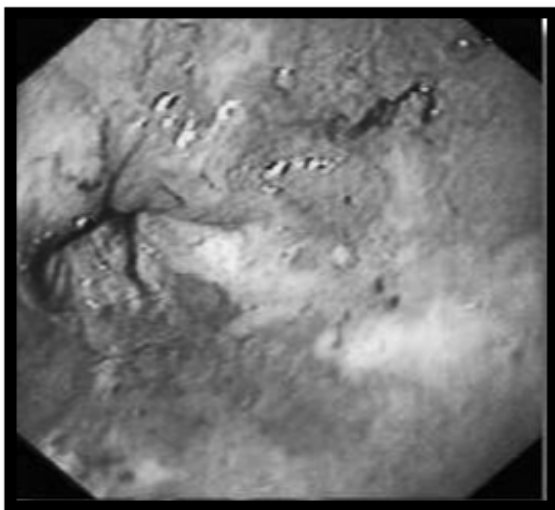
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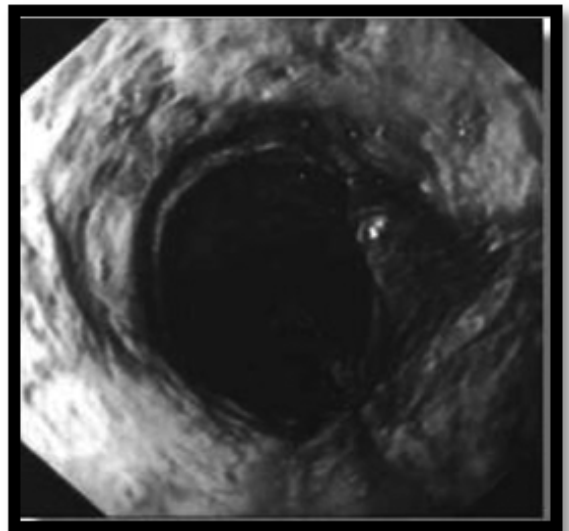
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5k.



5i.



5l.

Figure 5 (a-l). Different Stages of Gastro Esophageal Reflux Disease

observed in 23 and 31 children having gastric reflux with or without respiratory problems to find the onset. No significant differences in pH factors noted either in the proximal or distal esophagus in patients with gastric reflux without breathing. The proportion of patients with proximal gastric reflux in patients with respiratory symptoms was same from those without respiratory symptoms. Ultimately the proximal esophageal acid reflux has no role in the increase or decrease of persistent respiratory symptoms in children. The distal esophageal acid reflux is the predominant form of reflux in children with gastric reflux irrespective of the frequency of respiratory symptoms and dependent on its own systemic disorders (Jiang *et al.*, 2007).

Reflux patient's studies shows that the gastro esophageal reflux disease and age, both are the factors that have their effect on esophageal motility. The rate of peristaltic wave amplitude is significantly low as compared to non-gastro esophageal reflux disease patients and the ratio mimics in the old and young age. While Dantas and associates supports esophageal wave amplitude progressive reduction but denies the age factor (Gutscham *et al.*, 2011). Jayadevappa and associates analyzed the gastro esophageal acid-related disease, co-morbidity and medical care cost a retrospective cohort research which was carried out on six hundred patients with gastro esophageal reflux disease were randomly assigned and 600 patients without gastro esophageal reflux disease were assigned for age, gender, drug efficacy. The demographics, medical health care was assessed from organization for 3 years demographically were compared between gastro esophageal reflux disease and non gastro esophageal reflux disease group. Random coefficient log linear regression models analyzed vis a vis costs and to determine its relationship with all type diagnoses. Gastro esophageal reflux disease is a chronic disease that is mixed with forms of disorders and diagnoses that significantly treatment is low costs is high without gastro esophageal reflux disease. Therefore in ultimate analysis new disease in the diseases with gastro esophageal reflux will cost more in health care (Jayaddevappa and Chhatre, 2008)

Pereira has given detail account for the regression of gastro esophageal reflux disease symptoms using dietary supplement with melatonin, vitamins and amino acids and compared with *OMEPRAZOLE* "gastro esophageal reflux disease is increasing in communities". Gastro esophageal exhibits symptoms of regurgitation, heartburn, cough, hoarseness, dysphagia, or chest pain. The study was conducted to find that dietary supplement containing vitamin B6, vitamin B12, melatonin, folic acid, L-tryptophan, betaine and methionine can help to increase energy and execute this malaise and compared with 20 mg of *OMEPRAZOLE*. Melatonin inhibits the secretion of gastric acid and synthesis of nitric oxide. However it is understood that nitric oxide significantly affect the relaxation of lower esophageal sphincter that is reflux in patients with gastro esophageal reflux disease. One randomized blind study was conducted in two groups, A- 176 patients that were treated as above, B- 175 treated with the dosage form of 20mg of *OMEPRAZOLE*. Symptoms were assessed, items and changes in severity of symptoms recorded. All patients in group A reported 100% worsening of symptoms after 40 days of treatment. On the other hand, 115 persons reported 65.7% worsening symptoms *OMEPRAZOLE*. The significant difference between groups supports the withdrawal symptoms of gastro esophageal reflux disease and no side effects (Pereira, 2006). Dettmar *et al* gave a detail account on reflux and its consequences the laryngeal, pulmonary and esophageal manifestations, 30% of adult population is affected by the gastro esophageal reflux disease. The classical esophageal symptoms such as heartburn and acid reflux often overlap with atypical symptoms that affect the respiratory tract which is termed as non-esophageal reflux disease or laryngopharyngeal reflux that appears chronic cough, laryngitis, hoarseness, voice disorders and asthma manifestations. The clinical and non-clinical performa was preferred to find out the above mentioned condition. The refluxate of components such as acid, pepsin, bile acid and nonacid reflux, resulting from tissue damage and protection of the esophagus and laryngopharynx airways were analyzed. Clinical symptoms of reflux, the cause, including asthma, chronic cough, respiratory disease,

were examined at length. In addition to strategies for diagnosis and treatment of gastro esophageal reflux disease thereafter finding the results of non-acid reflux were proposed to be rendered as inclusion criteria (Dettmar *et al.*, 2011).

### SYMPTOMATOLOGY

After reviewing the research articles and consulting books the symptoms that may be developed in gastro esophageal reflux disease are as follows; Heart burn, chest pain, epigastric pain, acidic feeling in the mouth, regurgitation, sore throat, hoarseness of voice, wakeup during sleep, restless sleep, fatigue, decreased appetite, stress, discouragement, anorexia, unnecessary anxiousness, frustration and irritation lump in throat, swallow difficulty, vomiting, pain on swallowing, flatulence, belching/burping, nausea, tenesmus, constipation/diarrhea, general weakness (Zeneca and Molandal, 2005) cough, laryngitis (Dettmar *et al.*, 2011). Increase in appetite, dyspepsia, breathlessness, taste usually goes bitter but there may be possibility of tastelessness also, dry mouth (Ahmed), palpitation, abdominal cramps, abdominal pain, peripheral numbness, hematemesis, melena, dizziness (Kabiruddin).

### CAUSES OF GASTRO ESOPHAGEAL REFLUX DISEASE

Gastro esophageal reflux disease can be caused by the prolonged use of the following foods;

- Ø Spicy and fast food
- Ø Fried and heavy fat containing food
- Ø Betel nut, Pan, Gutca, Snuff
- Ø Alcoholic Drinks
- Ø Chocolate
- Ø Coffee, Tea, Cola
- Ø Tomato, Orange Juice (high acidic contents)
- Ø Peppermint, Onion, Garlic
- Ø Hot in temperature and cold food simultaneously
- Ø Over eating

Along with these foods the following risk factors are also involved in the development of the gastro esophageal reflux disease this has been elaborated in Figure 7 (Lafullarde *et al.*, 2001),

- Ø Self medication and excess medication like antidepressants, NSAIDs, Corticosteroids, Calcium Channel Blockers
- Ø Obesity and excess of abdominal fats
- Ø Age over 50 years
- Ø Smoking
- Ø Pregnancy
- Ø Asthma



Figure 6. Foods That Cause Gastro Esophageal Reflux Disease



**Figure 7.** Risk Factors of the Gastro Esophageal Reflux Disease

Gastro esophageal reflux disease may be developed through following basic ways;

1. Prolonged contact of gastric juice with esophageal epithelium
2. Unusual damage of esophageal epithelium with acidic contents
3. Frequent use of anti-acids and overflow of the stomach

The lower esophageal sphincter remain relax in gastro esophageal reflux disease and the gastric material invade in the esophagus while the esophagus functions properly. Hiatus hernia, an anatomical abnormality of stomach may develop gastro esophageal reflux disease. Normally the muscular sheet of diaphragm generates pressure to close lower esophageal sphincter. In case of hiatus hernia, the supporting pressure decreases or may be lost, such conditions provide ease to reflux. Hiatus hernia may be developed in any age but it is common in the age group of more than fifty years (NDDIC, 2007). The therapy for gastro esophageal reflux disease follows the continuous medication. When the medication stops the reflux relapse and its ratio goes up to 90%. medication along with lifestyle changes bring up the results more than three fourth of the patients. The patients that do not tolerate medicine and fed up with long term medication goes for surgery. Frequently used surgical procedure is called Laproscopic Nissen Fundoplication. The response rate is very encouraging in 5 year follow up i.e. 90%of the cases (Lafullarde *et al.*, 2001).

### **PATHOLOGY**

There may or may not be any pathology involved

in the gastro esophageal reflux disease. The major pathology we are studying here in this study is *Helicobacter pylori* (*H. pylori*). The easiest route of induction of the *H. pylori* infection is;

- Oral to oral
- Fecal to oral

### **HISTORY OF *HELICOBACTER PYLORI***

*Helicobacter pylori* is also known as *H. pylori*. It was firstly detected by the Bany Marshal and J. Robin Warren. They found an organism in the culture of the gastric biopsy tissues in 1982 and name it *Campylobacter pylori*. Its rate of infection, portal of exit and no animal reservoir has been found yet (Jacquelyn, 2005).

### **MECHANISM OF *HELICOBACTER PYLORI***

*H. pylori* have highest ability of genetic diversity than other human pathogens. It is due to the genetic strain differences. So, its role in different type of stomach cancer is 89%. It is a bacteria that survives in the acidic environment of the stomach. It happens due to a specific quality that it utilizes uric acid and produces ammonia, which neutralizes the acidity and provides suitable environment for survival and reproduction around the bacterial cells. They colonize directly above the epithelial layre of the stomach and penetrate into it. Their growth rate is slower in the laboratory culture due to the microaerophilic conditions. Identification markers for *H. pylori* is directly from gastric biopsies, for the evaluation of the enzyme urease and culturing specimens an special media, serologically specific antibody against *H. pylori* test is used for identification (Jacquelyn, 2005). In a susceptible host, *H. pylori* determine



chronic active gastritis that may lead, in turn, to duodenal and gastric ulcer disease, gastric cancer, and maltomas. *H. pylori* infection causes chronic active gastritis, which is characterized by a striking infiltrate of the gastric epithelium and the underlying lamina propria by neutrophils, T and B lymphocytes, macrophages, and mast cells. Mast cells, usually responsible for the immune response balance, may be important effectors cells in the pathogenesis of gastritis. However, *H. pylori* do not seem to invade the gastric mucosa, although evidence suggests that the mucus creates a niche wherein the germ is protected from gastric secretions (Santacroce and Bhuttani, 2011).

### PATHOGENESIS

Marshall *et al.* first of all cultured *Helicobacter pylori* in 1982 from gastric biopsy tissues and name it *Campylobacter pylori*. It survives in the highly acidic environment of the stomach because it develops ammonia around it from the uric acid that neutralizes the acidity around the bacterial cells and carried out the survival and reproduction by providing suitable environment. They colonize direct above the epithelial layer of the stomach and penetrate into it. During culture in laboratory their growth is slow because of the requirement of the microaerophilic conditions and an enriched medium. *H. pylori* have highest ability of genetic diversity than most of the other human pathogens because of its strain differences. So, its role is 89% indifferent types of the stomach cancers. No animal reservoir has been found yet (Strapoli, 2010).

*H. pylori* invade the body through food, fluids and contaminated utensils. Its Identification marker is directly from gastric biopsies for the evaluation of enzyme Urease and culturing specimens on special media. A sophisticated urea breath test is used to measure the quantity of the carbon dioxide developed in the stomach after oral presentation of urea. Serologically specific protein antibody test against *H. pylori* is used for identification. The final and the easiest approach that provides the accurate results is fecal antigen test (Zarling, 1998). The therapy for gastro esophageal reflux disease follows the continuous medication. When the medication stops

the reflux relapse and its ratio goes up to 90%. Medication along with lifestyle changes bring up the results more than three fourth of the patients. The patients that do not tolerate medicine and fed up with long term medication goes for surgery. Frequently used surgical procedure is called Laproscopic Nissen Fundoplication that shows very encouraging response rate in 5 year follow up i.e. 90% (Lafullarde *et al.*, 2001).

### CLINICAL PRESENTATION

Commonly the reflux may be found in any age, but it affects mostly the age group of 20 to 50 years. Male and females are equally victimized, and both are hospitalized. But in men the endoscopic findings of esophageal damage are two to three fold more than females of China and West (Kay *et al.*, 1994; Chang *et al.*, 1997; Liker *et al.*, 2005; Galmiche *et al.*, 2006). Esophageal reflux has basic symptoms of epigastric pain that starts after one hour eating and may lasts up to two hours, aggravates with the spicy food, citrus food, tomato, onion and alcohol etc. It starts with heartburn, refers to epigastric pain along with regurgitation. If it happens during sleep the symptoms of hyper salivation and bitter taste are also found (Zarling, 1998).

Galmiche and coworkers have reported that functional esophageal disorders of the esophagus are associated with esophageal symptoms such as heartburn, chest pain, dysphagia, a globe. These could not view from the perspective of structural disorders, movement disorders based on histopathology or gastro esophageal reflux. Gastro esophageal reflux is taken into account of the diagnosis of reflux esophagitis or esophageal acid exposure there, episodes of acid reflux or respond to anti reflux treatment. Management methods that modulate the central symptom (perception, noxious stimuli) of the esophagus were excluded. All this has resulted in the understanding of the symptoms, the new strategies and give a way to diagnosis and treatment (Zhang *et al.*, 1996).

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