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Correlation of Endoscopic Severity of Erosive Gastroesophageal Reflux Disease (GERD) with Body Mass Index (BMI)

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Abstract: **Background:** Gastro esophageal reflux disease (GERD) is aspectrum of disease with classic symptoms of heart burn and acid regurgitation, at one end, without any evidence of esophageal mucosal injury and erosive esophagitis, complications of Barrett's esophagus and esophageal adenocarcinoma at other end. Obesity is widely regarded as a pandemic with potentially disastrous consequences for human health. To date, many studies have reported on the association of obesity with gastro esophageal reflux disease (GERD), In light of this, we conducted this study to examine the association of obesity and erosive GERD. **Objective:** to assess the correlation of endoscopic severity of erosive gastro esophageal reflux disease (GERD) with body mass index (BMI).**Design:** cross sectional analytic study. **Place and duration of study:** Baghdad teaching hospital/Baghdad from April 2010 to February 2011. **Patient and method:** 100 untreated Patients with erosive GERD, on endoscopic examination, had been presented with typical symptom of GERD (heart burn and acid regurgitation). Classification of erosive GERD severity had been done according to Savary-Miller classification system. Body mass index (BMI) was calculated as body weight in kilogram (KG) divided by square of the body height in meter (m2). Patients were analyzed by using (SPSS.17) soft ware. Statistical evaluation using Spearman correlation coefficient (r) test (which measures how well the relationship between two variables can be described by a monotonic function). P value <0.05 statistically significant. **Results:** The mean BMI of patient's group who had grade 1 GERD (48 patients) was 25.09 kg/m2 ± 4.248 SD , and of those with grade 2 GERD (36 patients) BMI was 34.45 kg/m2 ± 4.665 SD , while those with grade 3 GERD (14 patients) BMI was 38.55 kg/m2 ± 4.245 SD and finally of those with grade 4 GERD (2 patients) BMI was 40.55 kg/m2 ± 4.879 SD, with significant statistical P value 0.000 measured by spearman correlation coefficient (r) test. This finding suggest that obesity and increased BMI is a risk factor for more serious mucosal lesion in the esophagus and will increase possibilities of complication of higher grade of GERD. **Conclusion:** Higher body mass index (BMI) seems to be associated with higher degree of endoscopic erosive GERD severity.

Keywords: GERD, BMI, Endoscopic.

INTRODUCTION

Gastroesophageal reflux disease (GERD) is a consequence of the failure of the normal anti reflux barrier to protect against frequent and abnormal amounts of gastroesophageal reflux (Richter, J. E. *et al*., 2010). A guideline issued by the American College of Gastroenterology defines GERD as symptoms or mucosal damage produced by the abnormal reflux of gastric contents into the esophagus (DeVault, K.R. *et al*., 2005). Another consensus statement (the Montreal Classification) defines GERD as "a condition that develops when the reflux of stomach contents causes troublesome symptoms and/or complications" (Vakil, N. *et al*., 2006). GER (gastroeosophagealreflux) itself is not a disease but rather a normal physiologic process. It occurs multiple times each day, especially after large meals, without producing symptoms or mucosal damage. In contrast, GERD is a spectrum of disease usually producing symptoms of heartburn and acid regurgitation. Most patients with GERD have no visible mucosal damage at the time of endoscopy (non erosive GERD), whereas others have esophagitis, peptic strictures, or Barrett's esophagus (Richter, J. E. *et al*., 2010).

Epidemiology:- GERD is one of the most common diseases in the western world based on the prevalence of heartburn. In the United States, about 45% of adults have heartburn at least once a month, about 20% once a week, and about 10% daily. Heartburn affects men two- to threefold more often than it affects women and is more common in whites than blacks. Although GERD rarely causes death, it reduces quality of life and has a morbidity rate of 10 to 15% secondary to ulceration, bleeding, stricture, Barrett's esophagus, and adenocarcinoma (Orlando, R. C, 2008).

Pathogenesis:- Abnormalities of anti reflux barrier ,hiatal hernia, esophageal acid clearance and gastric factors such as acid volume and emptying all play a role in the pathogenesis of GERD .multiple abnormalities are often present in the same patient (Freston, J. W, 2001). **Anti reflux barriers**, is an anatomically complex region including the intrinsic lower esophageal sphincter (LES), diaphragmatic crura, the intra-abdominal location of the LES, the phrenoesophageal ligaments, and the acute angle of His (1). As shown in figure (1) .

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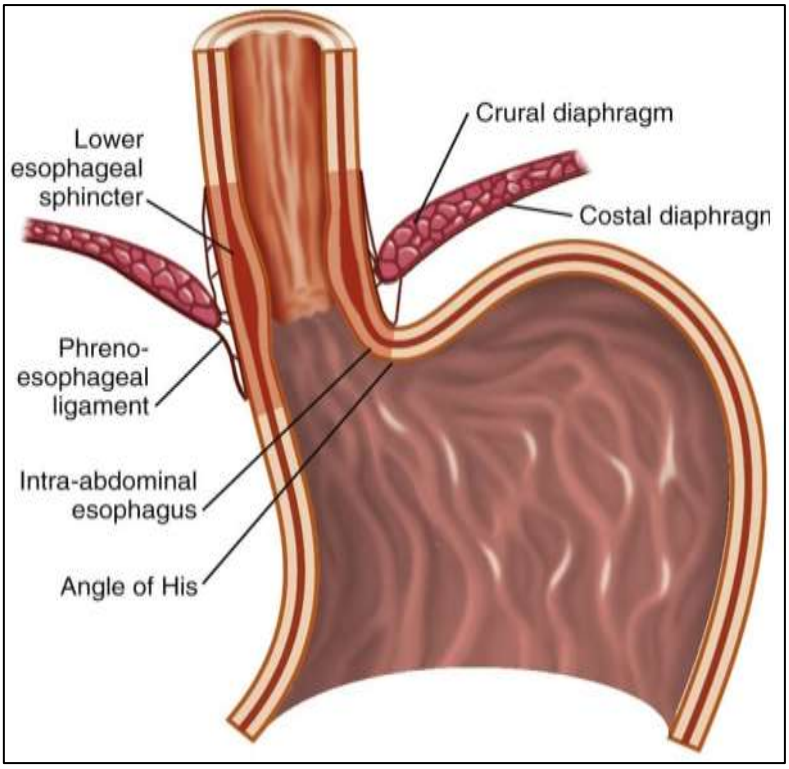

Figure (1): Anatomy of the gastroesophageal junction illustrating the major elements of the anti reflux barrier (Richter, J. E. *et al*., 2010).

Esophageal acid clearance: This phenomenon involves two related but separate processes: *volume clearance*, which is the actual removal of the reflux material from the esophagus by peristalsis, and *acid clearance*, which is the restoration of normal esophageal pH following acid exposure through titration with base from saliva and esophageal gland secretions. Although the competency of the antireflux barrier determines the frequency and volume of GER, esophageal acid clearance determines the duration of acid exposure to the mucosa and probably the severity of mucosal damage (Richter, J. E. *et al*., 2010).

Hiatus hernia causes reflux because the pressure gradient between the abdominal and thoracic cavities, which normally pinches the hiatus, is lost. In addition, the oblique angle between the cardia and oesophagus disappears. Many patients who have large hiatus hernias develop reflux symptoms, but the relationship between the presence of a hernia and symptoms is poor. Hiatus hernia is very common in individuals who have no symptoms, and some symptomatic Patients have only a very small or no hernia. Nevertheless, almost all patients who develop oesophagitis, Barrett's oesophagus or peptic strictures have a hiatus hernia(Palmer, K. R. *et al*., 2010).

Gastric factors (volume and components of the gastric refluxate) are potentially important in the production of reflux esophagitis**.** *Gastric acid screation* clinical series find that the degree of esophageal injury, from non erosive GERD to Barrett's esophagus, parallels the increase in the frequency and duration of acid reflux with a pH of less than 4. *Delayed Gastric Emptying* The importance of delayed gastric emptying in pathogenesis of GERD is controversial, recent investigations found only a 6% to 38% incidence of delayed gastric emptying of reflux patients, regardless of the severity of the esophagitis Nevertheless, delayed gastric emptying is a major factor contributing GERD in some groups such as diabetic patients with autonomic peripheral neuropathy (Richter, J. E. *et al*., 2010).

Clinical feature:-

Heartburn is typically described as a burning sensation in the retrosternal area (behind the breastbone) (3). **Regurgitation** is defined as the perception of flow of refluxed gastric content into the mouth or hypopharynx (3). **Dysphagia** is defined as difficulty in swallowing wich is common in the setting of long-standing heartburn and, in patients with erosive esophagitis, can resolve following treatment with a proton pump inhibitor (Vakil, N. B . *et al*., 2004) .**GERD-related chest pain** may mimic angina pectoris,

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and is typically described as squeezing or burning, located substernally and radiating to the back, neck, jaw, or arms, lasting anywhere from minutes to hours, and resolving either spontaneously or with antacids. It usually occurs after meals, awakens patients from sleep, and may be exacerbated by emotional stress (Richter, E, 1996) .**Water brash** or (hypersalivation) is a relatively unusual symptom in which patients can foam at the mouth, secreting as much as 10 mL of saliva per minute in response to reflux .**Globus sensation** is the almost constant perception of a lump in the throat (irrespective of swallowing), which has been related to GERD in some studies. However, the role of esophageal reflux in this disorder is uncertain. One study suggested that globus was associated with a hypertensive upper esophageal sphincter rather than with reflux (Corso, M. J. *et al*., 1998). **Odynophagia (painful swallowing)** is an unusual symptom of GERD but, when present, usually indicates an esophageal ulcer .**Nausea** is infrequently reported with GERD but may be a consideration in patients with otherwise unexplained symptoms. In one report, nausea resolved after therapy for GERD in 10 patients who previously had intractable symptoms (Brzana, R. J. *et al*., 1997) .**Extraesophageal manifestations** of GERD are due to reflux of gastric contents into the pharynx, larynx, trachea bronchial tree, nose, and mouth. It may cause chronic cough, laryngitis, and pharyngitis. Morning hoarseness may be noted. Recurrent pulmonary aspiration may cause or aggravate chronic bronchitis, asthma, pulmonary fibrosis, chronic obstructive pulmonary disease, or pneumonia. Chronic sinusitis and dental decay have also been ascribed to GERD (Goyal, R. K, 2008).

Differential Diagnosis:-
Symptoms associated with GERD may be mimicked by other esophageal and extra esophageal diseases including achalasia, Zenker's diverticulum, gastro paresis, gallstones, peptic ulcer disease, functional dyspepsia, and angina pectoris. These disorders usually can be identified by failure to respond to aggressive proton pump inhibitor (PPI) therapy and appropriate diagnostic tests. Although GERD is the most common cause of esophagitis, other etiologies (pills, infections, or radiation esophagitis) need to be considered in difficult-to-manage cases, older individuals, or immune compromised patient (Richter, J. E. *et al*., 2010).

Associated factors:- Several medical and surgical factors associated with GERD.The most common factors shown in table (1) .

Table (1): factors associated with GERD (12).

Pregnancy or obesity
Fat ,chocolate ,coffee or alcohol ingestion
Large meals
Cigarette smoking
Drugs-anti muscarinic ,calcium channel blockers ,nitrate
Systemic sclerosis
After treatment of achalasia
Hiatus hernia

Diagnostic Evaluation:- The diagnosis can be made by history alone in many cases. A therapeutic trial with a PPI such as omeprazole, 40 mg twice/day for 1 week, provides support for the diagnosis of GERD. Diagnostic studies are indicated in patients with persistent symptoms or symptoms in spite of therapy, or in those with complications. The diagnostic approach to GERD can be divided into three categories:

(1) Documentation of mucosal injury.
(2) Documentation and quantitation of reflux.
(3) Definition of the pathophysiology (Goyal, R. K, 2008) .

1. *Documentation of Mucosal Injury:* Mucosal damage is documented by the use of barium swallow, esophagoscopy, and mucosal biopsy**.** *Barium swallow* is usually normal but may reveal an ulcer or a stricture. A high esophageal peptic stricture, a deep ulcer, or adenocarcinoma suggests Barrett's esophagus. *esophagoscopy* May reveal the presence of erosions, ulcers, peptic strictures, or Barrett's metaplasia with or without ulcer, peptic stricture, or adenocarcinoma.(Goyal, R. K, 2008). Multiple classification systems for esophagitis have been proposed; some are confusing and none has worldwide acceptance. In Europe the most popular scheme is the Savary-Miller classification. The most thoroughly

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evaluated esophagitis classification is the Los Angeles system, which is gaining acceptance in the United States and Europe (Richter, J. E. *et al*., 2010). The two were described in table (2).

Table (2): Endoscopic Grading Systems for Esophagitis (Richter, J. E. *et al*., 2010).

Savary-Miller Classification	
Grade 0	Not applicable
Grade I	Single, erosive, or exudative lesion on one longitudinal fold
Grade II	Multiple erosions on more than one longitudinal fold
Grade III	Circumferential erosions
Grade IV	Ulcer, stricture, or short esophagus, isolated or associated with grades I through III
Grade V	Barrett's esophagus ? grades I through III
Los Angeles Classification	
Grade A	One or more mucosal breaks confined to folds, ≤5 mm
Grade B	One or more mucosal breaks >5 mm confined to folds but not continuous between tops of mucosal folds
Grade C	Mucosal breaks continuous between tops of two or more mucosal folds but not circumferential
Grade D	Circumferential mucosal break

Esophagoscopy is not diagnostic of GERD; it is normal in non erosive reflux disease(NERD) , which constitutes one-third to one-half of all cases of GERD (Goyal, R. K, 2008). *Mucosal biopsies and the Bernstein test* may be helpful in the diagnosis of NERD. Mucosal biopsies may show early changes of esophagitis, including dilation of intracellular spaces. The mucosal biopsies should be performed at least 5 cm above the LES, as the esophageal mucosal changes of chronic esophagitis are quite frequent in the most distal esophagus in otherwise normal individuals. The Bernstein test involves the infusion of solutions of 0.1 *N* HCl or normal saline into the esophagus. In patients with symptomatic esophagitis, infusion of acid, but not of saline, reproduces the symptoms of heartburn. Infusion of acid in normal individuals usually produces no symptoms. Supra esophageal manifestations are documented by careful otolaryngologic and pulmonary examination (Goyal, R. K, 2008).

2. *Documentation and Quantitation of Reflux:* Documentation and quantitation of reflux when necessary , can be done by ambulatory long-term (24–48 h) esophageal pH recording. Long-term pH recording may be performed using a pH-sensitive capsule (BRAVO) that is anchored into the esophageal mucosa via an endoscope, rather than the traditional nasally placed pH probe. For evaluation of pharyngeal reflux, a system of recording simultaneously from pharyngeal and esophageal sites may be useful. The pH recordings are helpful only in the evaluation of acid reflux. Endoscopic esophagitis does not correlate with gastroesophageal reflux. Documentation of reflux is necessary only when the role of reflux in the symptom complex is unclear, particularly in evaluation of supra esophageal symptoms, in cases with NERD, and in cases with non cardiac chest pain. Reflux of nonacid contents may be responsible for symptoms of regurgitation and extraesophageal manifestations of GERD. Reflux of nonacid contents can be documented by the use of an impedance test (Goyal, R. K, 2008).

3. *Determination of pathophysiologic factors:* Determination of pathophysiological factor in GERD is sometimes indicated for management decisions such as anti reflux surgery (Goyal, R. K, 2008). Esophageal manometry allows assessment of LES pressure and relaxation, as well as peristaltic activity, including contraction amplitude, duration, and velocity. However, esophageal manometry is generally not indicated in the evaluation of the uncomplicated GERD patient because most have a normal resting LES pressure (Dent, J. *et al*., 1998) .

Complications:-

Hemorrhage, ulcers, and perforation

GERD-related non-cancer deaths are rare (0.46 per 100,000 persons). The most common fatal causes are hemorrhagic esophagitis, aspiration pneumonia, ulcer perforation, and rupture with severe esophagitis, Clinically important hemorrhage has been reported in 7% to 18% of GERD patients and may result in iron deficiency anemia(Richter, J. E. *et al.,* 2010).

Peptic esophageal strictures

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Strictures occur in 7% to 23% of patients with untreated reflux esophagitis, and are especially seen in older men. They may be linked to chronic nonsteroidal anti-inflammatory drug (NSAID) use (Richter, J. E. *et al.,* 2010) .

Barrett's Esophagus

Barrett's esophagus is replacement of reflux-damaged squamous epithelium in the distal part of the esophagus by metaplastic, specialized columnar epithelium. It is found in 10 to 15% of patients with GERD, principally in white individuals. Barrett's metaplasia is more acid resistant than squamous epithelium and produces no symptoms. Barrett's metaplasia is a premalignant lesion that increases the risk for esophageal adenocarcinoma 30- to 125-fold over that of the general population. Factors that increase the risk for malignancy in Barrett's esophagus include white race, male sex, alcohol and tobacco use, obesity, and its length (4) .

Treatment:-Treatment of GERD is primarily medical, the mainstays being lifestyle modifications (Table3) and drug therapy.

Table (3): Life style modifications for reflux esophagitis (4) .

Elevate the head of the bed 6 inches
Stop smoking
Stop excessive alcohol consumption
Reduce dietary fat
Reduce meal size
Avoid bedtime snacks
Lose weight (if overweight)
Avoid chocolate, carminatives (spearmint, peppermint), coffee (caffeinated and decaffeinated), tea, cola beverages, tomato juice, citrus fruit juices
Avoid, when possible, anticholinergics, theophylline, diazepam, narcotics, calcium-channel blockers) ,beta adrenergic agonist (isoproterenol), alpha adrenergic antagonist (phentolamine) ,progesterone

The goals of treatment are to relieve symptoms and prevent relapse and complications. All patients should be advised about lifestyle modifications that help reduce symptoms and prevent relapse. Antacids or antacid-alginate combinations are recommended for safe, prompt, inexpensive relief of heartburn. The same agents, however, are poorly suited for regular use because of poor palatability and durability and side effects such as diarrhea, constipation, and possible magnesium or aluminum toxicity in renal patients. Protection against recurrence of heartburn is provided by acid-suppressing medications such as H_2-receptor antagonists and PPIs. H_2-receptor antagonists reduce gastric acid secretion moderately by inhibiting one of three acid-stimulating receptors on the basolateral membrane of the parietal cell. When prescribed twice a day, they can control symptoms in about 50% of GERD patients and heal erosions in about 30%. PPIs irreversibly inhibit the H^+, K^+-ATPase or proton pump, the final common pathway for acid secretion on the apical membrane of the parietal cell. Consequently, PPIs markedly reduce gastric acidity with once-a-day dosing and provide relief of symptoms and healing of lesions in about 80 to 90% of GERD patients. H_2-receptor antagonists (>30 years) and PPIs (≈15 years) have excellent safety profiles. PPI safety beyond 15 years remains unclear because of uncertainty about the long-term risk for chronic gastric hypoacidity and hypergastrinemia. Although vitamin B_{12} levels can be reduced with chronic PPI use, clinically significant vitamin B_{12} deficiency has not been reported, so an increase in vitamin B_{12} intake is not currently recommended.Early endoscopy is indicated for those with alarm symptoms. Endoscopy is also indicated for patients who fail once-a-day PPI therapy to confirm the diagnosis and assess severity, including the presence of Barrett's esophagus (see later). Testing for H. pylori is not recommended because the organism is not etiologic in GERD and, when eradicated, may make treatment more difficult.Failures with once-a-day PPI therapy are treated with twice-daily PPI therapy with or without H_2-receptor antagonists at bedtime for 6 to 8 weeks, and patients who fail this regimen undergo esophageal pH monitoring during therapy to assess for control of esophageal acidity. If the acidity is controlled, the symptoms are not mediated by acid. Effective therapy is often accompanied by relapse when medication ceases, especially in patients with erosive esophagitis, in whom maintenance therapy is indicated. Patients requiring maintenance therapy should undergo at least one endoscopy procedure to determine whether Barrett's esophagus is present. If endoscopy reveals NERD, no further endoscopy is

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necessary and treatment is guided by symptoms. If endoscopy reveals erosive esophagitis, treatment to healing should be documented by endoscopy so that Barrett's esophagus can be effectively established or excluded. Once Barrett's esophagus is excluded, endoscopy is unnecessary and treatment is guided by symptoms because subsequent relapse and treatment will rarely result in Barrett's esophagus. (Orlando, R. C, 2008)

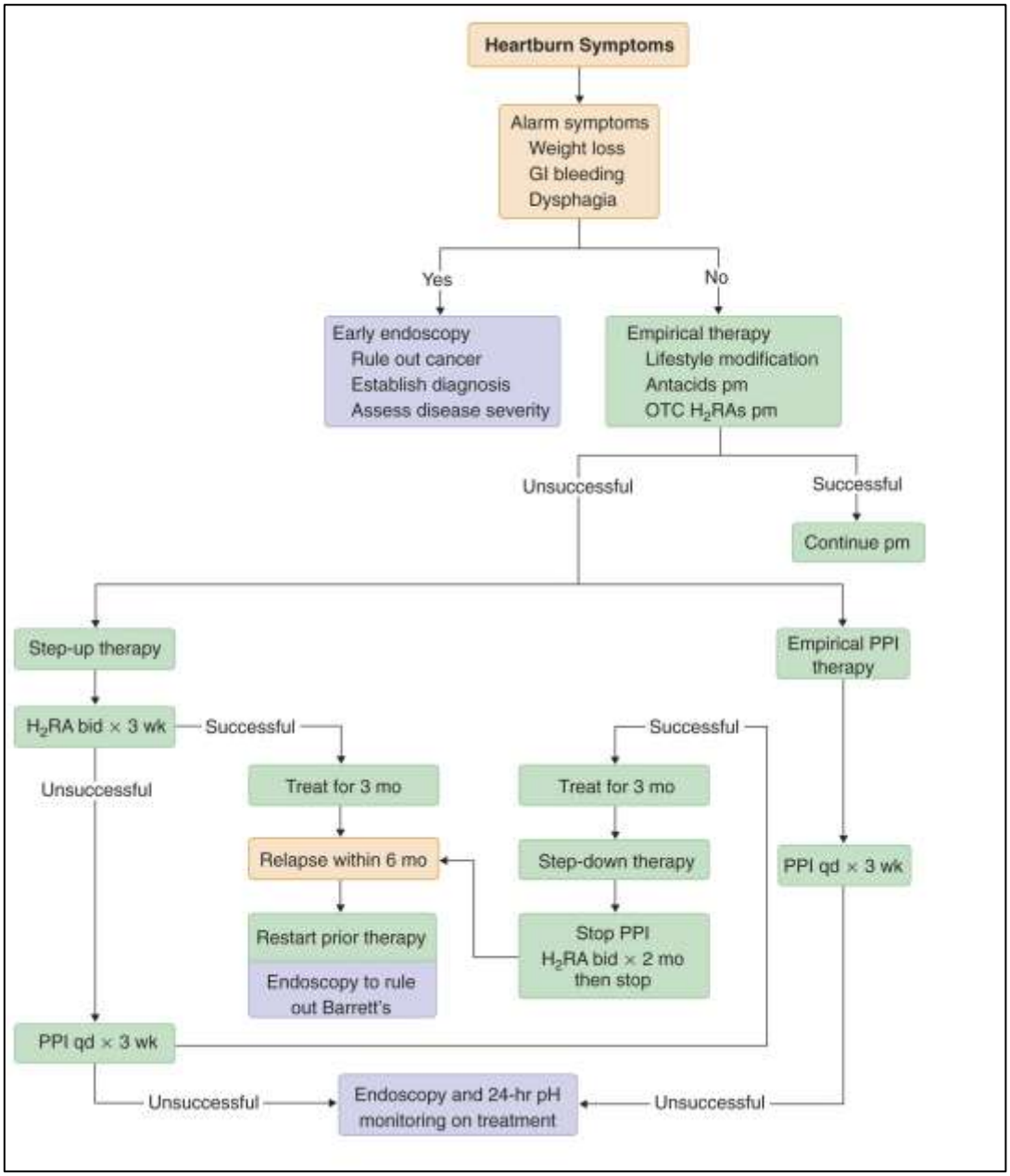

Figure (2): Algorithm for the management of a patient with heartburn. GI = gastrointestinal; OTC H_2RA = over-the-counter H_2-receptor antagonist; PPI = proton pump inhibitor; Rx = treatment (4) .

Antireflux surgery, in which the gastric fundus is wrapped around the esophagus (fundoplication), creates an antireflux barrier. The efficacy of the antireflux barrier depends on the type of surgery and experience of the operator. Open fundoplication has mostly been replaced by laparoscopic fundoplication, and endoscopic antireflux procedures are being vigorously tested. Laparoscopic or endoscopic antireflux procedures should be considered as alternatives in young patients who require long-term, high-dose PPIs. Ideal candidates for fundoplication are those who have classical GERD with good response to PPI therapy and in whom motility studies show poor LES pressures but normal peristaltic contractions in the esophageal body. Symptomatic GERD patients with low or no acid or alkaline (bile)

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reflux are also considered candidates for antireflux operations (Goyal, R. K, 2008).

Obesity:- Obesity is frequently considered to be a 'modern' disease—a reflection of the excesses of urbanized society. Hippocrates recognized that obesity posed a threat to health when he wrote that, 'sudden death is more common in those who are naturally fat than in the lean'. The recognition that obesity represents a serious medical disorder at a population level came with pooled life insurance data from the United States of America, showing that increasing degrees of overweight and obesity were important predictors of decreased longevity, much of which was attributed to cardiovascular disease. Obesity, defined as a BMI of more than 30 kg/m2, is a common condition in Europe and the United States of America. The precise measurement of body fat is quite challenging, and accurate methods are not applicable to large populations; therefore, surrogate markers such as the body mass index (BMI—weight in kilograms divided by the square of the height in metres) are most often used to define obesity in population studies and in the clinic (Farooqi, S, 2010). Body mass index (BMI) is now the recommended means to categorize weight relative to height for adults. BMI is calculated as weight (in kilograms)/height squared (in meters). To calculate BMI by pounds and inches, the formula is modified as follows: weight (pounds)/height (inches2) × 703. The weight classifications according to BMI are summarized in Table 4 below. Individuals who are overweight (BMI of 25.0 to 29.9) may or may not have excessive fat. Some men may be overweight because of increased muscle mass, which is a straightforward clinical judgment. Although in general the risk of developing weight-related health problems increases with a BMI above 25, the guidelines point out that intervention or discussion of weight issues with the patient may not be necessary for overweight adults who are entirely healthy or who are not over fat. On the other hand, some individuals in the BMI range of 27 to 29.9 develop serious metabolic complications of obesity that could be expected to improve with weight loss. These individuals are candidates for more aggressive treatment, including pharmacotherapy if it is needed. The risk of co morbidities increases considerably at BMIs above 30, the level at which an individual is defined as obese. Obesity is divided into three classes, also depending on BMI. Treatment approaches may differ for those who are overweight and for different classes of obesity.

Table (4): Classification of Overweight and Obesity by BMI (4).

	Obesity Class	**BMI (kg/m^2)**
Underweight		<18.5
Normal		18.5–24.9
Overweight		25.0–29.9
Obesity	I	30.0–34.9
Obesity	II	35.0–39.9
Extreme obesity	III	≥40

In addition to BMI, the National Heart, Lung, and Blood Institute guidelines recommend the waist circumferences as another office assessment tool that can help with the treatment decision-making process. A waist circumference of more than 102 cm or 40 inches for men and of more than 88 cm or 35 inches for women is an additional indication of risk for overweight and obesity (4).

Does Obesity Associated With Gastro Esophageal Reflux Disease?

The prevalence of obesity has reached epidemic proportions In the United States, 32% of the adult population is obese . Similarly, the prevalence of gastroesophageal reflux disease (GERD) has increased up to 20% in the western world . In addition, some studies have shown that GERD is highly prevalent in morbidly obese patients and that a high body mass index (BMI) is a risk factor for the development of GERD. The mechanism by which BMI affects esophageal acid exposure is not completely understood. It has been suggested that increased Intra gastric pressure, increased trans diaphragmatic gastroesophageal pressure gradient , incompetence of the lower esophageal sphincter (LES) , and increased frequency of transient LES relaxations , may all play a role in the pathophysiology of the disease in morbidly obese patients. To support the hypothesis that obesity increase esophageal acid exposure is the documented relation between increased BMI and the prevalence of GERD and its complications .Although many advances have been made in the understanding of the pathophysiology of GERD,

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many aspects of the pathophysiology of this disease in morbidly obese patients remain unclear. It has been suggested that the pathophysiology of GERD in morbidly obese patients might differ from that of non obese patients (Fisichella, P. M. *et al*., 2009).

How Does Obesity Increase The Risk of GERD? The precise pathophysiological link between obesity and GERD has not been fully elucidated. Individual studies have variably found reduced lower esophageal sphincter (LES) pressure, increased frequency of transient LES relaxations, increased prevalence of hiatal hernia ,an increased prevalence of esophageal motor disorders , and disorders of gastric accommodations in obese subjects. Elevated intragastric pressure in patients with central obesity has also been implicated as a contributing factor (Fig. 3) (Frank, K. *et al*., 2008).

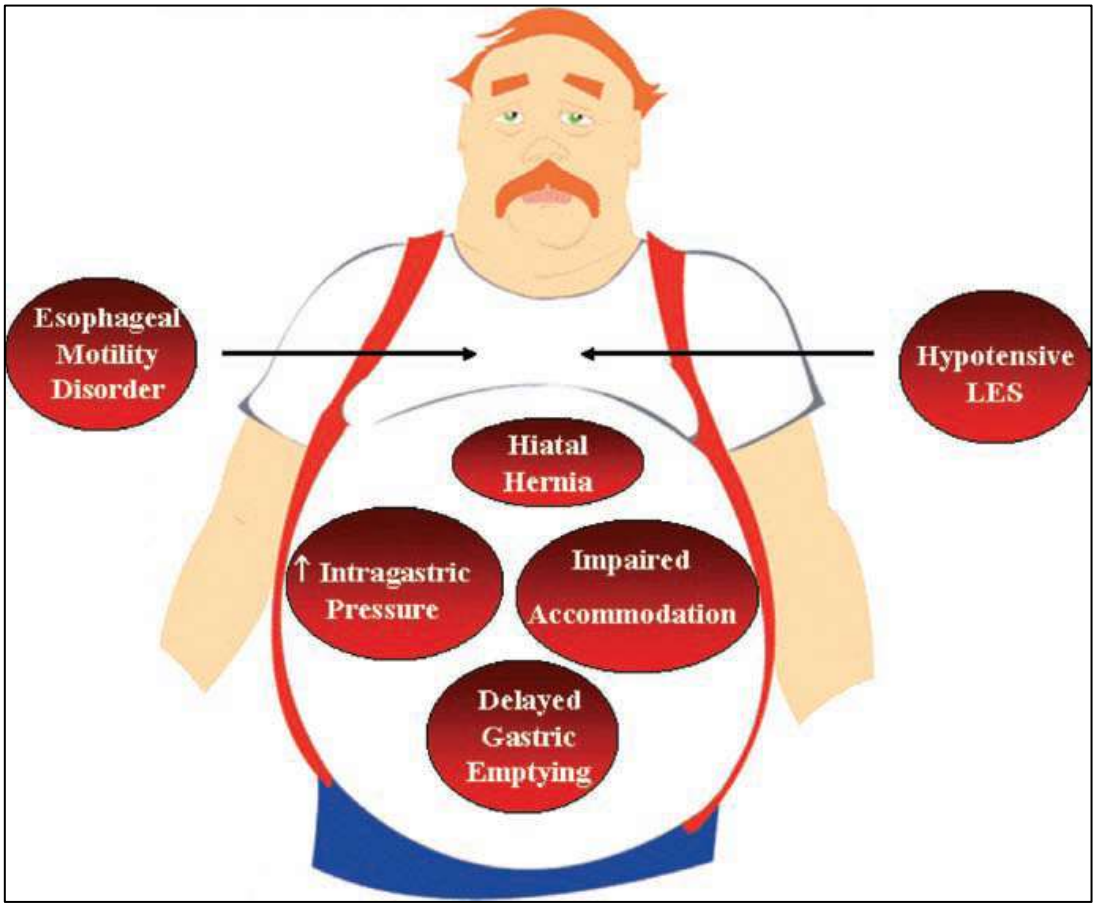

Figure (3): Proposed pathophysiological disturbances in obesity. (Frank, K. *et al*., 2008)

LES Abnormalities in Obesity

The LES is the major barrier against gastric reflux into the esophagus. Normal LES pressure is in the range of 10–35mmHg , A hypotensive LES (<10 mmHg) is a clear risk factor for the development of GERD and the correlation between BMI and LES pressure has been extensively investigated. One study assessed 43 morbidly obese patients for reflux symptoms, manometric abnormalities, and pH evidence of esophageal acid exposure . These patients were compared to 53 healthy control subjects. LES pressure was significantly lower in the obese group in comparison to the control group (11.9 ± 5.3 vs 15.9 ± 2.7 mmHg, respectively). In addition, the LES pressure of obese patients with GERD was significantly lower than obese patients with normal acid exposure (Frank, K. *et al*., 2008).

Transient Relaxations of the LES in Obesity:- Transient lower esophageal relaxations (TLESRs) are complete relaxations of the LES in the absence of swallowing . Several significant findings occurred during the postprandial period. First, overweight and obese individuals had a significantly higher rate of TLESRs during the 2-h period after meal ingestion. Second, the proportion of TLESRs accompanied by acid reflux and the total acid exposure times were significantly higher in obese and overweight subjects. A direct correlation between rising BMI, increased number of TLESRs, and an increased number of TLESRs

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associated with acid reflux was identified(Frank, K. *et al*., 2008).

Hiatal Hernia in Obesity:- Hiatal hernia is commonly associated with symptomatic GERD, and patients with abnormal esophageal acid exposure have a significantly higher prevalence of hiatal hernia . In a study by Suter *et al*., 181 of 345 (52.6%) morbidly obese patients selected for bariatric surgery were diagnosed with a hiatal hernia. In patients with a hiatal hernia, findings of either esophagitis (47.5% vs 15.8%) or abnormal low distal esophageal pH (7.4% vs 5.1%) were more common than in those without hiatal hernia (Frank, K. *et al*., 2008).

Esophageal Body Motor Abnormalities in Obesity:- Several studies have investigated esophageal motility abnormalities in morbidly obese patients, generally focusing on those seeking bariatric surgery. In the largest study, 85 of 345 (25.6%) patients had abnormal motility findings. The most common findings were nutcracker esophagus and nonspecific motility disorder (Frank, K. *et al*. *et al*., 2008).

Gastric Motor Abnormalities:- Several studies have investigated the role of gastric motor function in causing GERD symptoms. In a study of 31 obese patients referred for bariatric surgery and eight healthy volunteers, a barostat (highly compliant balloon) was used to measure proximal gastric compliance and tone .Nineteen of 31 obese patients had abnormal esophageal acid exposure, and these patients demonstrated a significantly higher prevalence of hiatal hernia (8 of 19 vs 1 of 12, P = 0.04). Minimal distending pressure (MDP, defined as the first pressure inducing an intra gastric volume >30 mL) was significantly higher in obese patients compared with lean healthy controls (11.8 ± 2.2 vs6.4 ± 3.0 mmHg; P < 0.001).The data with respect to gastric emptying in obese subjects is conflicting. Gastric emptying rate in obesity may be of importance because delayed gastric emptying in the setting of a filled, relatively large capacity stomach may result in frequent TLESRs and reflux episodes (Frank, K. *et al*., 2008).

AIM OF THE STUDY

To find association between obesity measured by body mass index (BMI) and severity of erosive gastroesophageal reflux disease (GERD).

PATIENTS AND METHODS

The study group included 100 patients who were referred to gastroenterology outpatient clinic, internal medicine outpatient clinic and endoscopy unit in Baghdad teaching hospital in the medical city between April 2010 to February 2011,and are discovered to have erosive gastro esophageal reflux disease (erosive GERD) during endoscopic examination**.** All Patients included in the study are present with typical symptom of GERD defined as **heart burn** is typically described as a burning sensation in the retrosternal area (behind the breastbone) (3) and **acid regurgitation** is defined as the perception of flow of refluxed gastric content into the mouth or hypopharynx (3). Severity of symptoms was reported as mild (ignored if patient do not think about it),moderate (can not be ignored but does not affect life style) severe (can not be ignored and affect life style) (Jacobson, B. C. *et al*., 2006) .

Inclusion criteria: 100 patient included in the study , had history of episodes of heartburn for one month or longer and episodes of moderate to severe symptom during the last 7 days prior to examination and had erosive GERD on endoscopic examination with savary - miller classification grade one to four (Tamis, G. T. *et al*., 2004).

Exclusion criteria:
1.Those with ongoing treatment for peptic ulcer with anti-secretory or anti-Helicobacter pylori therapy (proton pump inhibitors, H2- blockers, prokinetics, antibiotics) .
2. Concurrent diagnosis of IBS.
3. Other erosive or ulcerative gastric or duodenal lesions at the time of endoscopy.
4. Other significant medical or surgical diseases which could explain the symptoms.
5. Daily use of NSAIDS.
6. Major psychiatric illness or dementia were also excluded (Tamis, G. T. *et al*., 2004).

The endoscopic examination were performed by the senior endoscopist (Dr. Akram.A.Najeeb) using a standard video upper endoscope (Olympus GIF –C240Z,TOKYO,JAPAN) the procedure was carried out under local anesthesia(xylocaine 10% oral gel) .Erosive GERD was based on endoscopic findings and the severity was graded according to Savary-Miller classification of the disease severity from 1-4.

Anthropometrical measurement:- Body mass index (BMI) is the measurement of choice for many obesity researcher and health professionals. to measure the over weightedness and obesity in adults , BMI < 18.5 is underweight ,18.5-24.9 is normal ,25-29.9 is over wight , 30-34.9 is grade 1

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obesity , 35-39.9 is grade 2 obesity and ≥ 40 is grade 3 obesity as shown in table (4). The BMI is a direct calculation that describe relative body weight for height ,is not gender specific ,and is significantly correlated with total body fat content. Anthropometrical measurement were taken using standard apparatus. A digital scale used to measure body weight (BW),subject was weighed without shoes ,in light clothing .Standing body height (BH) was measured without shoes to the nearest 0,5 cm with use of the commercial stadiometer with shoulders in relaxed position and arms hanging freely .The BMI then calculated as BW in kilogram (kg) divided by square of the body height in meter (m2) (Zafar, S. *et al*., 2008) .

STATISTICAL ANALYSIS

Statistical Package for Social Sciences –version 17 (SPSS.17) used for data input and analysis. Continuous variables expressed as mean and standard deviation (SD), and discrete variables expressed as numbers and percentages. Chi square test for goodness of fit used to test the distribution of discrete variables. Spearman correlation coefficient (r) used to test the correlation between continuous and ordinal variables. which measures how well the relationship between two variables can be described by a monotonic function.T test for two independent variables used to test the significance of difference between continuous variables.

P value less than 0.05 considered significant.

RESULTS

During the 10 month period of the study, 100 patients (49 male and 51 female) were included , their age range from minimum (21y) to maximum (75y) with mean(41.33), with symptoms of GERD and endoscopy shows erosive GERD .Body mass index was measured for those patients and range from minimum (Frank, K. *et al*., 2008) (kg/m2) to maximum 46 (kg/m2) with mean of 30.65 (kg/m2) as seen in table (5).Distribution of study sample according to age categories show 24% between 20-29 year , 31% between 30-39 year ,12% between 40-49 year ,17% between 50-59 year , 9% between 60 -69 year and 7% for age ≥70 year with statistically significant p value=0.000.as seen in table (6) and figure(4).Gender distribution was 51% female and49% male with statistically in significant p value=0.841 as seen in table (6) and figure (5).

BMI distribution of study sample was 6% under weight , 13% normal weight , 29% over weight , 18% grade 1 obesity , 21% grade 2 obesity ,13% grade 3 obesity with statistically significant p value=0.002as seen in table (6) and figure(6) .

Table (5): mean age and BMI distribution of study sample.

	N=100	Minimum	Maximum	Mean	SD
Age (year)	100	21	75	41.33	15.345
BMI (kg/m2)	100	16	46	30.65	7.066
N; number, SD; standard deviation					

Table (6): Distribution of study sample according to some demographic characteristics & body weight

	N=100	%(100)	X 2	P
Age(year)				
20-29	24	24		
30-39	31	31		
40-49	12	12	26.000	0.000
50-59	17	17		
60-69	9	9		
≥70	7	7		
Gender				
Male	49	49	0.040	0.841
Female	51	51		
Body weight				
Under weight	6	6		
Normal weight	13	13		
Over weight	29	29	18.800	0.002
Obesity	18	18		
Obesity 2	21	21		
Obesity 3	13	13		
N; number, %;percent ,X2;chi square, P ;P value				

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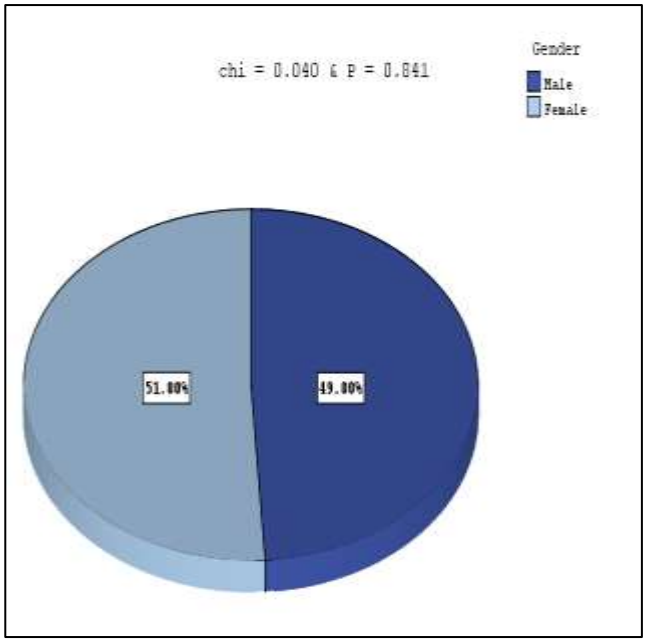

Figure (5): sex distribution of the study sample

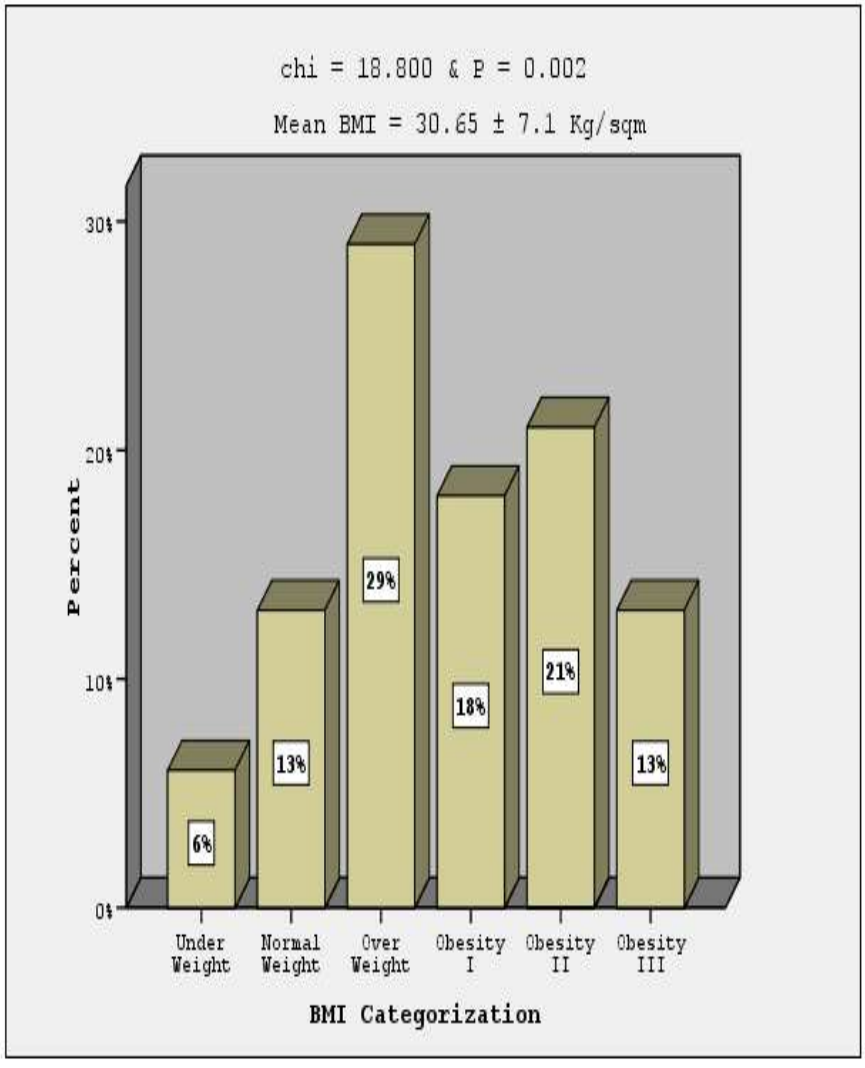

Figure (6): Distribution of study sample according to bodyweight.

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Study sample's distribution according to the severity of erosive GERD graded according to savary-miller endoscopic severityfrom grade1-4, which is shown in table(7) and figure(7) in which there is 48% of study sample was grade 1 GERD, 36% grade 2 GERD,14% grade 3 GERD and 2% grade 4 GERD.

Table 7: Distribution of study sample according to grades of erosive GERD.

Grades of GERD	N=100	% (100.0)	X^2	P
Grade I	48	48.0		
Grade II	36	36.0	52.000	**0.000**
Grade III	14	14.0		
Grade IV	2	2.0		
N; number, %; percent, X^2; chi square statistic, P; P value, GERD; gastro-esophageal reflux disease.				

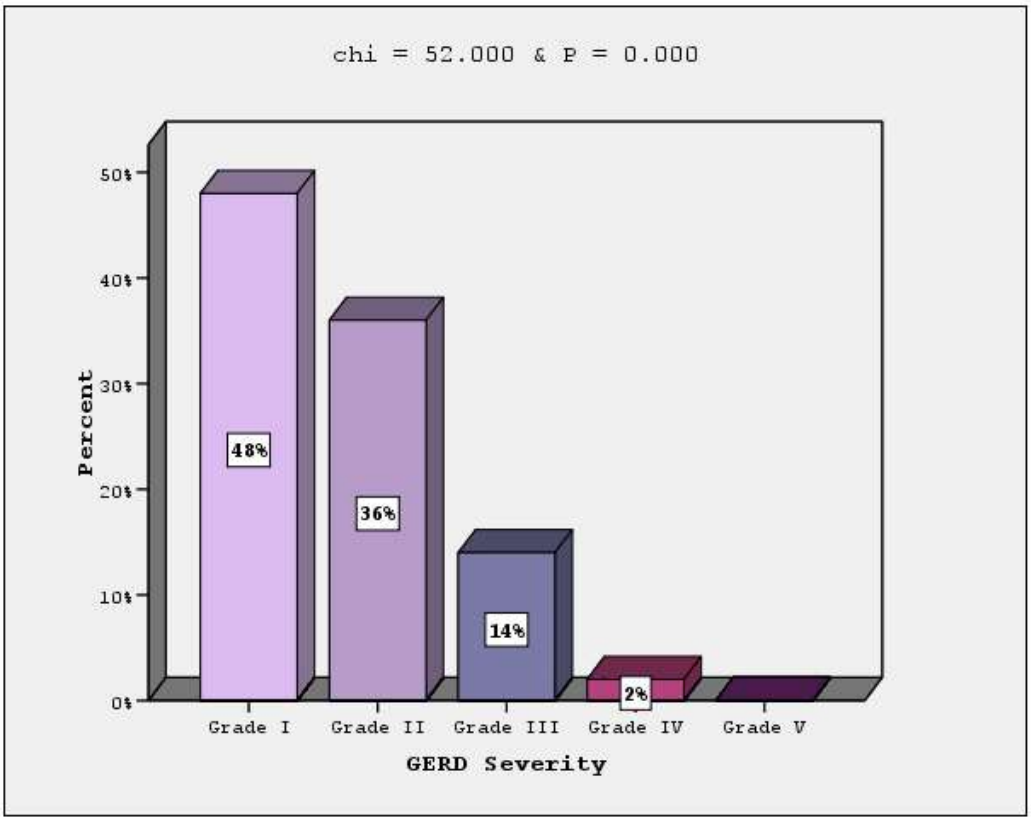

Figure (7): Distribution of study sample according to erosive GERD severity

The correlation between BMI and erosive GERD severity was shown in table (8) and figure (8) in which those patients with GERD grade 1(48) have mean BMI =25.09 kg/m2, GERD grade2 (36) patients have mean BMI=34.45kg/m2,GERD grade3(14) patients have mean BMI=38.55kg/m2 and GERD grade 4(2) patients have mean BMI=40.55 kg/m2. In this case, strong relationship was found between BMI and GERD severity by spearman correlation coefficient(r) test with statistically significant p value (0.000).

Table (8): Mean BMI according to severity of erosive GERD

GERD Severity	N=100	BMI (kg/m2) Mean ± SD	r	P
Grade I	48	25.09 ± 4.248	0.799	0.000
Grade II	36	34.45 ± 4.665		
Grade III	14	38.55 ± 4.245		
Grade IV	2	40.55 ± 4.879		
BMI; body mass index, GERD; gastro-esophageal reflux disease, r;Spearman Correlation coefficient, P; P value.				

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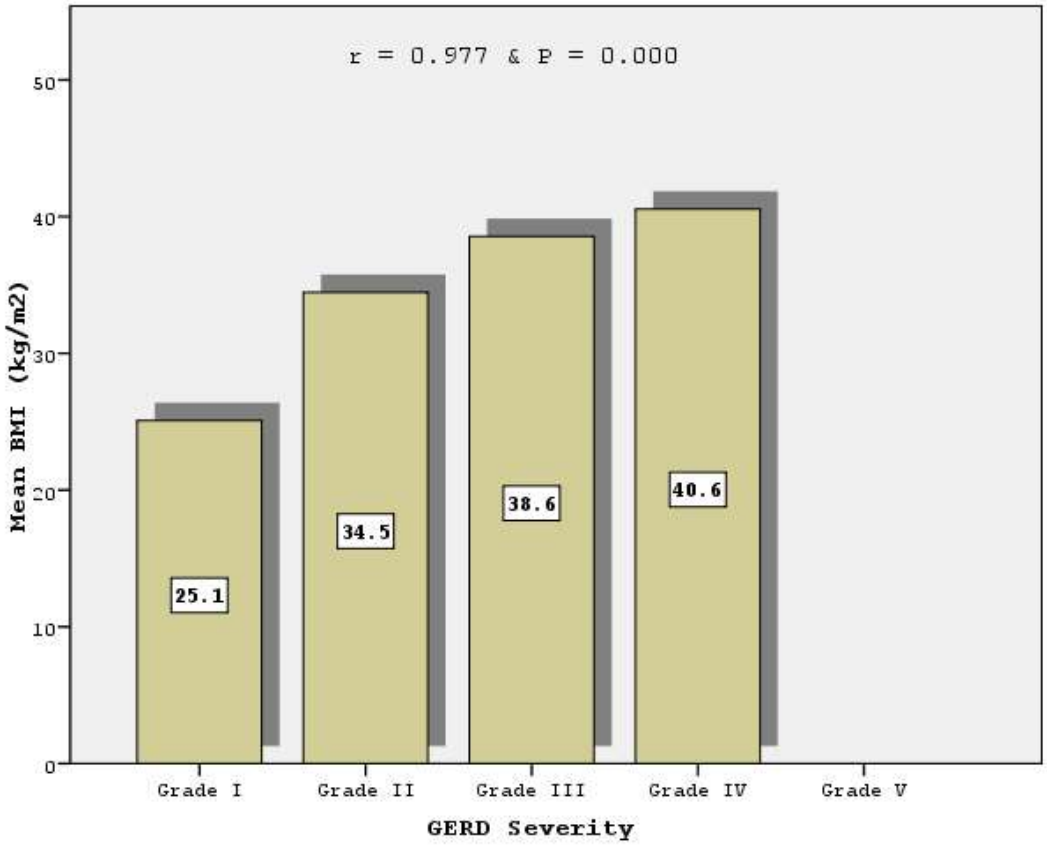

Figure (8): Mean BMI of study sample for each grade of erosive GERD.

DISCUSSION

Gastro esophageal reflux disease is spectrum of disease with classic symptom of heart burn and acid regurgitation, at one end, without any evidence of esophageal mucosal injury and erosive esophagitis, and complications of Barrettes esophagus and esophageal adenocarcinoma at other end. In our study, group of patient with untreated GERD was examined endoscopicaly and found to have erosive GERD. The association between BMI and endoscopicaly proven mucosal damage was analyzed in patient having symptom of GERD using savary- miller grading classification. It was utilized to categorize patient with erosive GERD into grade 1 - 4 severity groups. Patient with grade 1 GERD (48) have mean BMI 25.09kg/m2±4.248 SD , grade 2 GERD (36 patient) have mean BMI 34.45kg/m2±4.665 SD , grade 3 GERD (14 patient) there mean BMI 38.55 kg/m2±4.245 SD and those with grade 4 GERD (2 patient) have mean BMI 40.55kg/m2±4.879 SD, with significant statistical P value 0.000 measured by spearman correlation coefficient test (r) test. These finding suggest that obesity and increased BMI is a risk factor for more serious mucosal lesion in the esophagus with increased possibilities of complication of higher grade of GERD .The present study suggest that obesity, as defined by BMI, is significantly associated with severity of esophagitis which could be mediated by various mechanism like increased intra abdominal pressure, increased intra gastric pressure, increased lower esophageal sphincter relaxation, an abnormal diaphragmatic pinchcock and delayed acid clearance and even more than one mechanism may be applied .These potential mechanisms could explain a predisposition of obese patient to reflux of gastric content which might, among other things, decrease the effectiveness of the lower esophageal sphincter function and impair effective esophageal acid clearance (Zafar, S. *et al*., 2007). The relationship between obesity and overweight with GERD severity is a subject of many trials with controversial results. There are a large scale trials both in favor and against the relationship between BMI and GERD . Some studies have examined the degree of obesity and the existence and frequency of the GERD symptoms using surveys ,esophageal sphincter manometry or 24 hour pH monitoring .Two similar studies in the literature were estimating the severity of GERD in relation to

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obesity. A similar work by Tamis, *et al*., (2004) showed a significant relation with endoscopic severity of GERD by savary miller classification and increasing BMI detected by ANOVA test p=0.0501 and proved that obesity might not be the primary cause of GERD but risk factor for increasing severity in those already having the disease. Study by Shamail, *et al*., (2007) showed that there is strong significant correlation between GERD severity and BMI analyzed by los Anglos classification as detected by Wilcoxon's signed rank test p=0.001 and this study suggest that obesity and increased BMI is not necessarily the primary cause of GERD but could be a risk factor for more serious mucosal lesion in the esophagus increasing the possibility of complication of higher grade of GERD. A cross sectional study in the US (Locke, G. R. *et al*., 1999), demonstrated an odds ratio of 2.8 for at least weekly reflux symptoms in obese subjects. In this study, questionnaire was posted to the resident of Olmested County ,Menesota, and subject were asked whether they had symptom compatible with heart burn and acid regurgitation and, if so , the frequency with which they occurred.69% of subject with BMI≥30 were found to be symptomatic . They proved that obesity was the strongest for all risk factors for the development of GERD, surpassing family history, previous history of smoking and alcohol consumption as a risk factor for GERD. An association between GERD symptom and obesity has been shown by Hashim, *et al*., (2005) when they proved that over weight and obesity were strong in dependant risk factors for GERD and esophageal erosions, and amount and composition of dietary intake does not seen to be responsible for this. In Swedish base study (Lagergren, J. *et al*., 2000), no relation was found between BMI and severity of GERD symptoms and it was found that GERD occurred in dependant of BMI and weight reduction as a part of treatment of GERD. Mercer, *et al*., (1987) in a study of esophageal manometry in 8 a symptomatic lean and 8 a symptomatic obese subjects, reported that obese individual had significantly elevated gastroesophageal pressure gradient at both inspiration and expiration, and significantly elevated ratio of gastroesophageal pressure gradient to lower esophageal pressure. Korn, *et al*., (1997) found no significant correlation between overweight and GERD but patients with Barrett esophagus had significantly higher body mass index than the normal controls. GERD and obesity are known risk factors of Barrett's esophagus (El-Serag, H. B, 2002) and it is estimated that 8-14 % of chronic GERD patients may develop Barrett's metaplasia, which should be considered a primary etiologic factor of esophageal adenocarcinoma (Kim, R. *et al*., 1997) Since the incidence of esophageal adeno carcinoma (EAC) has been increasing faster than any other cancer in developed countries, approximately by 5- 10 % per year, identifying these risk factors is essential. Evaluation of a large population-based case control study (Mayne, S. *et al*., 2002) in the mid 1990s showed that BMI>30 increased the risk of esophageal adenocarcinoma by 16-fold compared to persons with BMI <22. In the Swedish nationwide Case-control study 2000 (Lagergren, J, 2000) higher severity of reflux symptoms together with elevated BMI increased the risk of esophageal adenocarcinoma in a dose dependent manner. They found GERD and obesity as strong and independent risk factors of esophageal adenocarcinoma. From a more practical point of view these two conditions(GERD and obesity) pose social and financial burdens since obesity increases the risk of GERD hospitalization (Ruhl, C. E. *et al*., 1999) and GERD symptom severity is associated with impaired health-related quality of life (Kaplan-Machlis, B. *et al*., 1999). On the other hand weight loss as the cheapest and a simple way of therapy has independent beneficial effect on GERD symptoms (Fraser-Moodie, C. A. *et al*., 1999).

CONCLUSION AND RECOMMENDATION

It is proved that higher BMI seems to be associated with higher degree of endoscopic erosive GERD severity which may worsen health related quality of life and increase the risk of barrett's esophagus and adenocarcinoma ,so:

- early detection and evaluation of GERD prevent the person from further complications specially barrett's esophagus and esophageal adenocarcinoma.
- Changes in gastroesophageal anatomy and physiology caused by obesity may explain the association. These include an increased prevalence of esophageal motor disorders, diminished lower esophageal sphincter (LES) pressure, the development of a hiatal hernia, and increased intragastric pressure. Weight loss, through caloric restriction and behavioral modification, has been studied infrequently as a means of improving reflux.

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LIST OF ABBREVIATIONS

1	GERD	Gastroesophageal reflux disease
2	NERD	None erosive reflux disease
3	BMI	Body mass index
4	LES	Lower esophageal sphincter
5	TLERS	Transient lower esophageal sphincter relaxations
6	MDP	Minimal distending pressure
7	NSAID	Non steroidal anti inflammatory drug
8	GER	Gastro esophageal reflux
9	EAC	Esophageal adeno carcinoma

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