Int. J. Adv. Res. Biol. Sci. (2015). 2(12): 252–261

International Journal of Advanced Research in Biological Sciences
ISSN: 2348-8069
www.ijarbs.com
Coden: IJARQG(USA)

Research Article

SOI: http://s-o-i.org/ 1.15/ijarbs-2-12-29

Frequency of Gastro-esophageal reflux disease in Egyptian Patients with Chronic Liver Disease

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Abstract

Background and Aim: Gastro-esophageal reflux disease (GERD), a highly prevalent disorder, is defined as reflux of gastro-duodenal content to the esophagus, and includes reflux esophagitis (RE) and Barrett's esophagus (Gisbert et al,. 2009)[1]. Symptomatic RE impairs the quality of life (QOL) of chronic liver disease patients, so treatment of symptomatic RE should be considered in order to improve the QOL of patients with chronic liver diseases (Suzuki et al,. 2008)[2]. We aimed to estimate the frequency of GERD in patients with chronic liver disease. **Patients and Methods:** This study was conducted on 170 patients with chronic liver disease who underwent upper GI endoscopy for different indications in the period from the first of August 2014till the 30th of june 2015 in Ain Shams university hospital. GERD, if present was classified according to Los Angeles Classification (Lundell et al., 2007)[3]. **Results:** Overall 170 patients with chronic liver disease, 41 patients were found to have GERD (24.1 %). The most prevalent was GERD grade (B). Symptomatic GERD was highly prevalent in patients with chronic liver disease, reported in about 48% of patients. Heart burn was the chief symptom present with a significant relationship between GERD and severity of the liver disease as assessed by Child-Turcotte-Pugh scoring system. A significant relationship between the severity of GERD and the degree of ascites was demonstrated, as GERD grade (C) was present more frequently in patients with marked ascites. The presence of GERD was significantly associated with the presence of esophageal varices, which could be a mechanical factor contributing to esophageal dysmotility and predisposing to GERD. **Conclusions:** A high frequency of GERD (24.1%) was demonstrated among upper endoscopies in Egyptian patients with chronic liver disease with overall 48.2 % of the studied patients were complaining of classical symptoms. Heartburn was the classical symptom of GERD, but it was not an indicator for the disease severity with a significant relationship was demonstrated between GERD and esophageal varices, ascites and signs of recent bleeding.

Keywords: Gastro-esophageal reflux disease; Esophageal varices, Chronic liver disease.

1. Introduction

Gastro-oesophageal reflux disease (GERD), a highly prevalent disorder, is defined as symptoms or mucosal damage produced by the abnormal reflux of gastric contents into the esophagus. However, only one-half of GERD patients present with oesophageal erosions, namely reflux oesophagitis (RE) [1].

Gastro-oesophageal reflux disease is a common condition affecting 25-40% of the population worldwide (Raghunath et al., 2003) [4]. It has a substantial impact on patient quality of life and use of health care resources (Ruigomez et al., 2004)[5]. The symptoms of GERD typically include dyspepsia, pyrosis, or tissue damage outside the oesophagus such as the pharynx, larynx, and trachea (Fock et al., 2008, hammer, 2009)[6,7].

Patients with chronic liver disease, especially patients with portal hypertension and liver cirrhosis, have clinical manifestations, such as oesophageal varices

and ascites. Some studies have been conducted regarding the role of oesophageal varices in the development of esophageal motor disorders and abnormal gastro-oesophageal reflux in those patients (Grassi et al., 2001, Suzuki et al., 2008)[8,2].

Ascites could be a factor promoting gastro-oesophageal reflux and it has been questioned whether or not reflux would favor the rupture of varices (Navarro-Rodriguez et al., 2003, Schechter et al., 2007)[9,10]. However, there are few studies on the prevalence of RE and factors related to RE in patients with chronic liver disease.

Reflux oesophagitis in cirrhotic patients with oesophageal varices (OV) has been studied for many years, and great importance had been paid to oesophageal dyspepsia as a risk factor for the rupture and bleeding of OV, as in cirrhotic patients increased contact time between dyspepsia and OV could lead to the eventual erosion of the mucosa and OV bleeding. (Garcia-Tsao et al., 2008, Okamoto et al 2008)[11,12].

2. Patients and Methods

2.1. Study Design and Duration:

This is a prospective study, during the period from the first of August 2014 till the 30th of june 2015 in Ain Shams university hospital.

2.2. Patients:

A total of 170 patients with chronic liver disease who underwent upper GI endoscopy for different indications in Ain Shams University Hospital after signing a written consent.

Inclusion criteria:

All patients with chronic liver disease, either having suggestive symptoms of GERD or not. unless there is a cause for exclusion.

Exclusion criteria:

Patients refused to undergo the procedure or to sign the consent.
Patients with systemic disease related to esophageal motor disorders and/or RE (progressive systemic sclerosis, diabetes mellitus and neuromuscular disorders).
Chronic users of drugs that influence esophageal motility (Calcium channel blockers, theophylline, and nitrates). Alcohol abusers until 6 months before this study.

Ethical Considerations:

This study has been performed in accordance with the ethical standards. Signed consent was obtained from all patients before enrollment in the study. Right to refuse participation was emphasized.

2.3. Methodology:

2.3.1. Clinical, Laboratory and radiological evaluation:

Full history taking stressing on GERD symptoms either typical or atypical with thorough clinical examination.

Laboratory Investigations including: Complete blood picture (CBC), erythrocyte sedimentation rate, Prothrombin time (PT) and INR, Liver profile (AST, ALT, total bilirubin, direct bilirubin, gamma-glutamyl transferase and serum albumin), Renal functions (serum creatinine and blood urea nitrogen), viral markers.

Evaluation of the severity of liver cirrhosis was obtained in each cirrhotic patient with Child-Turcotte-Pugh score. This system relies on clinical and laboratory evaluation including ascites, grade of encephalopathy, serum albumin, bilirubin and prothrombin time (Christensen et al., 1984)[13].

Abdominal ultrasound to assess liver texture, splenic size and amount of ascites.

2.3.2. Technique (Upper endoscopy):

Patients came to the endoscopy unit after an overnight fasting. Each patient was given intravenous sedation with midazolam, in a titrated dose of up to 0.1mg/kg before the endoscopy. Careful explanation of the procedure to the patient, including risks and benefits, with informed and written consent for the procedure.

GERD, if present was classified according to Los Angeles Classification (Lundell et al., 2007)[3]:

I- LA grade A: One (or more) mucosal break no longer than 5mm, that does not extend between the tops of two mucosal folds.

II- LA grade B: One (or more) mucosal break more than 5mm, which does not extend between the tops of two mucosal folds.
III- LA grade C: One (or more) mucosal break that is continuous between the tops of two or more mucosal folds, but which involves less than 75% of the esophageal circumference.
IV- LA grade D: One (or more) mucosal break but which involves at least 75% of the oesophageal circumference.

Esophageal varices (EV) were classified according to Maratka classification (1989) [14] according to the degree of protrusion into the lumen when the esophagus is maximally relaxed and inflated with air.
- Grade I: Varices were hardly noticeable protrusion.
- Grade II: Varices were protruded up to 1/4 of the lumen.
- Grade III: Varices were protruded up to 1/2 of the lumen.
- Grade IV: Varices were protruded greater than 1/2 of the lumen.

Portal Hypertensive Gastropathy:

Grading was done according to The New Italian Endoscopic Club into mild and severe portal gastropathy.

Esophageal Biopsies:

Whenever feasible lower esophageal biopsies were taken for histopathological examination, the biopsy was preserved in 10% formalin till examined.

2.3.4. Statistical Methods:

SPSS statistical software package (V. 17.0, Echo soft Corp., USA, 2008) was used for data analysis. Results were expressed as means ± standard deviation of the means (SD). Differences between groups were analyzed either by using the Chi square test or student's t test and nonparametric (Mann Whitney test) for comparison between two groups or ANOVA test for multiple group comparison. Spearman rank correlation coefficient was used to determine significant correlations among different parameters. The analysis was performed using Statistical Analysis System, version 6.03, on an IBM at personal computer.

1-SD: slandered deviation.
2-M: mean.
3-P: P-value.

3. Results

A total of 170 patients with chronic liver diseases were enrolled in this study that underwent upper GI endoscopy for different indications. There were 120 male versus 50 female patients (70.6% and 29.4% respectively), with age group ranging from 30 up to 78 years (mean age 50.50 ± 10.94). Sixteen patients (39%) with GERD were below 40 years and 25 (61%) patients with GERD were above 60 years. GERD was endoscopically evident in 41 patients of the studied patients (24.1%), 33 patients (80.48%) were males and 8 patients were females (19.5%) with GERD grade B is the most prevalent entity (43.9 %). Heartburn was the most presenting complaint in all symptomatic patients (82 patients i.e. 48.2%), followed by epigastric pain present in 65 patients (38.24%), while acid regurgitation was found in 47 patients (27.6%) (Table 1)

Table (1) Base line clinical symptoms of the studied groups

Characteristics CLD group (n= 170)	CLD group (n= 170)
Typical symptoms	82(48.2%)
Heart burn	82(48.2%)
acid regurgitation	47(27.6%)
Excessive salivation	9(5.2%)
Atypical symptoms	8(4.7%)
Throat clearing	8(4.7%)
Hoarsness of voice	1(0.5%)
Chronic cough	2(1.1%)
Nocturnal asthma	0(0%)
Other GIT symptoms	
Epigastric pain	65 (38.24%)
Vomiting	18 (10.6%)
Dyspepsia	50 (29.4%)

Heart burn was presented in 100% of patients with GERD grade (C), however, there was no statistical significant relationship between various reflux symptoms and the different degrees of GERD. P>0.05 (N.S) (Table 2).

Table (2) Typical and atypical symptoms in relation to different grades of GERD.

Characteristics	GERD (A) (n= 15)	GERD (B) (n= 18)	GERD (C) (n= 8)	P value
Heart burn	9 (60%)	10 (55.6%)	8 (100%)	**0.073 (NS)**
Acid regurgitation	6 (40%)	5 (27.8%)	5 (62.5%)	**0.245 (NS)**
Excessive salivation	3 (20%)	1 (5.6%)	0 (0%)	**0.222 (NS)**
Throat clearing	1 (6.7%)	0 (0%)	2 (25%)	**0.077 (NS)**
Hoarsness of voice	0 (0%)	0 (0%)	0 (0%)	---
Chronic cough	0 (0%)	0 (0%)	1 (12.5%)	**0.121 (NS)**
Nocturnal asthma	**0 (0%)**	**0 (0%)**	**0 (0%)**	---

Values are expressed as number (%). NS= Not significant= p> 0.05.

Ascites was manifested in 31 patients with GERD. The majority of GERD grade A patients were presented with tense ascites (33.3 %), half of the patients with GERD grade B had moderate ascites, while 87.5 % of patients with GERD grade C had marked ascites which is highly significant data concerning the relation between the different degrees of ascites and different grades of GERD, P< 0.001. (Table 3, Figure 1).

Figure 1 Association between different grades of GERD and degree of ascites

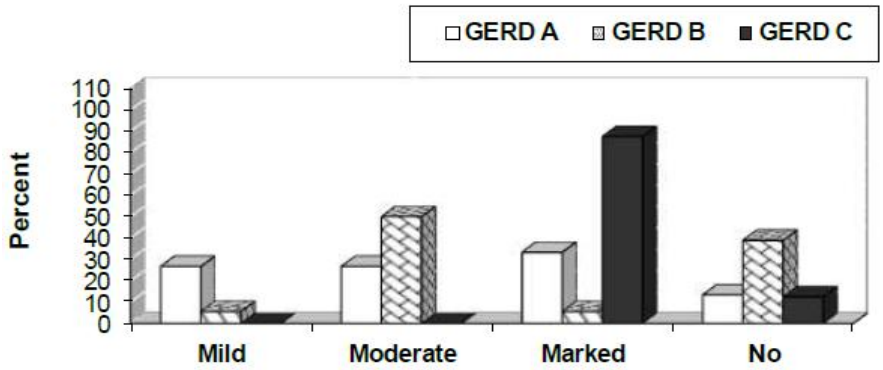

Table (3) Association between different grades of GERD and degree of ascites in the studied group.

Characteristics of ascites	GERD (A) (n= 15)	GERD (B) (n= 18)	GERD (C) (n= 8)	P value
Mild (n=40)	4 (26.67%)	1 (5.56%)	0 (0%)	0.001**
Moderate (n=47)	4 (26.67%)	9 (50%)	0 (0%)	
Marked (n=35)	5 (33.33%)	1 (5.56%)	7 (87.50%)	
No (n=48)	2 (13.33%)	7 (38.89%)	1 (12.50%)	

Values are expressed as number (%).**p< 0.001= highly significant.

In the studied group, 25 patients (14.7%) were classified Child A, 40 patients (23.5%) were classified Child B, 92 patients (54.1%) were classified Child C and 13 patients (7.6%) were having chronic hepatitis, showing statistically highly significant difference between GERD and modified Child score (severity of liver damage), p< 0.001. The majority of patients of GERD grade A, B and C were categorized as Child C (66.67%, 55.56% and 87.5 % respectively), however it was not statistically significant. P> 0.05 (non-significant). (table 4).

Table (4) Child-Turcotte-Pugh scoring system in relation to different grades of GERD.

Characteristics	GERD (A) (n= 15)	GERD (B) (n= 18)	GERD (C) (n= 8)	P value
Chronic hepatitis	0 (0%)	0 (0%)	1 (12.5%)	0.206 (NS)
Child A	2 (13.33%)	3 (16.67%)	0 (0%)	
Child B	3 (20%)	5 (27.78%)	0 (0%)	
Child C	10 (66.67%)	10 (55.56%)	7 (87.5%)	

Values are expressed as number (%).NS= Not significant= p> 0.05

In this study, 37 patients (90.2%) with GERD were having esophageal varices with different grades, while the rest of GERD patients (9.8%) were not with a significant statistical difference (P= 0.011). Sixty patients were having signs of recent variceal bleeding, 36 patients of them (60 %) were having GERD which is highly significant. (table 5).

Mild portal gastropathy was found in 45 patients (26.27 %), only ten of them were having GERD (24.39 %), on the other hand 10 patients (5.88 %) were having severe portal gastropathy, only two of them were having GERD (4.88 %) which is not significant.

It was possible to take lower esophageal biopsies in 27 patients (15.88 %) revealing no pathological evidence of reflux esophagitis in 2 non-symptomatizing patients, 12 patients (44.44 %) with mild reflux esophagitis activity, 12 patients (44.44 %) with moderate activity and only one patient was classified as reflux esophagitis with low grade dysplasia and this patient was not having GERD endoscopically (table 6).

Table (5) Association between GERD and PHG in the studied group.

Characteristics	GERD (A) (n= 15)	GERD (B) (n= 18)	GERD (C) (n= 8)	P value
Chronic hepatitis	0 (0%)	0 (0%)	1 (12.5%)	0.206 (NS)
Child A	2 (13.33%)	3 (16.67%)	0 (0%)	
Child B	3 (20%)	5 (27.78%)	0 (0%)	
Child C	10 (66.67%)	10 (55.56%)	7 (87.5%)	

Values are expressed as number (%).
NS= Not significant= p> 0.05.

Table (6) Association between GERD and pathology of the biopsies taken in the studied group.

Characteristics of pathology	No GERD (n= 129)	GERD (n= 41)
Normal (n= 2)	2 (100%)	0 (0%)
reflux oesophagitis of mild activity (n= 12)	6 (50%)	6 (50%)
reflux oesophagitis of moderate activity (n= 12)	6 (50%)	6(50%)
reflux oesophagitis with low grade dysplasia (n= 1)	1 (100%)	0 (0%)

Discussion

Gastro-esophageal reflux disease is one of the most common diseases in modern civilization, which greatly affects people's health and quality of life [1]. It is the most common gastrointestinal diagnosis recorded during visits to outpatient clinics [15]. GERD contributes in excess of 10 billion $ in annual direct health care costs, with the majority of cost directed to proton pump inhibitors (PPI) [16]. A guidelines issued by the American College of Gastroenterology (ACG) define GERD as symptoms or mucosal damage produced by the abnormal reflux of gastric contents into the esophagus [17]. GERD is associated with considerable morbidity and complications, such as esophageal ulcerations (5%), peptic stricture (4% to 20%) and Barrett's esophagus (8% to 20%). Furthermore GERD, as a chronic disease significantly impairs quality of life [18].

Symptomatic RE impairs the quality of life (QOL) of patients with chronic liver disease, thus, those patients should be assessed for the presence of symptomatic GERD, and if present, treatment should be considered in order to improve the QOL of these patients [2]. Patients with chronic liver disease, especially patients with portal hypertension and liver cirrhosis, have clinical manifestations, such as esophageal varices and ascites. Some studies have been conducted regarding the role of esophageal varices in the development of esophageal motor disorders and abnormal gastroesophageal reflux in those patients [2,8].

Ascites could be a factor promoting gastro-oesophageal reflux, and it has been questioned whether or not reflux would favor the rupture of varices [19,10].

In our series, GERD was more prevalent in male patients than females. This is in agreement with Li et al. [20], who stated that RE is more common in males than females. A more progressive clinical course and a predominance of cirrhosis with comorbid related factors contributing to GERD like esophageal varices and ascites were shown by Yu et al. [21] to be more common in males. On the other hand Kotzan et al. [22] found no correlation between sex and GERD.

We found that GERD was more prevalent in older patients with CLD; this is in agreement with Li et al. [20], who stated that there is a relationship between the high prevalence of RE among patients with chronic liver disease and age, and this also is in agreement with earlier studies done by Collen et al. [23] and Huang et al. [24] who found more severe gastroesophageal reflux and esophageal lesions in elderly patients as compared to younger patients. The abnormalities that appear to play a pathogenic role in GERD tend to be more severe in the elderly patients and lead to the increased rate of GERD complications. Also, multiple medications more frequently taken by the elderly for co-morbid illnesses such as NSAIDs, beta blockers and antidepressants, are well known to decrease LES pressure. Also many diseases that can negatively affect esophageal motility appear with greater frequency with advanced age.

In the present study, we reported that 82 patients (48.2%) experienced typical symptoms for GERD including heartburn, acid regurgitation and excessive salivation, and only 8 (4.7%) patients were complaining of atypical symptoms. This frequency of symptomatic GERD was more prevalent than the results of the study done by Zhang et al. [25] who reported that typical symptoms of gastroesophageal reflux disease were present in (32.05%) of patients. This may be explained, as Zhang and his colleagues studied only 78 patients with liver cirrhosis without esophageal varices, while our study was conducted on a larger number of patients most of them had esophageal varices, which was demonstrated as a positive mechanical factor contributing to GERD.

Suzuki and his colleagues [2] found that approximately 33.6% patients with chronic liver disease had symptomatic GERD which is higher in chronic liver disease patients than in the general population. They used (QUEST) questionnaire (Quality-of-Life and Utility Evaluation Survey Technology) for Diagnosis of symptomatic GERD in 238 patients with chronic liver disease, after exclusion of patients who were taking drugs that could affect gastric acid secretion including H2-receptor antagonists, PPI or patients were taking a gastrointestinal tract motility regulator.

In our work, heartburn was the most predominant symptom presented in all symptomatic patients with no statistically significant difference between different GERD symptoms and different grades of GERD ($P > 0.05$), denoting that there is no relationship between the symptoms of GERD and the severity of the disease. It is not possible to preview the endoscopic findings by the intensity or frequency of symptoms.

Similarly DeVault et al. [17] reported that heartburn is the classical symptom of GERD. Heartburn is caused by acid stimulation of sensory nerve endings in the

deeper layers of the esophageal epithelium. It agrees also with Schechter et al. [10] who found that, in face of typical symptoms, GERD should be suspected. However, a correlation between the presence or absence of symptoms and the intensity of reflux could not be found.

When GERD patients in our study were endoscopically assessed according to Los Angeles classification, it was detected in 41 patients (50 %) from the symptomatic individuals and represents (24.1%) of the total studied patients with chronic liver disease. GERD grade (B) was the most frequent grade and it was present in 43.9% of GERD patients. This is in agreement with Zhang et al. [25] who studied GERD in cirrhotic patients depending on upper endoscopy, esophageal manometry, and 24-h esophageal pH monitoring. They demonstrated that, there was a high incidence of RE (endoscopically) and pathologic reflux (by pH metry) in patients with severe chronic liver disease. Li et al. [20] stated that, the prevalence of RE was 36.4% (469/1280) in patient with chronic liver disease, which was significantly high.

Liver cirrhosis itself could be an important causative factor for the onset of gastroesophageal reflux. It seemed that not only the mechanical effects caused by esophageal varices or ascites, but also neural and humoral factors are related to the high incidence of GERD in patients with liver cirrhosis. Cárdenas et al. [26] demonstrated that nitrous oxide (NO) was found in large amounts in the systemic circulation of cirrhotic patients, NO has been shown to decrease the amplitude of distal esophageal peristaltic waves, and the velocity of the peristaltic contractions in the proximal esophagus, and all these can attribute to the high incidence of GERD in patients with liver cirrhosis.

On the other hand, out of 82 patients who had GERD symptoms, only half (41 patients) of them when assessed endoscopically were not having GERD. This is referred as nonerosive reflux disease (NERD). This is similar with the results shown by Schechter et al. [10] who studied the prevalence of GERD in cirrhotic patients with esophageal varices without endoscopic treatment, and found that, in 27 patients with typical reflux symptoms, 14 (52%) presented with abnormal reflux. A more prevalent percentage of NERD was reported by Zagari et al. [27] who performed a large epidemiologic study and demonstrated that 23.7% (out of 1,033 patients) had reflux symptoms at least twice a week, of those patients with reflux symptoms, 75.9% were found to have a negative endoscopy.

In a large population-based endoscopy study 1000 northern Europeans were randomly sampled, Ronkainen et al. [28] reported that two thirds of these patients who were having reflux symptoms had no esophagitis and there was imperfect correspondence between symptoms attributed to GERD and endoscopic features of the disease. Overall, the results of old and recent studies investigating patients with GERD-related symptoms have suggested that the prevalence of NERD is between 50% and 70%, and this could be due to the widespread of proton pump inhibitors (PPI). It is likely that some of the recent studies that determined the prevalence of NERD have been over estimated because of including healed erosive esophagitis subjects as NERD patients.

A highly statically significant difference ($P< 0.001$) between the degree of ascites and different grades of GERD was observed in our study, as the degree of GERD was higher in patients with marked ascites. GERD grade (C) was present more frequently in patients with marked ascites. These results were matched with Li et al. [20] who found a significant relationship between ascites and reflux esophagitis. Ascites increases the intra-abdominal pressure, compressing the stomach and its contents, and this may alter the anatomic anti-reflux elements that are naturally occurring against reflux, also gastric half-emptying of liquid food is delayed in patients with liver cirrhosis and ascites.

Similarly, Navarro et al. [19] observed that there was a trend of reduced reflux when intra-abdominal pressure was reduced by paracentesis. On the other hand, they oncluded that, although a significant reduction of intra-abdominal pressure occurred when the volume of ascites was controlled, it did not correspond to any alteration in the LES pressure, LES length and LES abdominal length.

Bhatia et al. [29] studied the effect of tense ascites on esophageal body motility and lower esophageal sphincter pressure; they concluded that esophageal body contraction wave duration was increased in the presence of ascites, and decreased after control of ascites, but the LES pressure was not affected by ascites. However, in an Egyptian study done by Iman et al. [30] concluded that the esophageal motility and the pressure of LES in patients with and without ascites had no significant difference, and this was in agreement with Avgerinos et al. [31].

In our study, there was a highly significant relationship (P< 0.001) between the presence of reflux esophagitis and the severity of chronic liver disease as graded by the Child- Turcotte-Pugh scoring system. However, there was no statically significant correlation (P=0.206) between different grades of GERD and the severity of liver disease. It was shown that, in advanced stages of liver diseases child (B) and (C) patients, GERD was more prevalent than child (A) patients. This could be attributed to the presence of ascites and esophageal varices that are frequent findings in decompensated liver cirrhosis. This is consistent with Zhang et al. [25] who stated that, the more severity of liver damage, the more abnormal parameters of acid and bilirubin reflux, also they found that the reflux incidence was also higher in Child B or C group than in Child A group. A stepwise increase of mixed reflux was demonstrated along with the severity of liver function damage. Also, this is comparable with Li et al. [20] who stated that there was a positive relationship between the severity of liver damage and RE and the highest prevalence of RE existed between patients with liver failure or Child B and C liver cirrhosis.

The results of our study showed that, there was a significant relationship (P=0.011) between the presence of esophageal varices and GERD, which is in agreement with Schechter et al. [10] and Zhang et al. [25] who found that esophageal varices itself, independent of the cirrhosis, delays the esophageal clearance and increases the contact time between acid and mucosa. Also these results go with Ahmed et al. (1993) who studied by pH metry 25 cirrhotic patients and 30 GERD patients without liver disease, they found that among the cirrhotic patients with GERD 81% were having esophageal varices; they concluded that GERD is common in cirrhotics with esophageal varices. They suggested that GERD is common in cirrhotics with esophageal varices, independent of their caliber. Passaretti et al. [32] and Iwakiri et al. [33] demonstrated that motor disorders in the esophageal body, a delay in the esophageal clearance time and abnormal gastroesophageal reflux occur in cirrhotic patients with esophageal varices.

On the other hand we found that, there was no significant relationship (P= 0.094) between the size of esophageal varices and GERD. This is in agreement with Li et al. [20] who found that there was no significant relationship between esophageal varices size and RE, also this coincides with Schechter et al. [10], who found that esophageal dysmotility occurs in the presence of varices due to the mechanical effect of the blood with in the varices, irrespective to their size.

Contradictory, when GERD was assessed by Iman et al. [30] by esophageal manometery, they demonstrated that patients with high-grade esophageal varices had significant decrease in esophageal body amplitude in middle and distal esophagus, they explain their results by the high mechanical effect of large varices which can diminish the amplitude and duration of the peristaltic waves and this predisposes to GERD.

Our study highlighted that, there was a significant relationship (P< 0.001) between the presence of GERD and the presence of signs of recent variceal bleeding. This is consistent with Lodato et al. [34] who observed that, high-grade varices and red color (RC) signs tended to be more frequently found on the right posterior wall of the esophagus rather than the other areas, however, bleeding varices with RC signs were more frequently found in the right anterior wall. Lodato and his colleagues found that mucosal breaks including erosions and ulcers in reflux esophagitis were most frequently found on the right anterior wall of the lower esophageal mucosa, probably because of the longer acid contact time of the right anterior wall of the lower esophagus. The longer acid contact time found on the right anterior wall may damage the esophageal mucosa and may increase the risk of variceal rupture, and this longer contact time is aided by the delayed acid clearance in patients with liver cirrhosis and comorbid factors.

We found that, there was no significant relationship (P=0.879) between portal hypertensive gastropathy and GERD. This is in agreement with Schechter et al. [10] who found that there was no relation between congestive gastropathy and abnormal reflux. Acid secretion may be decreased in patients with PHG due to several factors related to mucosal injury in PHG as mucosal surface hypoxia and generation of oxygen free radicals.

When lower esophageal biopsies were taken and were pathologically examined, some patients who were negative endoscopically, had GERD pathologically and one of those patients was having esophagitis with mild dysplasia.

Also Zagari et al. [27] had observed that a large number of patients who have GERD were negative at upper endoscopy. Dent [35] stated that, the use of histological characteristics help to diagnose GERD

and specifically NERD. Patients with NERD demonstrated the highest number of acid reflux events before sensed reflux event. This suggests that prior sensitization is needed for an acid reflux to be perceived in NERD patients who demonstrated a lower acid exposure compared with erosive esophagitis patients. Distal amplitude contractions, as well as mean lower esophageal resting pressure, are mildly reduced in NERD patients in contrast to patients with erosive esophagitis who demonstrate obvious peristaltic dysfunction.

In conclusion, A high frequency of GERD (24.1%) was demonstrated among upper endoscopies in Egyptian patients with chronic liver disease with overall 48.2 % of the studied patients were complaining of classical GERD symptoms. In addition heartburn is the classical symptom of GERD, but it is not an indicator for the disease severity, so it is not possible to preview the endoscopic findings by the intensity or frequency of symptoms with a significant relationship was demonstrated between GERD and esophageal varices, ascites and signs of recent bleeding.

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How to cite this article:
Ahmed Samir Abo Halima; Hossam El-Din M. Salem. (2015). Frequency of Gastro-esophageal reflux disease in Egyptian Patients with Chronic Liver Disease. Int. J. Adv. Res. Biol. Sci. 2(12): 252–261.