

Laryngopharyngeal Reflux in Gastroesophageal Reflux Disease: Does “Silent Laryngopharyngeal Reflux” Really Exist?

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Abstract

Background: Gastroesophageal reflux disease (GERD) is a disorder resulting from the reversed flow of gastroduodenal contents into the esophagus, and producing different symptoms, while laryngopharyngeal reflux (LPR) is a disorder resulting from the reversed flow of gastric contents into the hypopharynx. The aim of this work is to evaluate LPR in cases of GERD. **Methods:** The present study was performed on fifty GERD patients diagnosed by gastroscopy. LPR was assessed by reflux symptoms score (RSI) and reflux finding score (RFS). Accordingly, patients are classified into: Group I = 25 patients with manifest LPR, and Group II = 25 control patients without LPR symptoms. **Results:** GERD accounts for 17.4% of attendants of gastroscopy unit, where manifest LPR accounts for 29.1% of GERD cases recording mean RSI and RFS 16.48 and 8.44 respectively. Silent LPR accounts for 8% recording mean RFS 7. **Conclusion:** There is a significant direct proportional relationship between severity of GERD and the RSI and RFS ($p = 0.015$ and 0.005 respectively).

Keywords

Gastroesophageal Reflux Disease (GERD); Laryngopharyngeal Reflux (LPR); Reflux Symptoms Index (RSI); Reflux Finding Score (RFS)

1. Introduction

Gastroesophageal reflux disease (GERD) is diagnosed clinically or histologically due to abnormal exposure of the oesophagus to gastric contents [1]. Extraesophageal manifestations are the complicated GERD primarily involving the neighboring organs [2]. Laryngopharyngeal reflux (LPR) is common, but its diagnosis may be difficult, for its symptoms are nonspecific and its laryngoscopic signs are not always correlated with symptom severity [3]. Little gastric content can induce laryngitis as laryngeal tissue is more vulnerable to such injury than oesophageal one [4]. There is neither pathognomonic symptom nor sign for LPR, but both reflux symptoms index (RSI) and reflux finding score (RFS) were validated for its diagnosis [5].

2. Patients and Methods

This study was conducted on adult patients with GERD diagnosed at Gastrointestinal Endoscopy Unit, Faculty of Medicine, Cairo University. *Exclusion criteria:* a) Patients giving history of peptic ulcer disease or anti ulcer medications or previous anti ulcer surgery, b) Patients having local laryngopharyngeal affection and those having causes inducing GERD like allergy, alcohol, tobacco, drugs.

The selected patients were divided into 2 groups: Group I: patients complaining of any of the LPR symptoms, and Group II: control cases who were not complaining of any of the LPR symptoms.

All patients were subjected to: a) History taking, including evaluation of GERD symptoms as heart burn, regurgitation, halitosis, dysphagia and dyspepsia, and LPR symptoms, defined as RSI, including hoarseness, throat clearing, postnasal drip, dysphagia, irritant cough, dyspnea, and globus, as designed by *Belafsky et al. (2002)* [6], and shown in **Table 1**. Score > 13 is suggestive of LPR. b) Oesophagogastroduodenoscopy using Olympus endoscopy for evaluating GERD, where Los Angeles classification was applied [7] and GERD oesophagitis was graded as follows: A: One (or more) mucosal break ≤ 5 mm, that does not extend between the tops of two mucosal folds, B: One (or more) mucosal break > 5 mm long that does not extend between the tops of two mucosal folds, C: One (or more) mucosal break that is continuous between the tops of ≥ 2 mucosal folds but which involves <75% of the circumference, and D: One (or more) mucosal break which involves $\geq 75\%$ of the esophageal circumference. It was also done to examine the presence of contributing factors of GERD as hiatus hernia, and the presence of any complications as Barrett's esophagus, stricture, and esophageal carcinoma. c) Direct fiberoptic laryngoscopy for examination of LPR signs defined as RFS and designed by *Belafsky et al. (2002)* [6], and shown in **Table 2**. Score > 5 is considered abnormal.

The study was approved by the institutional ethical committee, and all patients provided an informed consent.

3. Results

This study was a cross sectional study, conducted on attendants of Gastrointestinal Endoscopy Unit, Faculty of

Table 1. Reflux symptoms index as designed by *Belafsky et al. (2002)*.

The reflux symptom index (RSI)	Grade: 0 = no, 5 = severe					Score
Within the past month, how did the following problems affect you?	0	1	2	3	4	5
Hoarseness or a problem with your voice.	0	1	2	3	4	5
Clearing your throat.	0	1	2	3	4	5
Excess throat mucus or postnasal drip.	0	1	2	3	4	5
Difficulty swallowing food, liquids, or pills.	0	1	2	3	4	5
Coughing after you ate or after lying down.	0	1	2	3	4	5
Breathing difficulties or choking episodes.	0	1	2	3	4	5
Troublesome or annoying cough.	0	1	2	3	4	5
Sensations of something sticking in your throat or a lump in your throat.	0	1	2	3	4	5
Heartburn, chest pain, indigestion, or stomach acid coming up.	0	1	2	3	4	5
Total = 45						

Table 2. Reflux finding score as designed by *Belafsky et al.* (2002).

Reflux finding item	Scale	Score
Pseudosulcus (infraglottic edema)	0 = absent, 2 = present	
Ventricular obliteration	0 = absent, 2 = present, 4 = complete	
Erythema/hyperemia	0 = none, 2 = arytenoids only, 4 = diffuse	
Vocal fold edema	0 = none, 1 = mild, 2 = moderate, 3 = severe, 4 = polypoid	
Diffuse laryngeal edema	0 = none, 1 = mild, 2 = moderate, 3 = severe, 4 = obstructing	
Posterior commissure hypertrophy	0 = none, 1 = mild, 2 = moderate, 3 = severe, 4 = obstructing	
Granuloma/grauation	0 = absent, 2 = present	
Thick endolaryngeal mucus	0 = absent, 2 = present	
Total		

Medicine, Cairo University from May 2012 to June 2013.

GERD was diagnosed in 17.4% of attendants (86/494 patients). GERD patients were then divided into 2 groups: Group I: constituted of 25 patients (29.1%) having LPR. All reported by symptoms and were confirmed by laryngoscope, therefore termed as “Manifest LPR”, and Group II: GERD patients without LPR symptoms which constituted of 61 patients (70.9%), however, 25 patients were further examined by laryngoscope to serve as control group. Most of the control group (23/25 patients; 92%) were laryngoscopically free while 2 only (8%) had LPR. Accordingly, group II is subdivided into IIA who are “LPR-free”, and IIB who are defined as “Silent LPR” respectively.

Demographic features of the studied groups are shown in **Table 3**. None of the demographic features showed a statistical difference between the 2 groups. Obesity was higher in Group I than in Group II but without recording a statistical difference, however, it is worth noting that obesity was reported by most of the studied patients (39/50 patients; 78%).

Gastrointestinal symptoms of the studied groups are shown in **Table 4**. Heart burn and regurgitation were the commonest symptoms (80% each) however, halitosis, dysphagia and nausea, which were less common, were significantly higher in Group I than in Group II ($p = 0.01$, 0.01 and 0.037 respectively).

LPR symptoms in manifest LPR (Group I) are illustrated in **Figure 1**. The mean score was 16.48.

Oesophagogastroduodenoscopic examination of the studied groups is shown in **Table 5**. Laryngoscopic examination (RFS) of the studied groups is shown in **Table 6**. Laryngoscopy detected positive signs of LPR in 2 patients in Group II (Group IIB). Both recorded erythema, vocal fold edema and diffuse laryngeal edema, while ventricular obliteration, posterior commissure hypertrophy and thick endolaryngeal mucus were detected in one of them. They recorded mean RFS = 7. Therefore termed as silent LPR.

Correlation between GERD grade and LPR symptom index and LPR finding score are illustrated in **Figures 2(a)** and **(b)** respectively. Predictability of RSI according to RFS is illustrated in **Figure 3**.

4. Discussion

GERD is a common disease that may present with disabling symptoms [8]. GERD was defined as backflow of gastric contents causing disturbing symptoms and/or complications. It was classified into esophageal and extra-esophageal syndromes. Recently, it became patient-centered approach independent of the laryngoscopic examination, subclassification of the disease into discrete entities e.g. laryngitis, cough, etc. and also Barrett’s esophagus [9].

In this study, GERD accounts for 17.4% among attendants of gastroscopy unit. This figure is intermediate. It was higher than that recorded in Asia (<5%) [10], and lower than that recorded in USA, being the 3rd digestive disease, and with the highest economic burden [11]. However, it was variably recorded in the western world as reported by Farrokhi *et al.* and Hershovici *et al.* i.e. approximately 35% - 40% and 10% - 20% respectively [4] [12].

In this study, neither sex nor age predilection was recorded in GERD. This is similar to Dent [10]. However,

Table 3. Demographic features of the studied groups.

Demographic parameter		Group I = manifest LPR (n = 25)	Group II no LPR symptoms (n = 25)	Total (n = 50)	p-value
Age	Mean \pm SD	40.4 \pm 12.9	39.8 \pm 10.7	40.1 \pm 11.8	0.92
Sex n (%)	Female/male	13 (52%)/12 (48%)	12 (48%)/13 (52%)	25 (50%)/25 (50%)	0.77
Residence n (%)	Urban/rural	15 (60%)/10 (40%)	14 (56%)/11 (44%)	29 (58%)/21 (42%)	0.77
BMI	Mean	32.9 \pm 5.6	31.6 \pm 5.5	31.8	0.99
	Absolute figure ≥ 25 / < 25	22 (88%)/3 (12%)	17 (68%)/8 (32%)	39 (78%)/11 (22%)	0.52

LPR: Laryngopharyngeal reflux, GERD: Gastroesophageal reflux disease, BMI: Body mass index.

Table 4. Gastrointestinal symptoms of the studied groups.

Gastrointestinal symptoms	Group I = manifest LPR (n = 25)	Group II = No LPR symptoms			Total (n = 50)	p-value (I vs II)
		A = LPR-free (n = 23)	B = Silent LPR (n = 2)	Total (n = 25)		
Heart burn	20 (80%)	17 (73.9%)	1 (50%)	18 (72%)	38 (76%)	0.73
Regurgitation	20 (80%)	17 (73.9%)	1 (50%)	18 (72%)	38 (76%)	0.73
Halitosis	15 (60%)	6 (26.1%)	0	6 (24%)	21 (42%)	0.01
Dysphagia	14 (56%)	2 (8.6%)	1 (50%)	3 (12%)	17 (34%)	0.01
Nausea	12 (48%)	5 (21.7%)	0	5 (20%)	17 (34%)	0.037
Appetite change	11 (44%)	7 (30.4%)	0	7 (28%)	18 (36%)	0.23
Vomiting	9 (36%)	6 (26.1%)	0	6 (24%)	15 (30%)	0.35
Haematemesis	2 (8%)	2 (8.6%)	0	2 (8%)	4 (8%)	-

LPR: Laryngopharyngeal reflux, GERD: Gastroesophageal reflux disease.

Table 5. Oesophagogastroduodenoscopic examination of the studied groups.

Oesophagogastroduodenoscopic findings	Group I = manifest LPR (n = 25)	Group II = no LPR symptoms (n = 25)			Total (n = 50)	p-value (I vs II)	
		A = LPR-free (n = 23)	B = silent LPR (n = 2)	Total (n = 25)			
A	15 (60%)	18 (78.3%)	1 (50%)	19 (76%)	34 (68%)		
GERD	B	8 (32%)	5 (21.7%)	1 (50%)	6 (24%)	14 (28%)	-
Esophagus	C & D	2 (8%)	0	0	0	2 (4%)	
	Sliding hiatus hernia	6 (24%)	4 (17.3%)	1 (50%)	5 (20%)	11 (22%)	0.73
	Barrett's esophagus	2 (8%)	0	0	0	2 (4%)	0.25
Stomach	Gastritis	18 (72%)	11 (47.8%)	2 (100%)	13 (52%)	31 (62%)	0.12
Duodenum	Duodenitis	9 (36%)	7 (30.4%)	2 (100%)	9 (36%)	18 (36%)	0.6
	Chronic active duodenal-ulcer	2 (8%)	1 (4.3%)	0	1 (4%)	3 (6%)	-

LPR: Laryngopharyngeal reflux, GERD: Gastroesophageal reflux disease.

El-Serag found GERD increased with age (highest in the 60 - 69 years range, with a slight decrease afterwards), meanwhile, women had a slightly higher risk at age > 50 years [13]. Similarly, Lee attributed this to the progressive decrease in abdominal lower esophageal sphincter length and esophageal clearance and motility [14]. Also, Johnson recorded severe erosive esophagitis ranging from 12% in patients aged < 21 years to 37% in patients

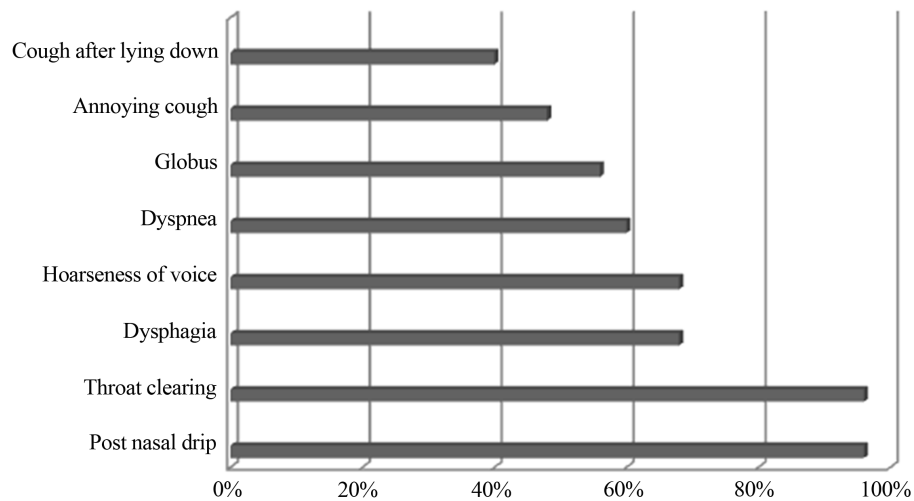


Figure 1. LPR symptoms of Group I.

Table 6. Laryngoscopic examination of the studied groups.

Laryngoscopic LPR signs	Group I = manifest LPR (n = 25)	Group II no LPR symptoms (n = 25)			Total (n = 50)	p-value (I vs II)
		A = LPR-free (n = 23)	B = silent LPR (n = 2)	Total (n = 25)		
Vocal fold edema	23 (92%)	0	2 (100%)	2 (8%)	25 (50%)	0.00
Diffuse laryngeal edema	21 (84%)	0	2 (100%)	2 (8%)	23 (46%)	0.00
Erythema/hyperemia	20 (80%)	0	2 (100%)	2 (8%)	22 (44%)	0.00
Posterior commissure hypertrophy	19 (76%)	0	1 (50%)	1 (4%)	20 (40%)	0.00
Thick endolaryngeal mucus	13 (52%)	0	1 (50%)	1 (4%)	14 (28%)	0.00
Granuloma	8 (32%)	0	0	0	8 (16%)	0.005
Pseudosulcus	6 (24%)	0	0	0	6 (12%)	0.009
Ventricular obliteration	5 (20%)	0	1 (50%)	1 (4%)	6 (12%)	0.09
RFS (mean)	8.44	0	7	0.56	-	0.00

LPR: Laryngopharyngeal reflux, GERD: Gastroesophageal reflux disease, RFS: Reflux Finding Signs.

aged >70 years, and conversely, found heartburn ranging from 82% in patients aged <21 years to 34% of those aged >70 years [15].

In the current study, 39 patients (78.0%) were obese (mean BMI = 31.8). Obesity was confirmed to be a strong predictor (95%) [16], link to GERD-related symptoms [17]-[19], and its complication up to esophageal adenocarcinoma [20].

Heartburn was reported by 3/4 of the studied patients (38/50 patients; 76%), comparably present in Groups I and II (20 patients; 80% and 18 patients; 72% respectively), meanwhile grade A was more in Group II than in Group I (19 patients; 76% versus 15 patients; 60% respectively), while grades B, C & D (moderate & severe) are more in the Group I than in Group II. This confirmed the fact that heartburn was the only symptom related to GERD and LPR severity [21].

Haematemesis was reported by 4 patients (8%), comparably present in Groups I and IIA. It is worth noting that they were following up their underlying oesophageal varices, complication of cirrhosis. This agrees with El-Serag who related history of haematemesis to positive GERD endoscopic examination [13].

Regarding LPR, manifest LPR was present in 25 patients (29%) which is lower than that reported in an international survey (60%) [22]. Also, Merati documented significant relation between acid reflux events and LPR (p = 0.003) [23].

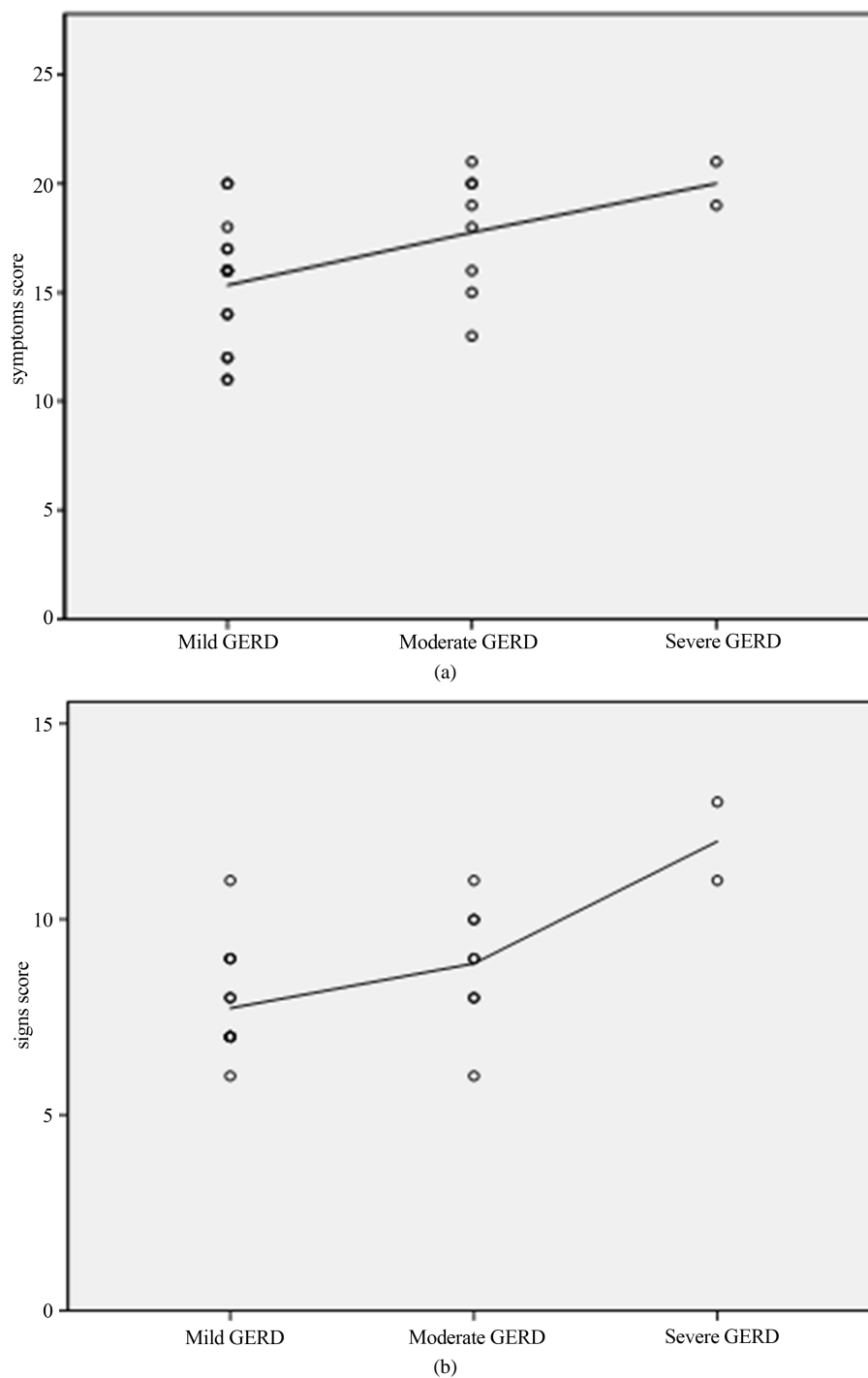


Figure 2. (a) Correlation between GERD grade and RSI, GERD: Gastroesophageal reflux disease, RSI: Reflux symptom index ($R = 0.482$, p value = 0.015); (b) Correlation between GERD grade and RF; GERD: Gastroesophageal reflux disease, RFS: Reflux finding score ($R = 0.544$, $p = 0.005$).

LPR was not significantly related to either sex or age. On the contrary, Patigaroo *et al.* in their LPR study, found gender and age predilection (male:female = 2:3, and patients mostly-40%-belonged to age range 31 - 40 yrs) [24]. Mean age recorded in manifest LPR was slightly higher than GERD (40.4 versus 40.1 years). This was higher than that recorded by previous studies *i.e.* 38 and 32.4 years [24] [25].

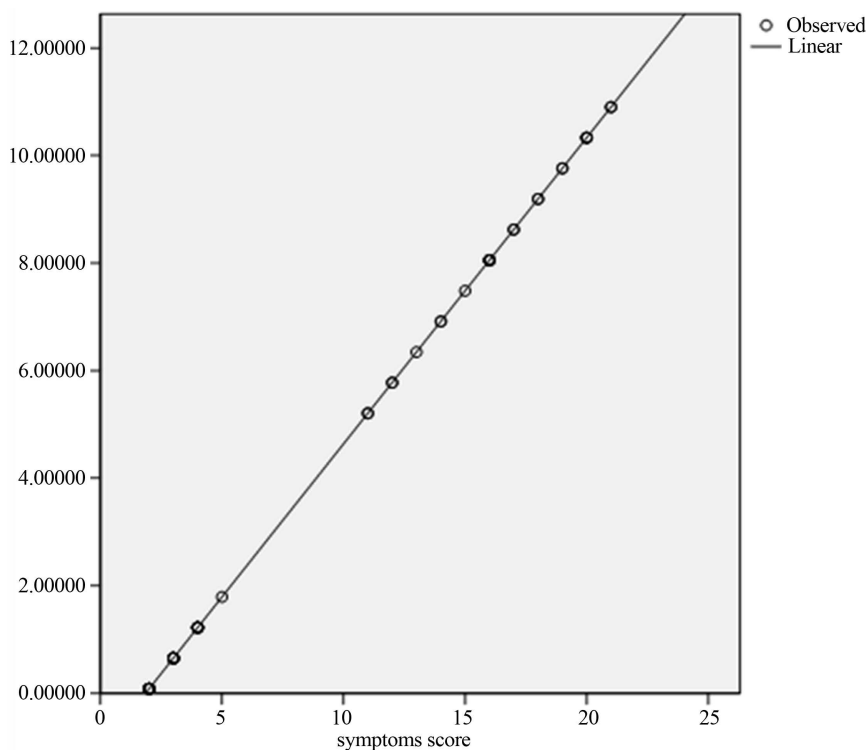


Figure 3. Predictability of RSI according to RFS. Overall accuracy = 98%, $R^2 = 0.86$, p-value = 0.00. Sensitivity = 100%, specificity = 95.8%, PPV = 96.3%, NPV = 100%.

In this study, postnasal drip and throat clearing were the most prevalent symptoms (96% each). Throat clearing is the most related symptom to LPR [21]. They were followed by dysphagia, hoarseness (68% each), and globus (56%). This agrees with other studies which stated that sore throat, hoarseness, and choking cough are the most reliable symptoms of LPR [26] [27]. While annoying cough and post prandial/positional cough were the least symptoms (48% and 40% respectively). This figure is close to that recorded in previous studies e.g. Irwin *et al.* (48%) who stated that chronic cough can be the sole symptom of GERD [28], and Patigaroo *et al.* (56%). GERD is generally considered one of the three main causes of chronic cough [29]. Also, 70% of LPR are found in patients with dysphagia [30].

These figures are less than that recorded by Kouffman; throat clearing (98%), persistent cough (97%), globus (95%), and hoarseness (95%) [22], and Said; persistent irritative cough (92%), sore throat (85%), globus (83%) [31]. On the contrary, Patigaroo *et al.*; clearing of throat (64%), globus (74%) [24], and less figures reported by Youssef and Ahmed recorded; cough (49%), followed by globus (46%), throat clearing (36%), and hoarseness (25%) [25], and Qadeer *et al.*; sore throat (40%), hoarseness (30%), and cough (20%) [27].

Meanwhile, hoarseness was intermediate to previous studies e.g. >50 [32], 62.8% [33], and 78.8% [34].

Accordingly, the mean (RSI) score in manifest LPR was 16.48, while Patigaroo *et al.* reported higher score *i.e.* 24.75 [24].

All of the studied GERD patients in this study had oesophagitis at variable degrees, as all of them were enrolled already diagnosed endoscopically, not on clinical suspect. Many other studies reported normal oesophogscopy (62.7%, 59.6%, 60% - 70%, and 50% [31] [35]-[37]). It was even found in the minority of patients [38] for poor correlation between GERD clinically and histopathologically [35]. Gastroscope revealed inverse relation between grade of GERD and its incidence *i.e.* A (68%), B (28%), while C & D (4%). This is almost similar to Mearin *et al.* findings; A (32%), B (38.8%), C (25%), and D (4.2%) [39].

Hiatus hernia was present in 11 patients (22%), comparably detected in both groups (6 and 5 patients in Groups I and II respectively). It was documented for its high specificity (95%) in predicting GERD [16], even stated as a *sine qua non* for GERD, and that both were formerly considered synonyms [40]. Also, Fein *et al.* detected it in 75.6% of GERD [41].

Barrett's esophagus was detected in 2 patients of GERD (4%), both belonged to Group I. It was lower than that recorded previously e.g. 7.4% [42], 10% [43], and 5% - 15% [44]. However, other studies reported extreme values e.g. 1% [13], and Koop who found it frequently in GERD patients [45].

None of the patients showed esophageal carcinoma. This agrees with the fact its risk is low despite being strongly associated with GERD [44].

The commonest laryngoscopic signs were vocal fold oedema, diffuse laryngeal oedema, erythema and posterior commissure hypertrophy (50%, 46%, 44%, 40% respectively). All were significantly higher in Group I than in Group II (92%, 84%, 80% and 76% versus 8%, 8%, 8% and 4% respectively). This is lower than that recorded in an international survey *i.e.* arytenoid erythema (97.5%), vocal cord erythema (95.7%) and edema (95.7%), posterior commissure hypertrophy (94.9%), and arytenoid edema (94.0%) [22]. However, they were higher than that recorded by Qadeer *et al.*; medial arytenoid wall erythema/edema (60%), interarytenoid erythema (50%), and arytenoid complex erythema/edema (50%) [27], Youssef and Ahmed; arytenoids erythema (54%), vocal cord oedema (27%) [25], and Said; posterior commissure injection 82%, vocal cord edema (74%), laryngeal erythema (77%) and subglottic edema (24%) [31].

Thick endolaryngeal mucus was detected in 14 patients (28%); mostly (13/14 patients; 92.8%) in Group I (52%), the left patient was nonsymptomized. This is higher than that recorded by Ylitalo and Ramel; 50% - 60% in LPR [46].

Laryngeal granuloma was detected in 8 patients (16%), all belonged to Group I (32%). This figure is intermediate to other studies e.g. Maronian *et al.* found GERD in all patients with organic subglottic stenosis and 71% with idiopathic subglottic stenosis. They concluded GERD a synergistic factor that stimulates laryngeal granulomatous reaction that may result in stenosis [47]. Also, Ylitalo and Ramel, and Ohman *et al.*; 65% - 74% respectively [46] [48]. On the contrary, Youssef and Ahmed (2%) [25] in LPR.

Pseudosulcus was detected in 6 patients (12%), all belonged to Group I. It is confirmed as a strong predictor (90%) for LPR [49].

Accordingly, mean RFS of Group I was 8.44, which is lower than that recorded by Patigaroo; 12 [24]. Moreover, 2 patients of Group II (Subgroup IIB = 8%), had positive laryngoscopic signs of LPR and both recorded RFS 6 and 8 (mean RFS = 7), therefore defined as "Silent LPR".

In this study, both RSI and RFS were significantly correlated with GERD grade ($p = 0.015$ and 0.005 respectively), and RSI was a significant predictor for RFS ($p = 0.00$), despite the stated fact that the endoscopic laryngeal signs do not correlate with LPR symptom severity, and treatment is recommended to continue for ≥ 6 months or until complete resolution of signs [3] [50]. Also accurate clinical assessment of LPR is likely to be difficult because laryngoscopic signs may show inter-observer variation [51]. Meanwhile, mild LPR can be confused with other laryngeal conditions [5]. LPR was detected in healthy people [33], reaching up to 86% of asymptomatic GERD volunteers [52].

5. Conclusion

RSI is a significant predictor for RFS, and both, RSI and RFS, are significantly proportionate to GERD, yet Silent LPR did exist among control patients.

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