

The prevalence of gastroesophageal reflux and helicobacter pylori in chronic non-specific pharyngolaryngitis

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Abstract

Aim: to identify the association incidence of *H. pylori* infection and gastroesophageal reflux in the patients suffering from chronic non-specific pharyngolaryngeal diseases symptoms.

Material and methods: Urea breath test, gastrointestinal (GI) endoscopy, flexible pharyngolaryngeal endoscopies from 76 adult patients suffering from chronic non-specific laryngeal and pharyngeal diseases symptoms

Result: Among 76 patients represented with chronic pharyngolaryngitis there were (41 ± 0.45) complaining of dysphagia (54 ± 0.45) of foreign body sensation (46 ± 0.5), of chronic dry cough (39 ± 0.5), with nocturnal choking (67 ± 0.48) with recurrent sore throat (48 ± 0.37), with post nasal drip, (63 ± 0.35) of frequent hawking (41 ± 0.48), voice fatigue (49 ± 0.5), of heart burn, (51 ± 0.47) with posterior laryngeal edema (51 ± 0.36), with vocal cord edema and erythema (12 ± 0.5) with vocal cord nodule, there were 42(55.2%) GER, 41(53.9%) with gastritis, with 21(27.6%) gastric ulcers and 27(35.5%) *H. pylori* positive patients and 7 (9.2%) non-GER non-*H. pylori* with significant p value (p<0.05). No significant relationships between *H. pylori* infection and GER found in the chronic non-specific pharyngolaryngitis and patients' demographic data, their unhealthy habits and reflux-related symptoms or signs were obtained.

Conclusion: There was a high prevalence association between both *H. pylori* infection and GER with chronic non-specific pharyngolaryngitis, and the GER is significantly higher in its association with chronic non-specific pharyngolaryngitis.

Introduction

It has been well demonstrated that gastroesophageal reflux is a retrograde flow of gastric contents into the esophagus, leading to disorders in organs other than the esophagus [1]. In contrast to the typical presentation of classic GER with heartburn and distal esophageal acid regurgitation after transient relaxation of the lower esophageal sphincter, extraesophageal reflux disease, termed laryngopharyngeal reflux often results in atypical manifestations with pharyngeal, laryngeal, and pulmonary disorders [2]. GER was well known to be a contributing factor in posterior laryngitis and laryngeal contact ulceration or granuloma formation, laryngeal cancer, chronic hoarseness, pharyngitis, asthma, pneumonia, nocturnal choking [3]. GER diseases were believed to cause esophageal reflux of gastric contents with direct contact and subsequent injury of the pharyngeal or laryngeal mucosal surfaces [4].

Because many patients are not aware of GERD as a possible causative factor for their varying medical complaints, they may present to otolaryngologists with symptoms such as dry or sore throat, Globus sensation, hoarseness, chronic cough, dysphagia, or buccal burning [5]. However, otolaryngologic examinations merely demonstrate striking pathological findings, and the underlying disease of LPR is not primarily diagnosed. Frequently, the misdiagnosed patients are commonly treated for (non-allergic) rhinitis with postnasal drip, nonspecific rhino pharyngitis, or recurrent sinusitis [6]. *Helicobacter pylori* infection caused by a gram-positive curved or spiral organism was considered as one of the most common gastric human bacterial infections, affecting

more than half of the world's population [7]. It had been proved that *H. pylori* played a significant role in the pathogenesis of chronic gastritis, duodenal and gastric ulcers, adeno carcinoma, and gastric lymphoma [8]. Although, the primary localization of this bacterium is the gastric mucosa, the recent literatures conducted that *H. pylori* might also be isolated from saliva, pharyngeal lymphoid tissue, nasal and sinus mucosa, oropharyngeal aphtha's ulcers, middle ear effusion, and larynx [9]. *H. pylori* could also cause vocal fold polyps, laryngeal cancer and other benign laryngeal lesions [10]. Some recent studies and had demonstrated that *H. pylori* could be an independent risk factor for the development of the hypopharyngeal carcinoma. Despite of the fact that modern scientists have been performing so many researchers on *H. pylori*, the routes of the bacteria entering the upper airway, as well as the relationship between gastroesophageal reflux and *H. pylori* in the upper airway also still unclear [10].

Patients and methods

The study was conducted at the ear, nose and throat (ENT) department Taiba hospital and GIT department Amiri hospital

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ministry of health, Kuwait from 2014 September to 2016 June. In 76 adult patients from 21 to 69 years old, who had experienced symptoms of chronic non-specific pharyngolaryngitis symptoms for 3 months or longer (dysphagia, odynophagia, Sore throat, heart burn, chronic cough, hemming, hawking, hoarseness of voice, post nasal discharge and foreign body sensation). The patients included 32 men and 44 women with a mean age of (46.9 ± 1.5) years. All patients were initially evaluated by complete medical history and physical examination with clinical ENT examination. CT scan of the para nasal sinuses were performed for all patients, neck ultrasound was also performed to exclude any thyroid or other neck swellings.

Nasopharyngeal endoscopy and flexible fiberoptic endoscopic laryngopharyngoscopy, complete assessment (function, shape, color, appearance) of the mucosa lining the vocal and ventricular folds, the laryngeal cartilages, the posterior commissure, the interarytenoid area, and hypo-pharyngeal regions.

Laryngeal changes were reported as, inflammation, oedema, ulceration, and nodules formation. Laryngeal changes with erythema of the posterior vocal folds and inter arytenoid area were coded as posterior laryngitis. Mucosal changes of posterior laryngitis were often accompanied by oedema of the vocal folds and inflammatory reactions of the interarytenoid area.

Nowadays, the 13C-urea breath test (UBT) is one of the gold standard and reliable non-invasive methods for the diagnosis of *H. pylori* infection. The examination is simple, innocuous when, easy to repeat, highly accurate, and requires a low number of precautions to obtain reliable results. It is particularly suitable for epidemiological studies in children and adults, in all clinical conditions where endoscopy is not strictly necessary, and to check the success of eradication regimens. The new and cheaper measuring equipment, the possibility of using a lower urea dose in capsules, and the patients had to be fasting for not less than 4 hours the take the capsule and then wait for 15 minutes and then blow, as well as shorter than usual sampling times, will certainly promote an increasingly broader application of this test [11].

Gastrointestinal evaluation was done by upper gastrointestinal (GI) endoscopy performed with (oesophago gastro duodenoscopy, and the Gastrointestinal physician was blinded for the laryngeal findings. Esophago gastro duodenoscopy is a well-established diagnostic test to evaluate mucosal injury and define the severity of esophagitis and gastritis. Informed consent was taken before doing the procedure, Propofol 100 mg IV was given and xylocain spray also was applied. In the present study, pH monitoring was not performed because not all the patients agreed to undergo this procedure. Verbal consent was from each patient before starting the management.

Patients with positive *H. pylori* were received medical triple regimen with 20 mg omeprazole twice daily for one month, Klacid 500 mg twice daily, and Amoxil 500mg three times daily for at least 15 days. Patients with reflux disease or gastritis, or both, received (20-40 mg) omeprazole daily for at least 4 weeks, depending on the severity of the mucosal finding according to Severity. All patients were advised to follow general anti reflux precautions including avoiding the spicy food, elevating the head of the bed and not eating for 2 or 3 hours before bedtime, stop smoking and start walking.

Results

Statistical method

The data were analyzed using IBM SPSS program (version 22). Data were expressed as (mean ± SD). The level of significance was taken as

p-value ≤ 0.05 and the results are presented in tables. Comparison of the study groups was done by Chi-square test (χ^2) and Macnemar test.

The demographic line data

The study contained 76 patients 32(42.1%) males and 44(57.9%) females as shown in Table 1. The age range was 44 to 66.3 years old with mean age (46.9 ± 1.5), 33(43.4) of them were smokers, 19 GER, 18 *H. pylori* positive and 1 non-GER non *H. pylori*. The patients presented with varying oral, pharyngeal, laryngeal, and pulmonary symptoms lasting for at least 3 months. There were 41 (53.9%) patients (22 GER, 16 *H. pylori* and 3 non-GER non *H. pylori* positive) complaining of dysphagia, 54(71.1%) (29 GER, 23 *H. pylori* and 2 non-GER non *H. pylori*) complaining of foreign sensation, 46(60.5%)(20 GER 22 *H. pylori* and 4 non-GER non *H. pylori*) were represented with chronic dry cough sensation, 39(51.3%) (22 GER,13 *H. pylori* and 4 non-GER non *H. pylori*) were complaining of chocking, 36(47.4%) (20 GER,13 *H. pylori* and 3 non-GER non *H. pylori*) were represented with hoarseness of voice, 67(88.2%) (37 GER , 23 *H. pylori* and 7 non-GER non *H. pylori*) complaining of recurrent sore throat, 48(63.2%) (26 GER,17 *H. pylori* and 5 non-GER non *H. pylori*)were represented with chronic post nasal drip, 63(82.9%) (35 GER,22 *H. pylori* and 6 non-GER non *H. pylori*) complaining of howking, 41(53.9%) (23 GER,12 *H. pylori* and 6 non-GER non-*H. pylori*)with voice fatigue,49(64.5%)of heart burn 29 patient in GER,16 in *H. pylori* and 4 in non-GER non *H. pylori*. As shown in Table 2.

There was a significant difference with p value <0.05 in smoking, dry cough and foreign body sensation being more presented in GER patients than the *H. pylori* positive patients, while in the other symptoms there were no significant difference in their presentations.

The result of Laryngopharyngeal endoscopies

Inflammatory disorders and allergic rhinitis of the nose and the para nasal sinuses were excluded by history, nasal endoscopy, and Water's view x-ray or computed tomography scan of the paranasal sinuses in all patients (Figure 1).

As shown in Table 3, There were 51(67.1%) (27 GER, 18 *H. pylori* and 6 non-GER non-*H. pylori*) had posterior laryngeal oedema, 44(57.8%)(24 GER,15 *H. pylori* and 5 non-GER non-*H. pylori*) had vocal cord oedema and erythema, 12(15.8%) (6 GER, 4 *H. pylori* and 2 non-GER non *H. pylori*) were represented with vocal cord nodule, with a significant difference with p value <0.05 for) for the incidence of GER, *H. pylori* patients and non-GER, non-*H. pylori* patients among chronic pharyngolaryngitis patients using chi square test while there were no significant difference (p value>0.05) for Posterior laryngeal oedema, Vocal cord oedema and erythema or Vocal cord nodule, as show in Figure 2.

The result of upper gastrointestinal (GI) endoscopy and urea breath tests

As shown in Table 3, there were 27(35.5%) of total 76 patients *H. pylori* positive and 42(55.3%) patients of total 76 patients were

Table 1. Showing the demographic data of the patients. No significance difference regarding to the age, sex for the groups of patients (p value >0.05)

Sex	Number (76)	P value
Male	32	0.94
Female	44	
Age	46.9 ± 1.5	

Table 2. Showing the demographic data of the patients. There is a significant difference (p value<0.005) for smoking and foreign body sensation using chi square test comparing all groups, but there is no significant difference (p value>0.05) for the other symptoms

	Number of total (76)	Percentage (%)	P value
Dysphagia	41		
GER	22	53.90%	
<i>H. Pylori</i>	16		0.7
non- GER, non- <i>H. Pylori</i>	3		
smoking	33	43.40%	
GER	23		0.05
<i>H. Pylori</i>	9		
non- GER, non- <i>H. Pylori</i>	1		
Horsness of voice	36		
GER	20	47.30%	
<i>H. Pylori</i>	13		0.96
non- GER, non- <i>H. Pylori</i>	3		
Voice weakness	41		
GER	23	53.90%	
<i>H. Pylori</i>	12		0.14
non- GER, non- <i>H. Pylori</i>	6		
Dry coughing	48		
GER	20	63.10%	
<i>H. Pylori</i>	22		0.019
non- GER, non- <i>H. Pylori</i>	4		
Foreign body sensation	54		
GER - <i>H. Pylori</i>	29	71%	
Non- GER non- <i>H. Pylori</i>	23		0.012
Post nasal drip	48		
GER	26	63.10%	
<i>H. Pylori</i> -Non GER, non- <i>H. Pylori</i>	17		0.88
Hawking	63		
GER - <i>H. Pylori</i>	35	82.80%	
Non- GER non- <i>H. Pylori</i>	22		0.95
Recurrent sore throat	67		
GER - <i>H. Pylori</i>	37	88.10%	
non- GER, non- <i>H. Pylori</i>	23		0.55
Heart burn	49		
GER - <i>H. Pylori</i>	29	64.40%	
non- GER, non- <i>H. Pylori</i>	16		0.6
<i>H. Pylori</i>	4		

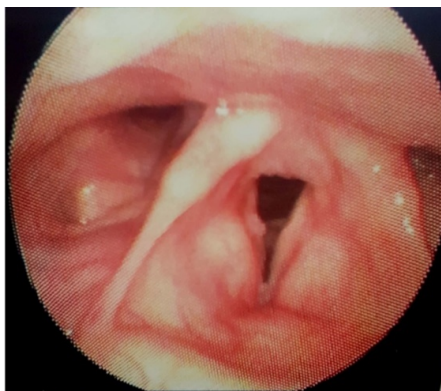


Figure 1. Right vocal cord minute nodule with posterior pharyngeal and vocal cords edema and congestion manifestation of GER

confirmed as GER disease positive and 7(9.7%) patients had no *H. pylori* nor GER diseases showing a significant difference at p value <0.005 by using Macnemar test for the chronic non-specific pharyngolaryngitis. Also, there were 41(53.9%) (14 GER, *H. pylori* and 0 non-GER non-*H. pylori*), had gastritis with a significant p value <0.005 (Figure 3).

Discussion

There is increasing evidence that GERD and helicobacter pylori may be associated with chronic non-specific laryngopharyngeal diseases [12]. Sometimes, patients seem not to be aware about the extent of GERD or *H. pylori* and their associated extraesophageal laryngopharyngeal symptoms may be the early presentation. Apart of that fact is the patients with GERD often may become symptomatic in the upper respiratory tract, and laryngopharyngeal findings are subtle and sometimes hard to detect. The patient was mainly complaining of dysphagia, horsiness of voice and chronic dry cough for more 3 months, post nasal discharge, foreign body sensation, chocking, recurrent



Figure 2. Inter arytenoids and vocal cords oedema and congestion

Table 3. There is a significant difference (p value<0.005) for the incidence of GER, *H. Pylori* patients and Non GER, Non *H. Pylori* patients among chronic pharyngolaryngitis patients, also for the incidence of gastritis among the groups of patients but there is no significant difference (p value>0.05) for Posterior laryngeal edema, Vocal cord edema and erythema or Vocal cord nodule

	No.	Name of test	P value
GER patient	42(55.3%)	Macnemar test	P<0.0001
<i>H. Pylori</i> patients	27(35.5%)		
Non-GER, non- <i>H. Pylori</i> patients	7(9.2%)		
Gastritis	41(53.9%)	Macnemar test	0.000
- GER - <i>H. Pylori</i>	14		
- non- GER, non- <i>H. Pylori</i>	27		
Posterior laryngeal oedema	51(67.1%)	Macnemar test	0.53
- GER	27		
- <i>H. Pylori</i>	18		
- non- GER, non- <i>H. Pylori</i>	6	Macnemar test	0.57
Vocal cord oedema and erythema	44(57.8%)		
- GER	24		
- <i>H. Pylori</i>	15	Macnemar test	0.62
- non- GER, non- <i>H. Pylori</i>	5		
<i>H. Pylori</i>			
Vocal cord nodule	12(15.7)	Macnemar test	0.62
- GER - <i>H. Pylori</i>	6		
- non- GER, non- <i>H. Pylori</i>	4		
<i>H. Pylori</i>	2		

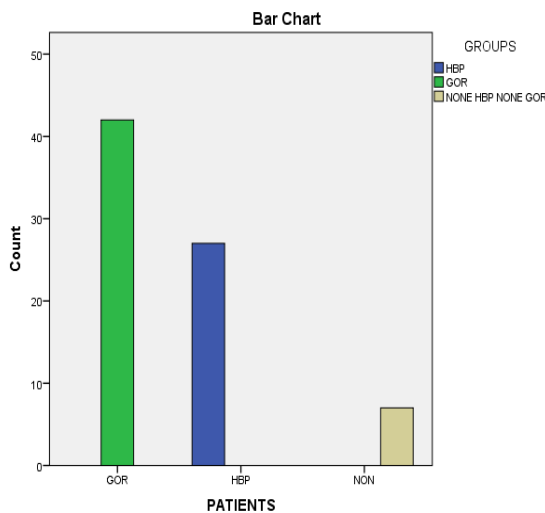


Figure 3. The prevalence of GER and H Pylori among the group of patients

sore throat, hawking, and heart burn those were the most common presentation of our patient group. Flexible pharyngolaryngoscopy showed posterior laryngeal oedema with erythema and oedema of the posterior part of the vocal cords, and minute vocal cord nodules and also it showed signs of chronic pharyngitis in all patients. The result of upper gastrointestinal (GI) endoscopy demonstrated GERD and some other upper gastrointestinal (GI) diseases. This result was also proved by Tauber et al, (13) who demonstrated that some of the laryngopharyngeal symptoms can be predictors of occult gastroesophageal diseases, including GERD or hiatal hernia. Symptoms such as dysphagia, sensation of Globus pharyngeus, postnasal drip, hoarseness, and other laryngeal disorders are not always caused by any primary otorhinolaryngological disease but may be related to upper GER diseases so a careful history, investigations and wide based knowledge of the disease syndromes are important for diagnosing GERD. In the present study, there were 53.9% of patients had different grads of gastritis being significantly higher in *H. pylori*.

In the present study, there were about (55.2%) of our chronic laryngopharyngitis had GER whereas, Deveney et al. [14] had demonstrated GERD by EGD in 43% of patients (13 of 28) with hypopharyngeal or laryngeal mucosal changes. other authors [14,15] proved that more than (62%) of their chronic pharyngolaryngitis patients had GER association, moreover from (30% to 86%) developed laryngopharyngeal reflux, as demonstrated by changes in the electrodes above the upper esophageal sphincter. Wilson et al. [16], conducted that at least 10% of all patients presenting to the ENT clinics have symptoms related to GERD4.

The wide ranges of GERD association incidence, which have been documented in all of those studies, might be explained by patient selection criteria, different laryngeal lesions, various definitions of "GER" disease, and also various methods of diagnosis GERD such as upper GIT endoscopy, 24-hour pH monitoring with single, double, or even triple probes, radiographic and manometric evaluation, and symptomatic assessment [17].

In the present study, there were (35.5%) 27 of 76 patients represented with *H. pylori* positive diagnosed by urea breath test (Figure 3). Some literatures [18] conducted 23% *H. pylori* positive in their study of total 30 patients. Tauber S et al. [13] showed that *H. pylori* infection in the biopsy material from the larynx was found in (45.5 %) of all the patients with chronic laryngitis and (46.2 %) in patients of

laryngeal cancer. Burduk PK et al. [18] conducted that that *H. pylori* is identified in almost half of the investigated patients with benign laryngeal diseases (in 40.6%-47.3 %) of cases. Izadi et al. [19] and Cekin et al. [20] had determined the association of *H. pylori* in 9.1-71.4 % by using an accurate method of (PCR), while identifying *H. pylori* DNA which support the hypothesis of a possible relationship between the etiological *H. pylori* and benign laryngeal diseases. Zhuo et al. [21] demonstrated that the risk of developing laryngeal cancer is two times higher for the subjects infected with *H. pylori*, than for those in the control group, in their study using both serological studies data that show immune response to *H. pylori*, a marker of prior infection with this organism, and the research data of the biopsy material from the laryngeal region, *H. pylori* is found in 46-70% of cases of the patients with laryngeal cancer, i.e., significantly more often than in the patients operated for benign laryngeal lesions, which suggests that *H. pylori* may be an independent factor of squamous cell carcinoma of the larynx

H. pylori is a (microaerophilic), gram-negative spiral organisms. *H. pylori* has been proved to be associated with Several factors causing epithelial damage including vacuolizing cytotoxin (VacA), cytotoxin associated gene A (cagA), surface lipopolysaccharide (LPS), bacterial urease, flagella, surface adhesins, oxidizing radicals and cytokines produced by leukocytes. *H. Pylori* had lipopolysaccharide in its cell wall, which was considered as a powerful immunologic agent, stimulating an inflammatory reaction leading to endothelial cells destruction. *H. pylori* need a microaerophylic environment and (5% of CO₂) is necessary for its reproduction. The produce urease enzyme which can alter the acidic environment to facilitate its colonization [22]. Although, the gastric mucosa was considered as the only habitat for *H. pylori*, it also was isolated from dental plaque, oral lesions, saliva, tonsils and adenoid tissue but the exact mechanism was still unclear. It was suggested that *H. pylori* contaminated gastric fluid enters to nasopharyngeal cavity by the GER and colonizes the pharyngeal and laryngeal mucosa. From these localizations, the bacterium ascends to the middle ear and the paranasal sinuses directly or by the reflux, and may trigger some pathological changes. Some literatures indicated that after nasopharyngeal mucosa exposure to gastric acid, Eustachian tube dysfunction developed also reflux of acidic gastric content to the nasopharynx and nose leads to oedema and congestion of nasopharyngeal mucosa, causing a disturbance of middle ear and paranasal sinus pressure regulation and clearance. This process predisposes the inflammation of upper respiratory system diseases [23]. The present study revealed a non-significant difference between the GER disease and *H. pylori* infection in relation to the age or the sex of the patients.

Conclusion

There was a high prevalence association between both *H. pylori* infection and GER with chronic non-specific pharyngolaryngitis, and the GER is significantly higher in its association with chronic non-specific pharyngolaryngitis.

Compliance with ethical standards

Conflicts of interest: All authors have read and approved the manuscript and have no conflict of interest related to this paper.

Informed consent: Informed consent was obtained from all parents of individual participants included in the study.

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Summary

- This study conducted the prevalence of GER and *H. pylori* infection in chronic pharyngolaryngitis patients.
- There was a significant higher association between GER and chronic pharyngolaryngitis.
- Sometimes patient is complaining of chronic cough or chocking for more than 3 months and he doesn't know that he has GER or *H. pylori* so ENT doctor has to investigate for them
- By good treatment for GER and *H. pylori* all the extra gastric symptoms will be improves.

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