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# Gastro-Esophageal Reflux Is Not a Common Cause of Chronic Cough: A Singapore Case Series

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## *Abstract*

***Background:*** *Gastro-esophageal reflux disease (GERD) is believed to be one of the common causes of chronic cough. There is a paucity of data on GERD-related cough (GERC) from Singapore. Our aim was to examine the prevalence, demographics and clinical features of GERC patients visiting a large teaching hospital in Singapore.*

***Methods:*** *We did a retrospective review of patients referred to the respiratory clinics of Changi General Hospital for evaluation of chronic cough (≥6 weeks in duration) during a 6-year period (March 2010 to June 2016). All patients diagnosed with GERC were further classified into 2 groups based on the likelihood of esophageal reflux being the cause of cough, 1) Likely GERC and 2) Possible GERC. We describe the demographics, clinical characteristics and the outcomes of these patients.*

***Results:*** *Of the 330 chronic cough patients seen over a 6 years period, 45 patients (13%) were diagnosed with GERC. Most were women (69%), the median age was 53 years and the median duration of symptoms was 26 weeks. Of all subjects, 14 patients were in the Likely group and 31 in the Possible group. Throat symptoms or signs were found in 77 % of the patients.*

***Conclusions:*** *Amongst patients referred for cough to a specialist clinic, GERD was not seen as a common cause. Throat signs and symptoms were common and could add weight to the diagnosis of GERC. There was no particular timing for the cough with regards to day or night.* ***(J Respirol Indones 2022; 42 (2): 156-60)***

***Key Words:*** *chronic cough; GERD; GERC; PPI*

# Refluks Gastroesofagus Bukan Penyebab Umum Batuk Kronik; Seri Kasus Singapura

## *Abstrak*

***Latar Belakang:*** *Penyakit refluks gastroesofagus (gastro-esophageal reflux disease/GERD) diyakini sebagai salah satu penyebab umum batuk kronik. Saat ini data yang tersedia mengenai batuk terkait GERD (GERD-related cough/GERC) dari Singapura masih terbatas. Tujuan kami adalah untuk mengetahui prevalens, demografi dan gambaran klinis pasien GERC yang berobat di rumah sakit pendidikan besar di Singapura.*

***Metode:*** *Kami melakukan tinjauan retrospektif terhadap pasien yang dirujuk ke klinik respirasi Rumah Sakit Umum Changi untuk evaluasi batuk kronik (durasi ≥6 minggu) selama 6 tahun (Maret 2010 hingga Juni 2016). Semua pasien yang didiagnosis dengan GERC selanjutnya diklasifikasikan menjadi dua kelompok berdasarkan kemungkinan refluks esofagus menjadi penyebab batuk, yaitu 1) Likely GERC dan 2) Possible GERC. Kami menggambarkan demografi, karakteristik klinis dan hasil dari pasien ini.*

***Hasil:*** *Dari 330 pasien batuk kronik yang datang berobat selama 6 tahun, 45 pasien (13%) didiagnosis dengan GERC. Sebagian besar adalah perempuan (69%) dengan median usia 53 tahun dan median durasi gejala 26 minggu. Dari keseluruhan subjek, 14 termasuk dalam kelompok Likely dan 31 dalam kelompok Possible. Tanda atau gejala klinis pada tenggorokan ditemukan pada 77% pasien.*

***Kesimpulan:*** *Di antara pasien yang dirujuk karena batuk di klinik spesialis, GERD tidak dilihat sebagai penyebab umum. Tanda dan gejala klinis pada tenggorokan biasa terjadi dan dapat memperkuat diagnosis GERC. Tidak ada waktu khusus untuk batuk baik pada siang maupun malam hari.* ***(J Respirol Indones 2022; 42 (2): 156-60)***

***Kata Kunci:*** *Batuk kronik; GERD; GERC; PPI*

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## INTRODUCTION

Gastro-esophageal reflux disease (GERD) has long been believed to be a common cause of chronic cough, especially in non-smokers with a normal chest radiograph. The exact prevalence is not known and estimates have varied widely from 0 to 40%.[1] Recently however, cough experts have admitted that the association is more complex than previously believed and the high prevalence of GERC reported in older studies was probably exaggerated.[2–4]

There is no good diagnostic test to prove GERC. 24-hour esophageal multichannel intraluminal impedance monitoring combined with pH-metry, which is the gold standard test for GERD, is not helpful for diagnosing GERC, even when used with symptom indices.[5] Current guidelines do not recommend using diagnostic testing for management of GERC.

There are a few factors adding to the controversy. One is the relatively high prevalence of GERD in the general population, reported to be as high as 20% in Western countries and 6–18% in Southeast Asia.[6] Therefore, even in patients with proven GERD, one cannot be certain that it is the reflux that causes the cough. Another reason is that GERD can sometimes present only with extra-esophageal symptoms (atypical GERD) and chronic cough is believed to be one of them. However, this is very difficult to prove and empiric treatment with proton pump inhibitors (PPI) in patients with non-specific cough has not shown benefit.[7,8]

A third controversial area is the possible association of cough with 'weakly acid' or 'non-acid' reflux. These patients do not respond well to PPI and may benefit better with the usage of promotility agents or Baclofen (which inhibits relaxation of the lower esophageal sphincter) to treat the cough.[9]

With all these uncertainties, probably the best way to make a clinical diagnosis of GERC is to see improvement in cough to therapy in patients who have esophageal symptoms of GERD. To our knowledge, no studies on GERC have been done in Southeast Asia and our main objective was to examine our local population.

## METHODS

The study was done in Changi General Hospital, which is a 1100-bedded teaching hospital in Singapore. The study was done on patients referred to the respiratory clinics from March 1, 2010 to June 30, 2016. In our two clinics, all referrals for chronic cough were subjected to a cough questionnaire during their first visit. We used these questionnaires and review of the charts to identify and collect data on patients who met the criteria of GERC. GERC was defined as cough ≥6 weeks and at least one esophageal symptom (heartburn or acid regurgitation) as per the 2006 Montreal definition of GERD. Exclusion criteria were 1) Age <21 years; 2) Prisoners and 3) Pregnant women. We classified GERC patients into two groups based on the likelihood that reflux was the primary cause of the cough.

A subject was classified as likely GERC when there was improvement in symptoms after therapy and the absence of any other etiologies for chronic cough, while possible GERC was defined as when someone had esophageal symptoms, but there was uncertainty about whether GERD is the cause of cough. These included patients who did not respond to GERD treatment OR who defaulted follow-up visits OR were non-compliant to treatment OR had other etiologies that also could cause cough (asthma, upper airway cough syndrome, smoking). We examined the demographics and clinical characteristics of these patients. For patients diagnosed with likely GERC, we examined the medications used and the duration of treatment. We followed these patients up until June 30, 2018. The study was conducted in accordance of the amended Declaration of Helsinki. Singhealth Centralized Institutional Review Board approval was obtained prior to the commencement of the study (CIRB Reference number 2016/2421).

## RESULTS

Over the 6-year period, 330 patients were referred for chronic cough (Figure 1). Among all of them, 45 (13%) were diagnosed with GERC.

Table 1. Patients' Characteristics

| Parameter | N = 45 | Median | Range |
|---|---|---|---|
| Age | | 50 years | 21–79 years |
| Gender | | | |
| Male | 15 | | |
| Female | 33 | | |
| Race | | | |
| Chinese | 33 | | |
| Malay | 7 | | |
| Indian | 5 | | |
| Others | 3 | | |
| Duration of cough | | 26 weeks | 6–30 years |
| Timing of the cough | | | |
| Any time | 18 | | |
| Evening/night time | 22 | | |
| Day time | 5 | | |
| Throat symptoms or signs | 35 (77%) | | |

Most of them (69%) were middle aged women with median age 53 years (Table 1). The median duration of cough was 26 weeks. Three patients had a past history of GERD (including one already diagnosed with GERC) and one had pre-existing hiatal hernia. We excluded three patients who had been given a diagnosis of GERD secondary to laryngopharyngeal reflux (LPR). These cases were diagnosed by ENT specialists either because their cough had responded to empiric PPI therapy or had features of LPR on endoscopy. All 45 patients received high dose PPI in the form of omeprazole 40 mg BD. All except one patient received additional domperidone (for promotility action).

Domperidone was used in varying doses (10–20 mg tds) for varying periods (2 to 6 weeks). All patients were given a pamphlet which had advice on lifestyle modifications. There was no particular timing for the cough (day or night). In all 45 cases, the cough improved or was absent altogether when sleeping. 77% of patients had associated throat symptoms or signs (itchy sore throat, globus, constant throat clearing, hoarseness, cobblestone appearance of the posterior pharynx).

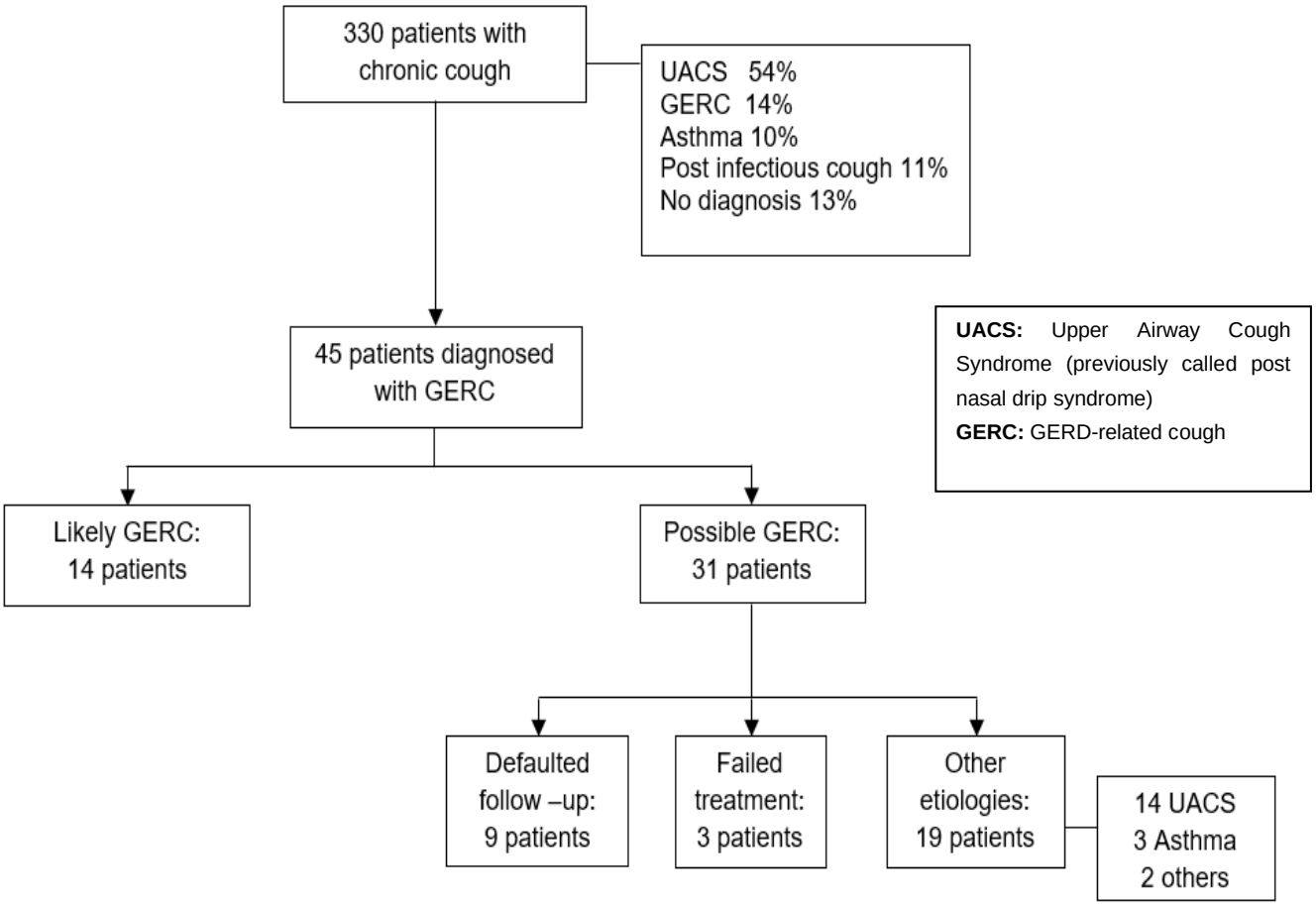


Figure 1. Flowchart of subject selection

The median duration for the next follow-up visit was 6 weeks (range 4 to 8 weeks). In the likely GERC group, most of the patients were middle-aged Chinese women with a median cough duration of one year. Throat signs/symptoms were seen in 7 patients. The median duration of initial therapy was 5.5 weeks (Table 2).

Table 2. Likely GERC

| Parameter | N = 14 | Median | Range |
|---|---|---|---|
| Age | | 48 years | 28–79 years |
| Gender | | | |
| Male | 5 | | |
| Female | 9 | | |
| Race | | | |
| Chinese | 9 | | |
| Malay | 2 | | |
| Indian | 1 | | |
| Others | 2 | | |
| Duration of cough | | 39 weeks | 6–15 years |
| Timing of the cough | | | |
| Any time | 5 | | |
| Evening/ nighttime | 5 | | |
| Day time | 4 | | |
| Throat symptoms or signs | 7 (50%) | | |
| Duration of initial therapy | | 5.5 weeks | 3–13 weeks |

As much as 69% were in the possible GERC group (see Figure 1). The most common reason to be included in this group was the presence of other etiologies that could have also caused the cough.

## DISCUSSION

Our study found that GERD was not a common cause (13%) of cough. If we were to infer the prevalence only from the Likely group, it would be much lower at 3%. A previous study done in Singapore on patients with unexplained chronic cough suggested that GERD was a common cause.[10] But these patients had no esophageal symptoms and were diagnosed either by response to empiric therapy or features of LPR on laryngoscopy. In the light of the recent literature, it is quite possible that the study overestimated the prevalence of GERC. In our study, most of our GERC patients were middle-aged women, which is in accordance to past studies which have shown that most patients with chronic cough belong to this demographic.[11]

Throat manifestations (sore throat, itchy throat, throat clearing, globus, cobblestoned pharynx) are well recognized in GERD and have been attributed to the refluxate bypassing the upper esophageal sphincter.[12] These were seen in majority (77%) of our patients. In our study, we did not include patients with endoscopic diagnosis of LPR, since this association is controversial.[11] Also, patients with severe cough might suffer from traumatic inflammatory changes in the larynx and there is a lack of agreement in literature about the laryngeal signs of LPR.[13] Although esophageal symptoms of GERD are mostly nocturnal, we found no time preference in our study group. This finding has also been seen in previous studies.[14]

Recent evidence suggests that PPI agents are not as efficacious as previously believed and is probably best used only in patients with esophageal symptoms.[8] Lifestyle modifications are possibly more beneficial and are recommended strongly in the 2016 CHEST guidelines.[4] Past guidelines had recommended a 3-month empiric therapy for non-specific cough to treat atypical GERD but evidence does not support such a practice and the latest guidelines advise against this practice.[3,4] Also, it may be difficult to convince patients to agree to a 3 months trial therapy. We did not prescribe empiric therapy in our patients. The median duration of initial therapy was 5.5 weeks. All cases except one were given the combination of PPI + domperidone, referred as “maximal medical therapy” by the 2016 ACCP guidelines.[4]

The rationale for adding a promotility agent like domperidone was to treat any non-acid reflux. Four patients did not respond to therapy. It is postulated that the cough might not have been due to esophageal reflux and just happened to co-exist with GERD or these were cases of GERD which were refractory to treatment. Another possibility is that the treatment period in these patients was inadequate (median 4 weeks, range 4–9 weeks). However, there is no evidence proving that the 3 months recommended by experts in the past is the optimum duration.

## CONCLUSION

In conclusion, the prevalence of GERC was low in our study. Since guidelines now use stricter criteria to diagnose and treat GERC, our findings may be just a reflection of the global population. Most of our patients had associated throat signs or symptoms. Although these are not specific for GERC, they may serve as adjuncts to the diagnosis. There is no nocturnal preference for GERC as is commonly believed.

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