

# Role of Comprehensive Lifestyle Interventions in Managing Gastroesophageal Reflux Disease Complicating COPD-OSA Overlap Syndrome

Iqbal Akhtar Khan<sup>1</sup> and Hamza Iltaf Malik<sup>2</sup>

<sup>1</sup> MBBS DTM FACTM PhD, Independent Scholar, Lahore-Pakistan.

<sup>2</sup> MBBS Northampton General Hospital, Cliftonville, Northampton, United Kingdom NN1 5BD.

**Corresponding Author:** Iqbal Akhtar Khan, Independent Scholar, Lahore Pakistan, profiakhan@gmail.com

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## Abstract

Although the term “lifestyle medicine” was first used as the title of a symposium in 1989 and of an article in 1990, its concept is not new. The towering figures in medicine: Huang Ti (2698-2598 BCE), Hippocrates (460-377 BCE) and Ibn Sina (980-1037CE) had the credit to link the natural effects of diet, lifestyle, emotion and environment with the preservation of health. Unhealthy lifestyle behaviors, a well proven primary source of the global burden of chronic diseases, are among the leading risk factors for increased disability-adjusted life years around the world. While, Gastroesophageal Reflux Disease and Chronic Obstructive Pulmonary Disease augment each other, COPD and Obstructive Sleep Apnea have a common pathophysiology and are known to coexist leading Flenley to coin the term “Overlap Syndrome”, in 1985. Behavioral therapy on each modifiable item, including diet and weight management, physical activity, smoking, sleeping pattern, stress and mood states have all been evaluated in the present study.

**Key Words:** lifestyle medicine, gastroesophageal reflux disease, chronic obstructive pulmonary disease, obstructive sleep apnea, behavioral modification

## Introduction

*“Lifestyle Medicine is the evidence-based practice of helping individuals and families adopt and sustain healthy behaviors that affect health and quality of life” [1].*

Although, American Cardiologist James Rippe has the credit to coin the term “Lifestyle Medicine”, the history of its evolution is deeply rooted in ancient medicine. *Nei Ching Su Wen*, the fundamental doctrinal source for Traditional Chinese Medicine, written by Huang Ti, known as the Yellow Emperor (2698-2598 BCE) beautifully links the natural effects of diet, lifestyle, emotion and environment with the preservation of health.

Influenced by Asclepius, the Greek god of healing, Hippocrates (460-377 BCE), the founder of medicine as a rational science, believed health to be the expression of a harmonious balance between the various components of man’s nature, the environment and lifestyle.

Ibn Sina (980-1037CE), in his Magnum Opus “Canon of Medicine”, has highlighted the key role of lifestyle and behavior modification (*Muddawa Salookia*) in maintaining and preserving health and he was the first to integrate psychological factors in theoretical and practical medicine.

The present study is aimed at defining the role of comprehensive lifestyle interventions in managing Gastro-esophageal Reflux Disease (GERD) complicating Chronic Obstructive Pulmonary Disease (COPD) and Obstructive Sleep Apnoea (OSA) Overlap Syndrome. These three interrelated conditions are discussed below.

### Gastroesophageal Reflux Disease (GERD)

GERD is a chronic and highly prevalent digestive disorder of multifaceted pathology. Whereas the discovery of proton pump inhibitors (PPIs) has revolutionised its management, serious concerns, however, have arisen in the recent past regarding their potential side effects, especially in the elderly. This has increased the importance of considering lifestyle interventions since these measures may reduce the need for acid suppression.

### Chronic Obstructive Pulmonary Disease (COPD)

COPD outstrips all the other comparators—heart failure, ischemic heart disease, diabetes and renal failure—as the cause of hospital admissions” [2].

COPD, a progressive inflammatory lung disease “*slowly robbing its sufferers of the ability to draw life-sustaining breath*” is a complex, multifaceted, under-diagnosed, debilitating, degenerative and

life-threatening global epidemic, killing on average one person every 10 seconds. It frequently affects people in their most productive years, gradually depriving them of their health and vitality. Although it is not fully reversible, much of its burden is either preventable or manageable with affordable and timely interventions. It is usually associated with significant concomitant chronic diseases, with pulmonary and extra-pulmonary manifestations and is an important public health challenge, throughout the world.

### Acute Exacerbations of COPD— (AECOPD)

AECOPD (acute or subacute worsening of symptoms mainly dyspnea) are a major cause of hospital admission and considerable healthcare costs. They have, therefore, become important events in the management of COPD as reduction in their frequency improves health related quality of life (HRQoL)

### Obstructive Sleep Apnea (OSA)

*“The worst thing in the world is to try to sleep and not to”*

These words of the great American fiction writer, Francis Scott Fitzgerald (1896-1940), describe what some 10 million Americans, with untreated OSA, endure every night. Defining OSA as an apnea-hypopnea index (AHI)  $\geq 5$  events/hour—as used by the Wisconsin Sleep Cohort—the prevalence is high; 24% in men and 9% in women aged 30 to 60 years.

COPD and OSA have common pathophysiology, for example smoking, and are known to coexist for which the term “Overlap Syndrome” was coined by Flenley in 1985. Consequently those with the dual burden have a much higher risk for worsening morbidity and early mortality, compared to those who only have one.

### Cause and Effect association between GERD and COPD

In a study, using the UK General Practice Research Database, to identify a cohort of patients with a first diagnosis of GERD (n = 4,391) and another cohort of patients with a first diagnosis of COPD (n = 1,628) during 1996, it was found that patients with a diagnosis of COPD are at a significantly increased risk of a diagnosis of GERD compared with individuals without COPD [3].

### GERD and COPD augment each other in three different ways:

#### (i)-- Impact of GERD on the severity of COPD

Whereas the prevalence of GERD in people with COPD ranges from 19% to 78%, it can adversely affect the clinical profile of those with moderate to severe COPD; the two possible mechanisms being pulmonary microaspiration and vagally mediated reflex bronchospasm [4].

#### (ii)—Impact of COPD on the severity of GERD

Whereas the prevalence of GERD in COPD patients is much more than the general population, wide variation exists in the reported prevalence. The prevalence of GERD in Japanese patients with COPD has been found to be up to 34% [5], in different studies. In a Korean National Cross-sectional Cohort Study, the figure was 28% [6] and in a prospective Spanish study pathological GERD symptoms were documented in 62% of COPD patients [7]. The use of bronchodilators (eg theophylline) and inhaled long-acting beta-agonists (LABA; eg salmeterol and formoterol), anticholinergics and corticosteroids may decrease the lower esophageal sphincter (LES) pressure, facilitating reflux of gastric contents. Thus a component of GER may be attributable to pharmacotherapy of concomitant COPD.

#### (iii)— Link between GERD and AECOPDs

It is known that GERD acts as a precipitating factor for AECOPD which were twice as frequent in patients with GERD than in those without [8]. In The Copenhagen City Heart Study of 9,622 patients [9], an American single-center retrospective analysis of 1,445 patients [10] and a nationwide Taiwan population-based study of 3,485 patients with COPD and symptomatic GERD [11], a protective effect of PPIs against worsening airway obstruction was reported.

### Lifestyle Interventions in the Triad of GERD, COPD and OSA

Lifestyle medicine “provides a nexus between public health promotion and clinical treatments, involving the application of environmental, behavioral, and psychological principles to enhance physical and mental wellbeing [12].

Behavioral therapy on each modifiable item, including diet and weight management, physical activity, smoking, sleeping pattern, stress and mood states (anxiety and depression) are all evaluated in the present study.

### Weight Management

Obesity, being of particular importance in the light of the global obesity epidemic, is a potential risk factor for GERD, COPD and OSA.

#### (A)- GERD

GERD has a proven connection with obesity, stronger in females. The American Society for Gastrointestinal Endoscopy identifies obesity as the leading cause of frequent GER. In a prospective cohort study, at the University of Kansas Medical Center, 332 adults (66% females) aged 18-65 years with BMI 25-39.9 kg/m<sup>2</sup> were enrolled in a structured weight loss program. Interventions included dietary modification, increased physical activity and behavioral change. Overall 81% of the participants had a reduction in GER score, 65% had complete resolution and 15% had partial resolution [13].

de Bortoli et al, from the University of Pisa, showed that voluntary and controlled weight loss can reduce symptoms, PPI use and dosage in patients with GERD [14]. In a large prospective population-based cohort, The Norwegian HUNT Study showed that weight reduction dose-dependently decreased GER symptoms [15].

#### (B)-COPD

In 650,000 subjects, evaluated as part of the Canadian National Health Survey, the prevalence of obesity was significantly higher in COPD subjects when compared to those without COPD (24.6% and 17.1%, respectively) [16]. The Copenhagen City Heart Study found that obesity was associated with a 20%–34% increase in the relative risk of all-cause mortality in patients with mild-to-moderate COPD compared with normal-BMI patients with comparable disease severity [17].

#### (C)-OSA

There is a strong bi-directional association between OSA and metabolic disorders such as obesity. In this sense, obesity is a well-established leading risk factor for OSA, and OSA itself may promote further weight gain. Young et al, in a community-based cohort of middle-aged subjects, showed that a 1-SD increase in BMI was associated with a fourfold increased risk for prevalent OSA [18]. In a randomized clinical trial at Kuopio University Hospital Finland of 81 patients (BMI 28-40) with mild graded OSA, followed for 1 year, intensive lifestyle counselling with a 10% weight reduction resulted in a 40% reduction in AHI (from 10 to 6 events/hour) [19]. Conversely, a 10% increase in body weight increased the AHI by 32% [20].

### Physical Exercise

*“There is growing evidence on the preventive value of exercise, and it is possible that, in the not too distant future, physical education will become a part of medicine”.*

Professor Peter Karpovich (1896-1975)

Exercise, according to WHO, is “*planned, structured, repetitive, and purposeful in the sense that the improvement or maintenance of one or more components of physical fitness is the objective*”. Its roots can be traced to the teachings of Maha Rishi Susruta (floruit 1500 BCE), who is believed to be the first to write a prescription for exercise.

#### (A)-GERD

In a cross-sectional Albanian study conducted on 1,000 adults ( $\geq 18$  years), a strong inverse relationship between physical activity and GERD was found [21]. In a large-scale Norwegian survey of a population of over 74,000 individuals (aged  $\geq 20$  years), a significant correlation was found between the number of exercise sessions, lasting at least 30 minutes, and decreased risk of GER [22].

#### (B)-COPD

In a German prospective cohort study, Waschki et al demonstrated that physical activity of patients with COPD decreases across all severity stages and this decline is parallel by a worsening of lung function and health status [23].

Conversely, Garcia-Aymerich et al, on the basis of a population based study in Copenhagen, demonstrated that COPD patients performing some level of regular physical activity had a lower risk of both hospitalization and mortality [24].

#### (C)-OSA

Evidence from epidemiological research suggests that individuals who are physically active have a reduced risk of OSA compared to individuals who are less active [25]. Kline conducted a randomized controlled trial to examine the efficacy of exercise training in the reduction of the severity of OSA in 43 sedentary, overweight adults aged 18-55 years who had an AHI  $\geq 15$ . A modest reduction in AHI was found despite minimal changes in body weight [26].

### Smoking

#### (A)-GERD

Smoking is known to impair esophageal acid clearance and reduce LES pressure. Multivariate analysis, in a prospective population-based cohort study of 3,153 GERD patients, revealed that the risk of GER was increased by 70% among daily smokers when compared with non-smokers [27].

#### (B)-COPD

Smoking is the leading cause of COPD and an important trigger factor for AECOPD. In the OLIN Cohort Study (Obstructive Lung Disease in North Sweden), it was reported that 50% of smokers eventually develop COPD [28]. Smoking cessation is the most effective strategy for slowing down the progression of COPD and reducing mortality in approximately 50% of smoker patients [29]. In the Lung Health Study, conducted in 10 clinical centers in United States and Canada, aggressive smoking intervention program showed significant reduction in the risk of hospitalization and total mortality [30].

#### (C)-OSA

Lin et al concluded that the effects of smoking on the pathophysiology of OSA include smoking-induced upper airway inflammation, stimulant effects of nicotine on upper airway muscles, and a "rebound effect" due to nightly short-term nicotine withdrawal [31].

### Diet (Type and Amount)

#### (A)-GERD

The amount of food, timing of meals and eating duration (interval between the first and last meal of the day), independent of energy intake, have been shown to play a major role in obesity (an important contributor to GERD, COPD and OSA). Most GER episodes occur within 3 hours after eating, possibly as a result of gastric distension. Patients complaining of GER are often advised to avoid large meals.

Different foods may influence the occurrence of GER events differently. In a Korean study, on patients attending the Digestive Disease Center, certain foods and drinks (hot spicy stews, rice cakes, ramen noodles, fried foods) were found to adversely affect variables such as LES pressure and esophageal acid exposure [32].

Whereas in an American cross-sectional study high dietary fat intake was associated with an increased risk of GER symptoms and erosive esophagitis, high fiber intake was linked to a reduced risk of GER [33]. A single-center open-label prospective study, conducted in Moscow, revealed that a fiber-enriched diet led to a significant increase of minimal lower LES resting pressure and a decrease of number of GER episodes [34].

#### (B)-COPD

There is an emerging evidence that nutrition can influence development and progression of COPD. A prospective cohort study of 44,335 Swedish men (aged 45-79 years) showed an association between consumption of fruits and vegetables and reduced incidence of COPD in both current and ex-smokers [35].

Two US prospective studies (Nurses Health Study and Health Professionals Follow-up Study) identified two major dietary patterns - the “prudent pattern”, with high intakes of fruit and vegetables, oily fish, poultry, whole-grain products and low-fat dairy products; and the “Western pattern”, characterized by a high consumption of refined grains, cured and red meats, desserts, French fries, and high-fat dairy products. Both studies consistently found that the “prudent pattern” was negatively and the Western pattern positively associated with a risk of self-reported newly diagnosed COPD in men and in women [36, 37].

#### (C)-OSA

The American Academy of Sleep Medicine recommends dietary-induced weight loss and exercise as lifestyle options for OSA. It has been found that the Mediterranean diet reduces mechanical loads and thus improves OSA severity compared to calorie-restricted low-fat diets.

### Eating Patterns (Dinner to Bed)

Dinner- to-bed time is the time between finishing the evening meal and going to bed. The American College of Gastroenterology Guidelines recommend that patients refrain from eating within 3 hours of sleeping.

#### (A)-GERD

The eating patterns implicated in GERD include avoidance of late-night eating and reduction in overall size and caloric density of meals. An age and sex matched case-control study, by Fujiwara et al, showed a significant association between a shorter dinner-to-bedtime interval and the risk of GER [38].

(B)-OSA

In a cross-sectional study of individuals aged 20-60 years with sleep apnea, it was found that those who had late meals and longer eating

duration had a worse sleep pattern and severity of apnea in addition to a higher risk of fatigue than individuals who were earlier eaters and those with shorter eating duration [39]. Trakada et al found that a high-fat meal before bedtime increased the number of episodes of apnea, suggesting that both meal timing and nutrient intake could affect AHI [40].

## Sleeping Postures

### (A)-GERD

Whereas gravity and anatomy play a pivotal role in finding relief from nocturnal GERD symptoms, the key to controlling nighttime GER is to keep stomach acid where it belongs— in the stomach.

#### (a) Head of Bed Elevation

GERD occurs more in the supine than in an upright position because of the effect of gravity. Hence, patients are traditionally advised to sleep propped up. Stanciu and Bennett studied the effect of head of bed elevation using 28cm blocks in 63 patients with GER. Those who slept with the bed head elevated experienced significantly fewer, shorter and less intense GER episodes. Acid clearance was faster compared with those lying flat [41].

#### (b) Left lateral versus right lateral decubitus position

The right lateral sleep position worsens GERD symptoms. Khoury et al reported that such patients have increased acid exposure and delayed esophageal acid clearance [42]. Moreover, this position tends to be associated with fluid regurgitation, cough, and choking, which can be alarming in the middle of the night.

When sleeping supine, acid escapes from the stomach and flows freely up the esophagus and beyond. Acid clearance from the esophagus is also poor leading to frequent symptoms of long duration. Sleeping in the left lateral decubitus position improves nocturnal esophageal acid clearance and refluxate composition compared with lying in the right lateral position [43]. It is the preferred position since the gastro-esophageal junction lies above the fundus of the stomach.

### (A)-COPD

Significant improvement in the quality of sleep has been shown with bed-head elevation and sleeping on a wedge. However, extra care is required in the selection of pillows. It is imperative that goose or duck feather pillows (triggers of COPD) be replaced by foam rubber material, for fear of harbouring the dust mite resulting in “feather duvet lung”.

### (C)-OSA

Whereas the supine sleep posture is consistently associated with more severe OSA indices, the relationship between apnea severity and prone posture is inconsistent [44]. Of note, the available positional therapy devices are quite useful. The slumber BUMP (essentially a belt with a pillow attached to the back) makes it uncomfortable to sleep on one's back, and promotes sleeping in a lateral position.

## Psychological Stress, Mood States (Anxiety and Depression)

### (A)-GERD

GER is significantly associated with psychosocial stress with severity proportionate to the degree of stress. Whereas GER aggravates stress and fatigue, the effect could be bi-directional. Stress has impacts on health-related behaviors such as smoking, diet, alcohol consumption, and physical activity, which in turn may influence the risk of GER.

### (B)-COPD

Depression and anxiety are prevalent among COPD patients and are associated with worse outcomes, including higher AECOPD rates, greater

functional limitation and increased mortality. In a population based cross-sectional study, there was a significantly stronger association of life event stress with depressive symptoms among individuals with COPD than among those without [45].

### (C)-OSA

In an individualized, prospective, longitudinal, interventional study, conducted at University Hospital São Paulo, it was found that nocturnal awakenings in OSA were associated with alterations in the hypothalamic-pituitary-adrenal axis (HPA). The resultant intermittent hypoxia, fragmentation, and sleep deprivation caused high levels of stress and cortisol release. Women were more vulnerable to stress than men, in all age groups [46].

## Conclusion

Referring to the definition of Lifestyle Medicine, by Garry Egger as “*the application of environmental, behavioural, medical and motivational principles to the management of lifestyle-related health problems in a clinical setting....Lifestyle medicine is not meant to be an alternative to conventional clinical practice, but rather a means to address the health challenges posed by changes to lifestyle in the past three to four decades*”[48], the present study has defined the pivotal role of comprehensive lifestyle interventions in the management of GERD complicating COPD and OSA Overlap Syndrome .

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## Conflict of Interest

Nothing to declare.

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