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The Association Between LPR, Obstructive Sleep Apnea, and Asthma - A Narrative Review

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Abstract

Background: Laryngopharyngeal reflux (LPR), obstructive sleep apnea (OSA), and asthma are common disorders increasingly recognized as interconnected conditions sharing inflammatory and mechanical mechanisms. Their coexistence may worsen symptoms and reduce quality of life.

Aim: To review current evidence regarding the association between LPR, OSA, and asthma, including shared pathophysiological mechanisms and clinical implications.

Material and Methods: A narrative review of meta-analyses, observational studies, and clinical reports examining prevalence, pathophysiology, clinical presentation, and treatment strategies related to LPR, OSA, and asthma.

Results: Studies demonstrate a significant overlap among these conditions. LPR is frequently observed in patients with OSA and asthma, while OSA prevalence is increased in asthmatic individuals. Proposed mechanisms include chronic inflammation, obesity, autonomic dysfunction, upper airway instability, and nocturnal hypoxia, creating a bidirectional cycle in which each disorder may aggravate the others. Continuous positive airway pressure (CPAP) therapy may improve reflux symptoms and asthma control, whereas proton pump inhibitor treatment for LPR often provides limited benefit.

Conclusions: LPR, OSA, and asthma may represent an overlapping clinical triad rather than isolated diseases. Awareness of their coexistence may improve diagnosis and support multidisciplinary management. Further prospective studies are needed to clarify causal relationships and optimize treatment strategies.

Keywords: Laryngopharyngeal reflux; Obstructive sleep apnea; Asthma; CPAP; Airway inflammation; Comorbidity

1. Introduction:

Laryngopharyngeal reflux (LPR) refers to a condition in which stomach contents (containing both stomach acid and digestive enzymes, including pepsin) are regurgitated beyond the esophagus (GERD- gastroesophageal reflux) all the way to the larynx and pharynx. This causes irritation of the upper respiratory tract [1] an inflammatory reaction of the laryngeal and nasopharyngeal mucosa occurs due to the reflux of gastric contents.

Gastroenterologists consider LPR to be a set of symptoms characteristic of GERD, whereas in otolaryngology, LPR is diagnosed as a separate disorder [2]. The symptoms of laryngopharyngeal reflux differ in part from the typical symptoms of GERD. Patients diagnosed with LPR most commonly complain of: chronic cough, hoarseness, dysphonia, as well as a sensation of a “lump” in the throat and frequent clearing of the throat. In contrast, the typical presentation of GERD includes heartburn, which is absent in LPR [1].

LPR is a relatively new clinical condition for which there is no clear-cut treatment protocol among specialists. The pathogenesis of LPR is not fully understood [3]. It appears that enzymes other than pepsin may play a key role in the inflammatory response of the mucosa; only a few studies have confirmed the presence of bile salts during the development of LPR there are no clear conclusions regarding bile salts in the inflammatory process [4,5]. Only a few studies [6,7] suggest that factors such as stress or autonomic nervous system dysfunction may likely contribute to the development of LPR.

It has now been demonstrated that the microbiota of the laryngeal and pharyngeal mucosa influences the homeostasis of these regions and limits the occurrence of inflammatory reactions within them. It appears that, unlike GERD, due to the structure of the laryngeal and pharyngeal mucosa, even small amounts of gastric contents can cause an inflammatory reaction and, consequently, LPR symptoms. Many studies point to attempts to treat LPR like GERD through the use of PPIs [9].

In a meta-analysis of the efficacy of PPIs in alleviating LPR symptoms conducted by C. Liu et al. [9], no significant benefits were demonstrated for the use of proton pump inhibitors compared to placebo. Patients continued to report coughing, hoarseness, and a sensation of a "lump" in the throat after treatment. The authors, C. Liu et al. [9], using 8 studies (one was a randomized, controlled crossover trial; the rest were randomized controlled trials), concluded that although the quality of the included studies cannot be unequivocally determined, the results indicate that PPIs have a clinical effect similar to that of placebo.

LPR often coexists with other respiratory disorders, including upper airway diseases, which supports the concept of a unified respiratory system. Such disorders include asthma and obstructive sleep apnea.

Obstructive sleep apnea (OSA) is a disorder characterized by obstruction of the upper airways during sleep. In a 2021 study by Abbasi et al., it was described that upper airway collapse occurs as a result of changes in the muscle tone of these airways. This leads to OSA (which can be either partial or complete), and consequently, episodes of hypopnea and/or apnea are observed [10].

OSA is a condition that falls under the umbrella of sleep-disordered breathing (SDB), which also includes two other disorders: obesity hypoventilation syndrome (OHS) and central sleep apnea. Abbasi et al., however, note that OSA is the most common condition among SDBs, and it is OSA that leads to the development of the greatest number of comorbidities, such as hypertension, atrial fibrillation, heart failure, and others. The pathogenesis of atrial fibrillation associated with OSA is caused by hypoxemia and hypercapnia during apnea episodes. This leads to structural changes in the myocardium and, consequently, atrial fibrillation due to oxygen stress [10].

During episodes of obstructive sleep apnea (OSA), arterial blood oxygen saturation decreases, leading to autonomic nervous system dysfunction; in chronic OSA, this consequently also leads to impaired cardiovascular and respiratory function, as well as neurocognitive dysfunction [10]. It has been demonstrated that OSA is associated with elevated levels of CRP and IL-6 in the blood; in these cases, CPAP therapy effectively reduces inflammatory markers in patients with obstructive sleep apnea [10].

In 2019, Benjafield et al. [11] conducted a comprehensive review to estimate the prevalence of OSA in sixteen different countries around the world, including Germany, Spain, and Switzerland. Compiling this data revealed that approximately 1 billion people aged 30–65 suffer from OSA, and 425 million of them have been diagnosed with moderate or severe obstructive sleep apnea [11].

This enabled the identification of numerous risk factors for OSA that can be detected during a physical examination. These include, among others: male gender, age over 50, and menopause in women. A linear correlation has also been demonstrated between a high BMI indicating obesity and OSA. Neuropathies and myopathies of the upper airway muscles, particularly the genioglossus muscle, may also contribute to the development of apnea. According to Benjafield et al., craniofacial structure in the Asian population is also a factor increasing the likelihood of OSA [11].

The diagnosis of OSA is based entirely on the clinical presentation of patients; however, there are no symptoms specific to obstructive sleep apnea [11]. Patients most commonly complain of fatigue, excessive daytime sleepiness, snoring, drooling, as well as headaches and/or falling asleep while driving [12].

Asthma is one of the most common inflammatory diseases affecting the lungs. In a 2015 article, T. Holgate et al. [13] stated that asthma involves both small and large airways and causes an inflammatory response that is simultaneously associated with structural remodeling of these airways. These changes may begin as early as the prenatal period, and interestingly, numerous studies have shown that the disease has a variable course and may go into remission, only to reappear during adolescence [13]. Periods of remission in late childhood and adolescence are more common in the course of the disease in men, whereas in women, remission is less frequently observed; on the contrary, in the same age group, women are at greater risk of developing de novo asthma.

Asthma is a heterogeneous disease, meaning that there are two types: allergic (IgE-mediated) and non-allergic. Allergic asthma is caused by IgE-mediated hypersensitivity to common environmental allergens and thus typically develops during childhood [13]. In contrast, non-allergic asthma remains poorly understood; it is primarily defined by the absence of inflammatory markers characteristic of IgE-mediated asthma [16]. These markers include, primarily, interleukins (IL)-4, IL-5, IL-13, and eosinophils. To illustrate the significant discrepancy between the prevalence of allergic and non-allergic asthma, it is worth noting that in >80% of the children studied and in most adults, the inflammatory response is T2-cell-mediated and occurs in response to hypersensitivity to environmental allergens such as dust mites, fungi, and pollen [14,15].

In the pathophysiology of asthma, during the inflammatory response, T2 lymphocytes are accompanied by various inflammatory cells primarily eosinophils, which form characteristic infiltrates, but also mast cells, basophils, neutrophils, and macrophages along with monocytes. Asthma-specific mast cell activation is stimulated by the release of inflammatory mediators. This is followed by mast cell degranulation, and eosinophil vacuolization is also observed [13]. In allergic asthma, the mechanism of eosinophil activation proceeds as follows: dendritic cells present antigens to T lymphocytes via MHC class II. This leads to the differentiation of T lymphocytes into Th-2 lymphocytes, which, when activated, secrete pro-inflammatory cytokines such as IL-3, IL-4, IL-5, IL-9, IL-13, and GM-CSF, a factor stimulating the growth of granulocyte and macrophage colonies [13]. This is followed by the activation of the mast cell response, eosinophilia, and IgE. As described above, these factors are markers indicating the development of IgE-mediated asthma.

The most characteristic symptoms of asthma include, above all: wheezing, chest tightness, and shortness of breath. In the initial diagnosis, greater attention is paid to: recurrent cough, waking up at night, and symptoms caused by external triggers environmental allergens, viral infections, physical exertion, or cold air. Clinically visible manifestations such as eczema, food allergies, or allergic rhinitis and conjunctivitis may also occur in the context of IgE-mediated asthma [13]. In adults, a history of bronchitis in childhood aids in the diagnosis of asthma. However, these symptoms do not allow for a definitive diagnosis of asthma, as they are not specific to this disease. To make a diagnosis, appropriate tests must be conducted, including: spirometry, determination of eosinophil counts in secretions or in a complete blood count, as well as FeNO that is, the concentration of nitric oxide in exhaled air. The symptoms of this hypersensitivity are clinically evident, for example, in the form of eczema, food allergies, or allergic rhinitis and conjunctivitis [13].

The relationship between LPR, OSA, and asthma suggests the existence of a pathophysiological "vicious cycle." The negative intrathoracic pressure generated may promote the regurgitation of gastric contents up to the larynx, which will exacerbate reflux. Excessively severe and untreated reflux, in turn, stimulates inflammation of the laryngeal mucosa and may exacerbate asthma symptoms. It is also worth noting that the correlation between these three conditions is further supported by the fact that increased secretion of pro-inflammatory factors including IL-6, which is characteristic of the course of both LPR, OSA, and asthma is observed in each of them.

Elaboration:

The relationship between OSA and LPR

A growing body of research indicates that the prevalence of laryngopharyngeal reflux is increasing among patients with OSA. In their meta-analysis, Jie He et al. report that the prevalence of LPR in patients with OSA was 49%. Other studies, however, indicate that this prevalence must be higher than 49%. This points to a correlation between LPR and OSA in populations in Europe and the United States [17]. It is believed that the occurrence of reflux is directly dependent on the severity of OSA symptoms; Payne et al. confirmed that 90% of patients with obstructive sleep apnea had inflammation in the throat consistent with a diagnosis of LPR.

Various studies have examined the potential reasons why LPR develops in the aforementioned patients. [18] One hypothesis suggests that the specific generation of negative intrathoracic pressure that occurs during an OSA episode leads to the aspiration of gastric contents. However, recent studies refute this theory, according to Kuribayashi et al. [19, 20] and Shepherd et al. [21] The barrier provided by the lower esophageal sphincter (LES) actually becomes more pronounced during apnea episodes- this prevents the aspiration of gastric contents and, consequently, is not the cause of LPR. It is worth noting, however, that obesity is a risk factor common to both OSA and LPR. Numerous studies have demonstrated the negative impact of a high BMI on the proper functioning of the open airways. [18] conducted an objective assessment of GER and esophageal function parameters in obese individuals from a control group without OSA, and to investigate the role of OSA itself, these parameters were evaluated

in obese and non-obese individuals with moderate or severe OSA. The studies showed that in the group of obese individuals with and without OSA, the number of reflux episodes during sleep was identical and nearly four times higher than in non-obese individuals. This led to the conclusion that obesity, which is a factor increasing the incidence of OSA, also increases the prevalence of LPR.

Studies have also observed an inverse correlation; that is, the presence of LPR contributes to the worsening of symptoms and the development of OSA. In the pathophysiology of this mechanism, a so-called vicious cycle is observed; first, Jie He et al. note that laryngopharyngeal reflux not only damages the mucosa of the upper respiratory tract but can also lead to swelling of the throat and larynx as a result of inflammation. Furthermore, with each episode of laryngeal reflux, some acidic gastric contents are regurgitated, leading to irritation of the nerve endings in the tracheal mucosa and consequently to its collapse. It is also possible that this same content leads to irritation of chemoreceptors in the lower part of the esophagus, which triggers a vagal reflex. All of these factors lead to irritation of receptors in the mucosa of the upper airways, and consequently to their narrowing and reduced permeability (obstruction), which directly leads to an episode of sleep apnea.

Continuous Positive Airway Pressure (CPAP) is used to treat both OSA and LPR. Numerous studies [22, 23, 24] have shown that the CPAP mask, by maintaining positive pressure in the upper airways, prevents the aspiration of gastric contents. This confirms that CPAP therapy completely or partially prevents the occurrence of reflux symptoms during nocturnal OSA episodes. It is speculated that CPAP also reduces reflex contraction of the LES (lower esophageal sphincter), which further contributes to the therapeutic effect observed for both OSA and LPR.

The relationship between LPR and asthma:

LPR symptoms are frequently observed in patients with asthma, particularly in those whose condition is poorly controlled. However, not all researchers agree on whether the correlation between these two conditions is merely coincidental.

[25] One reason for more frequent asthma exacerbations in patients with LPR is that regurgitated gastric contents reach as far as the upper airways including the trachea, bronchi, and even the lungs. Because the upper and lower airways lack adequate protective mechanisms primarily peristaltic movements and cilia- to protect the mucous membrane, the acidic contents cause bronchoconstriction. This leads to an exacerbation of asthma symptoms: shortness of breath, chest tightness, etc.

The trachea and bronchial tree are exposed to microaspiration of gastric contents; this most often occurs during sleep and involves the entry of small amounts of gastric contents into the trachea and bronchi. Repeated microaspiration leads to chronic inflammation and swelling caused by hydrochloric acid and pepsin contained in gastric contents, which increases the risk of infection and may also lead to aspiration pneumonia. As a result of swelling in the upper

airways and bronchi, there is also increased stimulation of the vagus nerve this leads to further narrowing of the airways. Such chronic irritation causes a cough reflex, as well as hoarseness and a sensation of a “lump” in the throat, which are well-known symptoms of LPR.

The cough mentioned above often worsens in asthma patients when their condition flares up. A noticeable nocturnal cough then occurs, which is usually most severe at the beginning of the night. [26] Many studies point to a possible cause: it is believed that changing from a standing to a lying position may affect lung physiology and thereby increase the reflux of gastric contents (LPR), consequently increasing airway swelling and leading to an asthma attack and a cough reflex. It is worth noting that the aforementioned cough reflex is a symptom caused by inadequate asthma treatment as well as an insufficient response to medications used for LPR.

The gold standard for treating laryngopharyngeal reflux is the use of proton pump inhibitors (PPIs). However, many studies indicate that PPIs have a therapeutic effect similar to that of a placebo. In a meta-analysis [9] of the efficacy of PPI therapy in LPR, no significant difference from placebo was demonstrated in improving the cough reflex. It is believed that one reason for this may be that LPR symptoms are not specific to the condition; it is therefore possible that LPR has been overdiagnosed in place of another disease. However, the fact that LPR treatment is not sufficiently effective leads to worsening of symptoms.

The association between OSA and asthma:

Numerous studies indicate a correlation between the prevalence of asthma and OSA. De-Lei Kong et al. [28] note in their meta-analysis that, after analyzing multiple databases, it appears that the prevalence of OSA among patients with asthma is 49.5%, and the risk of OSA is 27.5%. This suggests that asthmatics are at higher risk of developing symptoms of obstructive sleep apnea. It is also worth noting that an increased prevalence of SDB (19.65%) has been observed in patients with asthma.

Numerous studies [29] support the hypothesis that OSA is associated with more severe and harder-to-control asthma. The impact of OSA on lung function requires further confirmation; however, it is believed that the presence of apnea complicates asthma treatment and is associated with an increased incidence of asthma exacerbations. Chronic edema, inflammation, and, consequently, remodeling of the bronchial wall (mucosa) impede airflow through the airways. Thus, it causes obstruction during ventilation and may lead to episodes of OSA. During these episodes, there is an increase in vagal nerve activity and reflexes, which can cause bronchoconstriction. Another notable factor is the oxidative stress that develops during OSA it leads to inflammation of the airways and, consequently, to an increased frequency of asthma attacks.

CPAP therapy is a common treatment for OSA. Its use creates positive pressure inside the chest. This, in turn, reduces apnea, thereby helping to maintain adequate oxygen saturation; the body is not in a state of oxidative stress, so inflammatory mediators are not released, which would otherwise lead to asthma exacerbations. It is reported that [29] CPAP therapy resulted in improvements in daytime and nighttime symptoms, the frequency of bronchodilator use,

disease recurrence (i.e., asthma), quality of life, and morning and afternoon peak expiratory flow rates.

Among the proposed mechanisms linking OSA to asthma are intermittent hypoxia, systemic inflammation, and sleep fragmentation, all of which may exacerbate lower airway dysfunction [29]. As previously mentioned, during OSA episodes, blood oxygen saturation decreases, leading to tissue hypoxia. During such chronic, recurrent hypoxia, the secretion of pro-inflammatory molecules such as IL-6, TNF-alpha, and CRP increases. This leads to inflammation of the airway mucosa. Chronic inflammation leads to so-called airway remodeling; there is hypertrophy and hyperplasia of bronchial smooth muscle, deposition of collagen I, III, and V, and subepithelial fibrosis. This causes the bronchial wall to become thicker and stiffer. As can be seen, this is a “vicious cycle” mechanism in which episodes of OSA lead to asthma exacerbations. Furthermore, nocturnal asthma causes frequent awakenings and poor sleep quality. It is speculated that these additional asthma symptoms may increase carotid body hypersensitivity, which would lead to changes in other phenotypic features such as the arousal threshold or the tendency of the airways to collapse. These features, in turn, are known contributors to the pathogenesis of OSA [29].

Common pathophysiological mechanisms:

Although asthma, obstructive sleep apnea, and laryngopharyngeal reflux are distinct clinical entities, they often occur concurrently because they share several interrelated pathophysiological mechanisms: chronic inflammation, obesity, autonomic imbalance, upper airway dysfunction, and sleep disorders. These conditions are not isolated disorders but can form a multidirectional network of interconnections, within which each contributes to the onset or progression of the others.

4.1 Chronic Inflammation

Asthma, obstructive sleep apnea, and laryngopharyngeal reflux all are associated with increased production of systemic inflammatory mediators. As mentioned above, these are primarily: interleukin-6, TNF-alpha, and CRP [29]. This persistent inflammation promotes airway remodeling, worsens the condition, increases the frequency of symptoms, and exacerbates them. It is worth noting that this also leads to poorer disease control and hinders or reduces the effectiveness of treatment. In cases of overlapping conditions, the inflammatory burden may be cumulative rather than specific to a given disease.

4.2 Obesity as a common factor

Obesity is one of the strongest common risk factors for all these diseases. Adipose tissue fills the chest cavity, mechanically contributing to impaired diaphragmatic movement and increased susceptibility of the upper airways to collapse during sleep. At the same time, abdominal obesity causes increased intra-abdominal pressure; adipose tissue functions as an active endocrine organ, producing pro-inflammatory cytokines, leading to systemic inflammation and thereby increasing the risk of LPR, asthma, and OSA.

4.3 Neurogenic and Autonomic Disorders

Excitation and stimulation of vagal nerve endings during episodes of OSA, LPR, and asthma can lead to bronchial hyperreactivity stimulating bronchoconstriction and mucus secretion. This leads to airway destabilization and reflex responses triggered by esophageal irritation, such as coughing. Recurrent nocturnal hypoxia and awakenings occurring in the course of OSA may disrupt normal autonomic balance, contributing to sympathetic overactivity and further respiratory instability.

4.4 Upper Airway Vulnerability

Inflammation of the mucous membrane in the throat and larynx leads to swelling and pain. This, in turn, predisposes them to collapse during sleep, which consequently impairs ventilation and may cause OSA symptoms. It is also possible that, as a result of the aforementioned persistent inflammation, a chronic cough, dysphonia, and hoarseness will persist, which hinder asthma control.

4.5 Sleep Fragmentation and Feedback Loops

Recurrent, repeated awakenings and poor sleep quality impair asthma control; they lead to chronic fatigue, make it difficult to adhere to treatment recommendations, and may exacerbate respiratory symptoms characteristic of obstructive sleep apnea, asthma, and laryngopharyngeal reflux.

4.6 A shared perspective

In summary, asthma, OSA, and LPR can be viewed as coexisting conditions that share common inflammatory, metabolic, neuronal, and mechanical pathways. These shared mechanisms may help explain persistent symptoms, treatment resistance, and the diverse clinical presentation, while also promoting a more integrated, multidisciplinary approach to diagnosis and management.

Clinical Approach:

Studies show that awareness of the association between OSA, LPR, and asthma is of significant importance in medical practice. It allows for the diagnosis of patients who have persistent respiratory symptoms despite treatment for one of the aforementioned conditions. A broader diagnostic approach can improve symptom control and enhance quality of life.

5.1 Screening for OSA in patients with uncontrolled asthma

Undiagnosed OSA in patients with asthma may manifest as follows: loud snoring, hoarseness, observable apneas, and excessive daytime sleepiness. In such cases, asthma may be difficult to control, and these patients should be evaluated for OSA. Episodes of apnea may contribute to asthma exacerbations and treatment difficulties through frequent hypoxia, inflammation, and sleep fragmentation. Diagnosis of OSA and CPAP therapy can lead to significant improvement in asthma management in such patients.

5.2 Consideration of LPR in cases of chronic cough and hoarseness

LPR can occur without typical heartburn or classic symptoms of gastroesophageal reflux, which is why less specific symptoms such as chronic cough, hoarseness, clearing of the throat, and a sensation of a "lump" in the throat are often overlooked. Interestingly, the irritation of the laryngeal and pharyngeal mucosa associated with LPR may resemble poorly controlled asthma. A diagnosis of LPR can therefore help guide treatment in a way that alleviates asthma symptoms.

5.3 The Importance of Multidisciplinary Care

LPR, OSA, and asthma involve overlapping systems: the respiratory, sleep, and upper gastrointestinal tracts. Collaboration among pulmonologists, sleep medicine specialists, otolaryngologists, gastroenterologists, and primary care physicians can improve diagnostic accuracy and enhance treatment effectiveness. Integrated care is particularly valuable in patients with treatment-resistant symptoms, recurrent exacerbations, or multiple comorbidities.

5.4 Management Strategies

In addition to standard pharmacological treatment for asthma, LPR, and CPAP therapy for patients with OSA, treatment should include the reduction of risk factors for these conditions. Clinicians should pay closer attention to patients' BMI, sleep hygiene, smoking habits, and adherence to medication regimens. All of these factors contribute to reducing the frequency of episodes of these conditions and make them easier to manage. For example, weight loss in obese individuals can simultaneously improve asthma control, reduce reflux, and alleviate the severity of apnea.

5.5 Summary

In clinical practice, persistent or unexplained respiratory symptoms should prompt consideration of comorbid conditions, rather than merely escalating treatment for existing OSA, LPR, or asthma. Early diagnosis of these comorbid conditions can reduce the symptom burden and enable more comprehensive, patient-centered treatment

Limitations:

The current state of knowledge regarding the correlation between these three conditions (LPR, OSA, asthma) remains limited due to several significant methodological challenges. These limitations should be taken into account when interpreting published results and drawing conclusions regarding clinical management.

6.1 Heterogeneity of LPR Diagnostic Criteria

One of the main limitations is the lack of standardized diagnostic criteria for LPR.

Studies have utilized a wide range of tools, including symptom-based questionnaires such as the Reflux Symptom Index (RSI), laryngoscopic scoring systems such as the Reflux Finding

Score (RFS), the empirical response to proton pump inhibitor therapy, and objective reflux monitoring. Because these methods vary significantly in terms of sensitivity, specificity, and reproducibility, it is difficult to compare the results of individual studies.

6.2 Limited Number of Participants

Most available studies evaluating the associations between asthma, obstructive sleep apnea (OSA), and laryngopharyngeal reflux (LPR) include relatively small groups of patients, often recruited from single centers or specialized clinics. Small sample sizes reduce statistical power, increase the risk of selection bias, and limit the ability to generalize results to broader populations. This is of great importance in the objective evaluation of these studies' results regarding, for example, response to treatment.

6.3 The predominance of observational studies

Most of the current literature consists of cross-sectional studies, case-control studies, or retrospective observational studies these do not allow for the determination of temporal relationships or the establishment of a causal link. As a result, it often remains unclear whether one condition directly contributes to the onset of another, or whether they simply coexist due to shared risk factors. The number of high-quality prospective cohort studies and randomized intervention trials remains limited.

6.4 Confounding factors related to obesity and other risk factors

Obesity is a major confounder in studies of asthma, OSA, and gastroesophageal reflux. It is independently associated with an increased risk of all three conditions and may exaggerate the observed associations between them. Additional confounding factors, such as age, smoking, medication use, allergic diseases, and lifestyle factors, are not always adequately controlled. Consequently, some reported associations may reflect shared background risk rather than direct pathophysiological interaction.

6.5 Summary

Future studies should use standardized diagnostic definitions, include larger and more diverse populations, and better control for confounding variables in order to clarify the true nature of the associations between OSA, LPR, and asthma.

7. Directions for Further Research

Current data indicate clinically significant associations between asthma, OSA, and laryngopharyngeal reflux (LPR). Future studies should focus on improving methodological quality, refining diagnostic methods, and determining whether integrated treatment can improve therapeutic outcomes reducing the frequency of episodes and exacerbations of symptoms in these overlapping conditions.

7.1 The Need for Prospective Longitudinal Studies

Most available data come from cross-sectional or retrospective studies, which limits conclusions regarding causality and temporal relationships. Well-designed prospective cohort studies are needed to clarify whether one disorder predisposes to the development of another, or whether they occur simultaneously due to shared risk factors such as those mentioned above obesity, smoking, and poor sleep hygiene.

7.2 Standardization of LPR Diagnosis

One of the main priorities is to develop more consistent and evidence-based diagnostic criteria for LPR. Current studies use a variety of symptom assessment scales, laryngoscopic findings, empirical evaluation of treatment response, and different methods of reflux monitoring, which makes it difficult to compare results it is also not sufficiently objective, meaning that the clinician's preference may influence diagnostic accuracy. Standardized definitions combining clinical assessment with validated objective measurements would improve the quality of research and facilitate more accurate identification of patients in clinical practice.

7.3 Interventional studies on comorbid conditions

Future randomized controlled trials should assess whether treating one condition can improve outcomes for the others. For example, further studies are needed to determine whether CPAP therapy for OSA improves asthma control or reflux symptoms, whether effective reflux treatment reduces chronic cough, hoarseness, or nocturnal asthma symptoms, and whether asthma treatment reduces sleep-related respiratory instability. Such studies would help determine the most effective sequence and combination of therapies.

7.4 Summary

Further progress in the diagnosis of OSA, LPR, and asthma will depend on prospective studies, standardized diagnostic criteria for LPR, and interventional studies evaluating integrated therapeutic approaches.

Conclusions

Available data indicate that laryngopharyngeal reflux (LPR), obstructive sleep apnea (OSA), and asthma are clinically related conditions that frequently coexist and may exacerbate one another. Although each of these disorders has a distinct underlying pathophysiology, they appear to share several overlapping mechanisms, including chronic inflammation, obesity-related effects, autonomic nervous system dysfunction, upper airway instability, and sleep fragmentation. These interactions may create a self-perpetuating cycle that contributes to persistent symptoms, poorer disease control, and reduced quality of life.

Current literature indicates that OSA is more common in patients with asthma, while reflux-related symptoms are frequently observed in both the asthma and OSA populations. At the same

time, LPR may remain undiagnosed because its symptoms often mimic those of respiratory diseases and may occur without typical reflux symptoms, such as heartburn. This underscores the importance of considering overlapping diagnoses in patients with chronic cough, nocturnal symptoms, hoarseness, unexplained shortness of breath, or an inadequate response to standard therapy.

From a clinical perspective, management should go beyond treating a single disorder. Screening for OSA in cases of uncontrolled asthma, evaluating possible LPR in patients with chronic upper respiratory tract symptoms, and addressing shared risk factors such as obesity can improve treatment outcomes and facilitate the management of these conditions.

However, significant limitations remain. Much of the current evidence is based on observational studies, small patient cohorts, and inconsistent diagnostic criteria—particularly in the case of LPR. Therefore, more robust prospective studies and randomized trials are needed to establish a cause-and-effect relationship and determine optimal treatment strategies.

In summary, LPR, OSA, and asthma should not always be viewed as distinct clinical entities. Instead, they may constitute an overlapping clinical triad in selected patients. Greater awareness of these associations may lead to earlier diagnosis, more personalized treatment, and better long-term patient care.

8. Disclosure:

8.1. Supplementary Materials.
No supplementary materials are available.

8.2. Author Contributions.
Conceptualization: Matylda Będkowska-Kuśmierek
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8.5. Informed Consent Statement.
Not applicable.

8.6. Data Availability Statement.
The study did not report any data.

8.7. Conflicts of Interest.
The authors declare no conflict of interest.

During the preparation of this work, the authors used ChatGPT for the purpose of language editing to improve clarity and readability. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the substantive content of the publication.

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