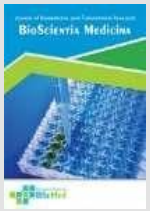
eISSN (Online): 2598-0580



Bioscientia Medicina: Journal of Biomedicine & Translational Research

Journal Homepage: www.bioscmed.com

Relation between Chronic Rhinosinusitis and Gastroesophageal Reflux in Adults: A Systematic Review

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ARTICLE INFO

Keywords:
Acid
Chronic rhinosinusitis
Gastroesophageal reflux
Inflammation

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All authors have reviewed and approved the final version of the manuscript.

https://doi.org/10.37275/bsm.v7i9.860

A B S T R A C T

Background: It is not entirely apparent how chronic rhinosinusitis (also known as CRS) develops. Since the 1970s, medical professionals have debated whether or not gastroesophageal reflux (GOR) could be a factor in the development of certain patients' conditions. The purpose of this research is to the relation between chronic rhinosinusitis and gastroesophageal reflux in adults. **Methods:** By evaluating the preferred reporting items for systematic review and meta-analysis (PRISMA) 2020 standards, this study demonstrated that it met all of the requirements. This enabled the researchers to ensure that the study was as up to date as feasible. Publications published between 2000 and 2023 were included in the search strategy, which included a variety of electronic reference databases (including Pubmed and SagePub). We did not consider review papers, duplicate publications, or half completed articles. **Results:** In the PubMed database, the results of our search brought up 133 articles, whereas the results of our search on SagePub brought up 69 articles. The results of the search conducted for the last year of 2000 yielded a total of 20 articles for PubMed and 8 articles for SagePub. In the end, we compiled a total of 21 papers, six of which came from PubMed and three of which came from SagePub. We included nine research that met the criteria. **Conclusion:** According to the findings of most studies, the number of cases of CRS seen in patients with GERD is around two to three times higher than that seen in the general patient group.

1. Introduction

Chronic rhinosinusitis (CRS) is an inflammatory disorder of the paranasal sinuses that produces chronic sinonasal symptoms. It is estimated that between 1% and 5% of the population in the United States suffers from chronic rhinosinusitis. It is a curable disease that annually costs the United States billions of dollars in direct and indirect health care costs.[1] As the pathophysiology of chronic rhinosinusitis in children is very different from that in adults, and because the pharmacological and surgical therapies for children and adults are also notably different from one another.[2,3] Because of its inflammatory origins, chronic rhinosinusitis is associated with asthma and allergic rhinitis. Certain inflammatory and immunodeficiency illnesses can also cause chronic rhinosinusitis. However, the symptoms are distinct.[3] Chronic rhinosinusitis, nasal crusting, and epistaxis can be caused by granulomatous diseases such as vasculitis and sarcoidosis. Chronic sinonasal symptoms are the most common manifestation of several forms of vasculitis, such as granulomatosis with polyangiitis and eosinophilic granulomatosis. Immunodeficiency and insufficient

mucociliary clearance can result in chronic sinus infections and rhinosinusitis.[4,5]

However, it is difficult to establish a clear association between CRS and gastroesophageal reflux disease (GERD) because both conditions are relatively frequent, which makes it easier for them to coexist independently.[6,7] This makes it difficult to establish a direct relationship between CRS and GERD. Several hypotheses concerning a connection between acid reflux and CRS have been proposed. The first factor is the direct exposure of the nasal and nasopharyngeal mucosa to gastric acid, which leads to inflammation of the mucosa and decreased mucociliary clearance. This, in turn, may lead to obstruction of the sinus ostia and recurrent infections.[8–10] Another possibility is a relationship mediated by the vagus nerve, a mechanism that has been demonstrated in the lower airway and nasal mucosa of rhinitis patients, but not in CRS patients. A malfunction of the autonomic nervous system can result in reflex sinonasal edema and inflammation, as well as subsequent obstruction of the ostia.[11,12] Wong et al.[13] demonstrated that by infusing saline with hydrochloric acid into the lower esophagus of healthy volunteers, there was an increase in nasal mucus production, an increase in nasal symptom score, and a decrease in peak nasal inspiratory flow, supporting this theory. The purpose of this research is to discover whether or if there is a connection between chronic rhinosinusitis and gastroesophageal reflux disease in adults.

2. Methods

The author of this study ensured that it was up to date and followed all applicable rules by adhering to the preferred reporting items for systematic review and meta-analysis (PRISMA) 2020 criteria. This stage is critical since it ensures that the investigation's findings are reliable. The findings of this investigation revealed relation between chronic rhinosinusitis and gastroesophageal reflux in adults. The most efficient way to accomplish this goal in a timely manner is to first evaluate previous research on the issue. The significance of the issues raised will be demonstrated in this section as part of an effort to accomplish the goal of this essay.

To be permitted to participate in the investigation, researchers were required to provide proof that they met the following requirements: 1) In order to be considered for publication, the paper must be written in English and its primary concentration must be on the relation between chronic rhinosinusitis and gastroesophageal reflux in adults. 2) For the purposes of this evaluation, works published after 2000 but before the evaluation period will be considered. Examples of research that cannot be published include editorials, applications lacking a digital object identifier (DOI), previously published review articles, and entries that are nearly identical to previously published journal articles.

We used between “chronic rhinosinusitis” and “gastroesophageal reflux” as keywords. The search for studies to be included in the systematic review was carried out from June, 7th 2023 using the PubMed and SagePub databases by inputting the words: ("chronic"[All Fields] OR "chronical"[All Fields] OR "chronically"[All Fields] OR "chronicities"[All Fields] OR "chronicity"[All Fields] OR "chronicization"[All Fields] OR "chronics"[All Fields]) AND ("rhinosinusal"[All Fields] OR "rhinosinusitis"[All Fields]) AND ("gastroesophageal reflux"[MeSH Terms] OR ("gastroesophageal"[All Fields] AND "reflux"[All Fields]) OR "gastroesophageal reflux"[All Fields]) used in searching the literature.

We considered both the abstract and the title of each study when determining its credibility. They then examined additional historical documents. This conclusion is founded on a synthesis of findings from multiple analyses employing the same methodology. Comments must be written in unpublished English. Only those works that met a set of predetermined criteria were considered for inclusion in the systematic review. Consequently, the purview of the search results is reduced.

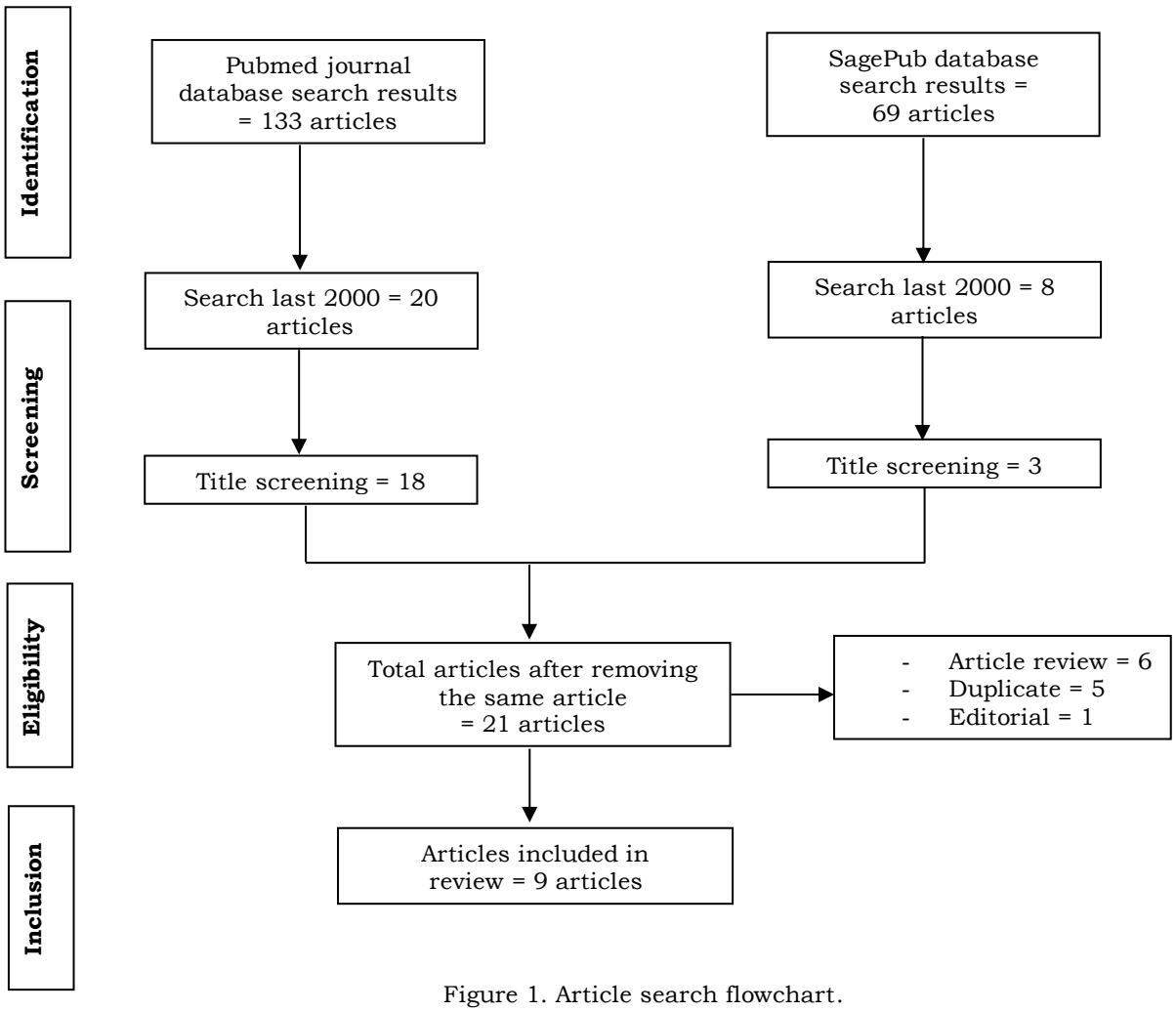

Figure 1. Article search flowchart.

There is insufficient analysis of the research's findings. Afterwards is the analysis. Who the subjects were, who penned the paper, when it was published, where the study was conducted, what it was about, and its parameters are described in the paper. The paper also includes information about the author and publication date. Endnote eliminated all instances of duplicate entries from the results list. Two separate evaluators analyzed the titles and abstracts of the articles.

Initially, their comprehensive papers were analyzed to determine if they were eligible for the study and to generate data. In the past, genome-wide association study (GWAG) and numerous other health issues have been the subject of conference presentations and investigations. During the course of deliberations, the justices reached a verdict. Before deciding which papers to analyze in greater detail, each author read the abstracts and titles of all of the papers. The following phase will be to investigate all of the papers that should be included in the review because they meet the inclusion criteria. After that, we will choose the review topics based on what we have learned about the numerous subjects. In this fashion, both the research papers and the review papers are selected.

3. Results

In the PubMed database, the results of our search brought up 133 articles, whereas the results of our search on SagePub brought up 69 articles. The results of the search conducted for the last year of 2000 yielded a total of 20 articles for PubMed and 8 articles for SagePub. In the end, we compiled a total of 21 papers, six of which came from PubMed and three of which came from SagePub. We included nine research that met the criteria. Finocchio, et al (2021)[14] showed prevalence of gastritis and GERD grew from

participants who did not have nasal disturbances (22.8% = 323/1414) to those who had AR (25.8% = 152/590), and then from subjects who had NAR (36.7% = 69/188) or sinusitis (39.9% = 276/691) it reached its highest point. The combination of gastritis and GERD was associated with a four-fold increase in the risk of non-allergic rhinitis (RRR = 3.80, 95% CI 2.56-5.62) and sinusitis (RRR = 3.70, 2.62-5.23) when compared to controls; however, it was associated with a much smaller increase in the risk of allergic rhinitis (RRR = 1.79, 1.37-2.35).

Bengtsson, et al (2019)[15] showed 2.7% of the total population of people who did not have nasal symptoms in the year 2000 developed CRS. CRS was associated with difficulties inducing sleep (aOR = 2.81 [95% CI = 1.67-4.70]), difficulties maintaining sleep (2.07 [1.35-3.18]), early morning awakening (3.03 [1.91-4.81]), insomnia (2.21 [1.46-3.35]), excessive daytime sleepiness (2.85 [1.79-4.55]), and snoring (3.31 [2.07-5.31]). Early morning awakening was also associated with CRS. Three symptoms of sleeplessness at baseline were associated with an elevated risk of CRS at follow-up by a factor of 5.00 (1.93-12.99). Study by Kim, et al (2019)[16] showed incidence of gastroesophageal reflux disease (GERD) was significantly greater in the CRS group (17.1%; 4020 out of 23,489 cases), as compared to the control group (9.1%; 8522 out of 93,956 cases; p <0.001). In the CRS group, the adjusted OR of GERD was 2.04, with a 95% confidence interval ranging from 1.96-2.13 and a significance level of p 0.001. The findings from each of the subgroup analyses were on par with one another.

Table 1. The literature included in this study.

Author	Origin	Method	Sample	Result
Finocchio, 2021[14]	Italy	Cross sectional study	2,887 subjects	According to the findings of the study, there is a link between gastritis / GERD and nasal disturbances. This link is more significant for non allergic rhinitis (NAR) and sinusitis than it is for allergic rhinitis (AR).
Kim, 2019[16]	Korea	Cross sectional study	23,489 CRS participants	The CRS participants had a higher likelihood of developing GERD. This association was true across all age ranges as well as between the sexes.
Bengtsson, 2019[15]	Sweeden	Cross sectional study	16,500 individuals	Incident CRS has been linked to poor sleep quality as well as an excessive amount of daytime sleepiness. The presence of insomnia symptoms is associated with an increased chance of developing CRS.
Mahdavinia, 2017[17]	United State of America (USA)	Retrospective study	1,066 patients with CRS	Atopic disorders and asthma are less likely in CRS patients without GERD. CRS patients without GERD had the same asthma risk. Atopic illness and GERD may increase CRS risk.
Zelenik, 2015[18]	Checz	RCT	90 patients	EER is high in CRS with nasal polyps and bronchial asthma. These patients should receive antireflux treatment. Further studies must confirm the effect.
DeConde, 2014[19]	USA	Cross sectional	229 patients with CRS	Patients electing endoscopic sinus surgery (ESS) for CRS with and without comorbid GERD have comparable baseline characteristics and quality-of-life (QOL) outcomes following surgery.
Bohnhorst, 2013[20]	Denmark	Cross sectional	82 patients with GERD	This study suggests that GERD may play a role in CRS's aetiology. CRS patients with GERD had a lower sinus and nasal passage quality of life.
Wong, 2010[13]	Australia	Cross sectional	45 patients with GERD	This suggests a vagus nerve-mediated esophageal-paranasal sinus reflex. Neuropathy-induced reflex-mediated rhinitis may produce CRS in GER patients. GER-CRS interactions need more research.
Ozdek, 2003[21]	Turkey	Prospective cohort study	12 patients with CRE	Some people with CRS can have *H. pylori* in their sinus mucosa, which makes it easy to find it. But it is not known if *H. pylori* causes CRS or if it is a symptom of CRS.

Mahdavinia, et al (2017) showed 112 of 1066 CRS patients had GERD. GERD was linked to higher BMI, older age, and female sex in CRS patients. The odds ratios (OR) for asthma and allergic rhinitis in the CRS group with GERD compared to the CRS group without GERD were 2.89 (95% CI = 1.905-4.389) and 2.021 (1.035-3.947). GERD also prolonged CRS. The prospective study involved 90 CRS patients and 81 controls. Asthma was related with GERD in CRS (OR = 4.77; 95% CI = 1.27-18.01). CRS in GERD patients was longer-lasting and younger-onset. In controls, GERD did not affect asthma or allergic rhinitis (OR = 0.67; 95% CI = 0.09-5.19). Zelenik, et al (2015)[18] conducted a RCT with 90 patients, who 30 participants assigned to each group. When compared to group I and group II, group III had a considerably higher prevalence of pathological EER in all aspects evaluated (RYAN score, number of EER episodes, total percentage of time below pH 5.5). In addition, individuals who fell into group III had a longer history of undergoing many surgical procedures. EER is high in CRS with nasal polyps and bronchial asthma. These patients should receive antireflux treatment. Further studies must confirm the effect.

DeConde, et al (2014)[19] showed patients with comorbid GERD and CRS were equivalent across all baseline patient characteristics ($p > 0.050$), but those with a history of GERD were older (53.8 vs 47.6 years) and less likely to have allergy testing ($p < 0.002$). CRS patients without GERD had comparable baseline objective and subjective illness parameters ($p > 0.050$). Both groups had significant QOL improvements across all QOL constructs ($p < 0.021$), and patients with and without GERD had similar improvements ($p > 0.050$). Active GERD medical therapy (n = 49) also improved QOL ($p > 0.050$). Bohnhsorst, et al (2013)[20] showed prevalence of CRS in the general population was 8.5% (95% confidence interval [CI] = 6.8%-10.2%), which is substantially lower than the prevalence of CRS among patients with GERD, which was 20.7% (95% CI = 12.0%-29.5%). When compared to patients with CRS from the background population, patients with GERD and CRS had an average Sino – Nasal Outcome Test (SNOT – 22) score of 43.8, whereas patients with CRS from the background population scored an average of 28.1. In patients with CRS, having GERD resulted in a 15.7 point rise in their mean SNOT-22 score (95% CI = 6.5-24.9).

Wong, et al (2010)[13] conducted a study. They showed, there was a trend towards an increase in the production of nasal mucus after esophageal stimulation with either normal saline or HCl. 45 minutes after the acid injection, this restored to the level that was considered normal. A parallel pattern was also seen with the assessments of nasal symptom scores and, to a lesser extent, nasal inspiratory peak flow. Both of these patterns followed the same general direction. Ozdek, et al (2003)[21] showed DNA from *Helicobacter pylori* was found in four of the twelve patients diagnosed with CRS, however it was not found in any of the patients diagnosed with concha bullosa. Complaints linked to gastroesophageal reflux disease were present in three out of the four individuals whose tests came back positive for *H. pylori*. They conducted a study with collect mucosal tissue samples from ethmoid cells of 12 patients with CRS and the removed mucosal part of the middle concha of 13 patients with concha bullosa who were treated surgically in our institution.

4. Discussion

Gastroesophageal reflux disease (GERD) is a common condition defined by chronic retrograde movement of gastric contents into the esophagus which causes various symptoms and complications in patients. The prevalence of GERD in South America, Western Europe and North America has the highest rates ranging from 20-40%.[22] Caucasian and African American patients have a high incidence of GERD. However, African Americans have a lower prevalence and lower likelihood of developing esophagitis.[23] The pathophysiology of GERD is a complex topic and involves several mechanisms that impair the protective capacity of the esophagus to cope with reflux of acid, pepsin, duodenal bolus and pancreatic enzymes. Mechanisms involved include motor

anomalies, anatomy, and mucosal resistance.[24] GERD-associated symptoms arise from lesions of the mucosa lining the esophagus and may manifest as esophageal (regurgitation and heartburn) or extraoesophageal (chronic cough, asthma, dental erosions, laryngitis, and non-cardiac chest pain) findings. These atypical manifestations of GERD known as extraesophageal syndromes (EOS) have received a lot of attention in the last few decades.[25]

The findings of the majority of studies indicate that the number of cases of CRS found in patients with GERD is around two to three times higher than that seen in the patient population as a whole. The connection between acid reflux and chronic rhinosinusitis has been linked to a number of possible mechanisms for explaining the connection. It has been demonstrated that people who suffer from chronic rhinosinusitis are more likely to experience proximal gastroesophageal reflux than healthy controls. To begin, exposure to gastric acid has the potential to aggravate inflammation within the mucosa of the upper airways and sinuses. This can also hinder the movement of mucociliary cells, which can lead to the obstruction of sinus ostia and increase the likelihood of recurring infections.[26,27]

Vagally-mediated neuroinflammatory alterations represent a potential alternative pathway.[28] Reflex sinonasal edema and inflammation can be caused by autonomic dysfunction, which can then lead to obstruction of the ostia. This idea was given experimental support by Wong et al.[13], who demonstrated through their study that infusion of saline with hydrochloric acid in the lower esophagus enhanced nasal mucus production as well as nasal symptom score. In addition, it has been hypothesized that *Helicobacter pylori*, also known as *H. pylori*, might play a part in the disease because this bacteria has been found not only in the stomach but also in the oral and nasal mucosa.[29] In particular, *H. pylori* has been discovered in nasal polyps, but not in control tissue. It has also been discovered in patients who have both chronic rhinosinusitis and GERD. In addition, *H. pylori* is the root cause of not just gastritis but also systemic inflammation, which may also affect the mucosa of the nasal passages. The study backs up the idea that extraesophageal reflux (EER) is linked to CRS that doesn't respond to medicine or surgery. The fact that pepsin was found in nasal lavages suggests that direct touch between the refluxate and the paranasal sinus mucosa may play a role in how CRS happens in this group of patients. Lastly, checking for pepsin in nasal fluid may be a good way to tell if refluxate is in the nose and paranasal sinuses.[28]

5. Conclusion

According to the findings of most studies, the number of cases of CRS seen in patients with GERD is around two to three times higher than that seen in the general patient group.

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