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Original Research Article

Prevalence of Chronic Rhinosinusitis in Chronic Obstructive Pulmonary Disorder Patients: Outcome of an Observational Case-Control Study

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Abstract

Background: Studies have persistently demonstrated that lower and upper airway diseases often coexist however the available data is limited.

Aim: we aimed to evaluate the prevalence of chronic rhinosinusitis in chronic obstructive pulmonary disorder patients at a tertiary care hospital in northern India.

Methods: In the present prospective case-control study, we recruited cases with COPD and according to Gold criteria visiting both OPD and admitted in the IPD block of GMC Srinagar age, gender and district of residence matched subjects as controls for the evaluation of CRS.

Results: we recruited 200 cases and control each. The mean age (±SD) was 64.4 (±12.1) years. Males showed an over representation than females (ratio 2.4:1). CRS was present in 14.5% of COPD cases compared to controls (8.0%). We observed nearly two-fold risk for developing CRS in patients with COPD (OR=1.97 95% CI:1.06 – 3.83). Unlike anosmia, we also observed a significant association of nasal discharge obstruction, posterior nasal drip and facial pain anosmia with the risk of COPD ($p<0.005$). However, we did not find any correlation of symptoms based of LK scoring between cases controls ($p>0.05$).

Conclusion: We observed that COPD and CRS can frequently co-exist. The presence of CRS should be assessed in COPD patients, especially in those with severe diseases. Further research is needed understand the overlapping pathophysiological mechanisms underneath COPD and CRS.

Keywords: Chronic Rhinosinusitis; Chronic Obstructive Pulmonary Disorder; Prevalence; Kashmir, Pathogenesis; Coexistence.

Introduction

Chronic rhinosinusitis (CRS) is a heterogeneous condition in which the sinuses (air-filled spaces in the bones around the nose) and the lining of the nasal passages become inflamed and swollen for an extended period of time. CRS is characterised by the presence of at least two out of four cardinal symptoms (i.e., facial pain/pressure, hyposmia/anosmia, nasal drainage, and nasal obstruction) for at least 12 consecutive weeks.

Clinically CRS is diagnosed with evidence of mucosal inflammation upon physical examination and focused sinonasal history with associated comorbidities. Globally, a spectrum of diseases, CRS affects ~11% of adult population and brings significant health and socioeconomic burden to large sections of people. The aetiology of CRS is poorly understood, and the possible risk factors for CRS include allergies, infections, environmental, anatomical, genetic, factors, and comorbid diseases [1]. Chronic obstructive pulmonary disease (COPD) is a common chronic respiratory condition that leads to a slow worsening of its symptoms. Although COPD is preventable but cannot be cured once established. However, effective self-management approaches can alleviate the severity and improve quality of life [2]. Globally chronic obstructive pulmonary disease (COPD) has a very high morbidity and mortality rates. COPD significantly impacts patients' health and related quality of life. Based on WHO estimates there that 65 million people worldwide suffer from COPD and is expected to become the leading cause of global deaths [3]. Moreover, with the advancement in diagnostic approaches including chest high-resolution computed tomography previously unrecognized radiographic bronchiectasis has also been identified [4].

Studies have persistently demonstrated that lower and upper airway diseases often coexist, developing the idea of the "united airways" [5]. Previous studies have shown up to 88% of COPD patients have daily nasal symptoms but, due to poor clinical

evaluation of the sinonasal cavity lack CRS diagnostics using[6]. Nonetheless, a high prevalence of CRS has been observed in the patients who primarily diagnosed for COPD. Given these observations, it is speculated that that CRS and COPD share the pathogenesis of however although the underlying mechanism remain speculative. In the current study we evaluated the prevalence of CRS in COPD patients a tertiary care hospital in norther India.

Material and Methods

The present prospective case-control study was conducted at a tertiary care Hospital (Govt Medical College, SMHS Srinagar) for a period of 18 months between September 2020 to November 2022. All the subjects who were diagnosed with COPD according to Gold criteria visiting both OPD and admitted in the IPD block of GMC Srinagar were enrolled as cases. We also recruited age, gender and district of residence matched subjects controls attending the hospital as an attendant with the patient or for some ailment other than COPD and CRS.

All the cases with the history of sinus surgery, pulmonary malignancy, or nasal malignancy were excluded from the study. Patients with diagnosed COPD evaluated for the presence of CRS by Questionnaire, Diagnostic nasal endoscopy and Para Nasal Sinus CT scan wherever needed.

CRS was diagnosed according to European position paper on Rhinosinusitis and nasal polyposis (EPOS-2020) according to which presence of two or more symptoms, one of which should be either nasal obstruction/ blockage/congestion/ nasal discharge (anterior or posterior nasal drip) + Facial pain/pressure, + Anosmia/Hyposmia, Duration of which should be equal or more than 12 weeks, with characteristic endoscopic findings:-Nasal Polyps and or Mucopurulent Discharge primarily from Middle Meatus and/or oedema/mucousal obstruction primarily in middle meatus and /or CT changes:- Mucousal changes within the Osteomeatal complex and/or sinuses. COPD was diagnosed according to Gold criteria, further were evaluated on HRCT chest wherever indicated. The study was reviewed and approved by the ethical committee of our institute. An informed consent was taken from the subjected before recruiting in the study.

Statistical Analysis: The recorded data in a spread sheet (Microsoft Excel) and statistical analyses were performed using statistical software Statistical Package for Social Sciences (SPSS; Version 26, IBM). Categorical variables were described as frequency and percentages whereas continuous variables were described as mean and standard deviation. Chi square test was used to analyse the relationship between two categorical variables. A p-value of <0.05 was considered statistically significant.

Results

In the current study we recruited 400 subjects including 200 cases and control each. The mean age (±SD) was 64.4 (±12.1) years. Males showed an over representation than females (ratio 2.4:1). CRS was present in 14.5% of COPD cases compared to controls (8.0%). We observed emphysema in ~51% and chronic bronchitis in ~49% of COPD. We observed nearly two-fold risk for developing CRS in patients with COPD (OR=1.97 95% CI:1.06 – 3.83). Unlike anosmia, we also observed a significant association of nasal discharge obstruction, posterior nasal drip and facial pain anosmia with the risk of COPD ($p<0.005$) (Table 1).

However, we did not find any correlation of symptoms based of LK scoring between cases controls ($p>0.05$)(table 2).

Table 1: Comparison between Presenting Symptoms and CRS

Feature/symptom	Case (N=200)	Control (N=200)	OR (95% CI)
Gender			p=1.00
Male	142 (71.0%)	142 (71.0%)	-
Female	58 (29.0%)	58 (29.0%)	-
CRS			p=0.040
Absent	171 (85.5)	184 (92.9	Referent
Present	29 (14.5)	16 (8.0)	1.97 (1.06 – 3.83)
Nasal Obstruction			p=0.003
Absent	158(79.0%)	180(90.0%)	Referent
Present	42(21.0%)	20(10.0%)	2.39 (1.35 – 4.20)
Nasal Discharge			p=0.019
Absent	165(82.5%)	183(91.5%)	Referent
Present	35(17.5%)	17(8.5%)	2.28 (1.25 – 4.18)
Posterior Nasal Drip			p=0.016
Absent	166(83.0%)	183(91.5%)	Referent
Present	34(17.0%)	17(8.5%)	2.20 (1.20 – 4.05)

Facial Pain			p=0.041
Absent	164(82.0%)	180(90.0%)	Referent
Present	36(18.0%)	20(10.0%)	1.91 (1.04 – 3.43)
Anosmia			P=0.079
Absent	160(80.0%)	174(87.0%)	Referent
Present	40(20.0%)	26(13.0%)	1.67 (0.96 – 2.81)
Emphysema	103 (51.5)	0	-
Chronic Bronchitis	97 (48.5)	0	-

OR: Odds Ratio, CI: Confidence Interval, Chi-square test was used to calculate ORs and 95% CIs

Table 2: Comparison between endoscopic findings and CRS

	Case (N=200)	**Control (N=200)**	**OR (95% CI)**
LKS Mucopurulent Discharge (Right)			p= 0.442
Absent	173(86.5%)	179(89.5%)	Referent
Present	27(13.5%)	21(10.5%)	1.33 (0.71 – 2.44)
LKS Mucopurulent Discharge (Left)			p=0.098
Absent	174(87.0%)	185(92.5%)	Referent
Present	26(13.0%)	15(7.5%)	1.83 (0.95 – 3.49)
LKS Oedema (Right)			0.839
Absent	186(93.0%)	188(94.0%)	Referent
Present	14(7.0%)	12(6.0%)	1.179 (0.55 – 2.64)
LKS Oedema (Left)			p=0.091
Absent	175(87.5%)	186 (93.0%)	Referent
Present	25(12.5%)	14 (7.0%)	1.89 (0.94 – 3.22)
LKS Nasal Polyposis (Right)			p>0.99
Absent	199(99.5%)	199 (99.5%)	Referent
Present	1(.5%)	1(.5%)	1 (0.05 -19.01)
LKS Nasal Polyposis (Left)			p=0.347
Absent	188(94.0%)	193(96.5%)	Referent
Present	12(6.0%)	7(3.5%)	1.76 (0.71 – 4.53)

LKS: Lund Kennedy Scoring, OR: Odds Ratio, CI: Confidence Interval, Chi-square test was used to calculate ORs and 95% CIs.

Discussion

CRS is a spectrum of diseases that bring significant health and socioeconomic burden to large sections of people globally. In absence of a systematic approach to diagnose CRS diagnostics due to poor clinical evaluation of the sinonasal cavity the coexistence of COPd a CRS remains underreported. We undertook the current observational, case-control study, wherein we enrolled 400 subjects including 200 case (with COPD) and 200 control (without COPD) subjects and evaluated them for CRS at a tertiary care hospital and evaluated them for CRS.

In the current stud we found male overrepresentation than females presenting CRS. The results from the epidemiology studies reporting prevalence of CRS in patients with or without COPD have shown mixed results [7, 8]. Similar to our results, Colins et al found that men were 2.5 times more likely than women[9], while as Barnes et al reported that COPD is commonly seen in women [10]. No convincing mechanisms or pathophysiological explanations have been offered so far for these gender-based differences (Collins et al. 2002). Given these contrary results in the literature, additional mechanistic studies are warranted to unveil the underlying gender based pathophysiological factors that could be contributing to these observations [11].

In our study, (11%), 45 out of 400 subjects had CRS out of which 14.5% (29 out of 200) were also suffering from COPD while 8% (16 out of 200) were undiagnosed and untreated for their CRS. An earlier study by Ardanal et al, reported that 22.5% of COPD patients had CRS based on EPOS guidelines [12]. Our observed CRS prevalence is lower than hat was reported by Arndal et al [12], but is higher than the questionnaire-based population prevalence of 10.9% (range 6.9–27.1%), wherein it is important be noted that the Swedish, Finnish and Danish CRS prevalence was 7.8% and did not include clinical evaluation of the patients [13]. Higher CRS prevalence has been previously published from different groups across different ethnicities; 48.5% (Yang et al. China) and 53–64% (Kelemence et al. Turkey). In these studies, evaluation and nasal endoscopy by an otorhinolaryngologist was not performed, and this may have resulted in an overestimation of CRS. Differences in study population and sample size may also contribute to the observed variations in

prevalence. Moreover, higher levels of air-pollution, smoking habits and ethnicity are known to affect CRS prevalence [14].

In the current study, we found a nearly two-fold risk for developing COPD in patients with CRS. CRS is also a considered as a risk factor for cystic fibrosis, asthma, and even COPD [15]. However, based on the "united airways disease hypothesis" there is currently a debate as to whether it is a cause or a coexistent phenomenon [16]. The coexistence of COPD and CRS could result from the simultaneous irritation of the lower and upper airways by exhaling tobacco smoke through the nose. Such an association could be demonstrated by the investigation of inflammatory cells and markers and the examination of tissue samples throughout the affected portions of the respiratory mucosa. [17]. However, the current study lacked laboratory investigations that might indicate a possible immunopathological mechanism common to CRS and COPD, warranting further research in the field.

Similar to an earlier study by Arndal et al [12], we found a positive correlation of presenting symptoms with CRS and COPD. Nasal obstruction is a diagnostic symptom for both acute and CRS [18]. Earlier studies have also reported nasal obstruction to be the main symptom presented by most of the patients with CRS [19, 20]. Nasal congestion is an acute vascular response to inflammation caused by any form of nasal irritation, and by infection and allergy. Anterior nasal discharge, and posterior discharge (post-nasal drip) are common symptoms of CRS [21]. The nasal discharge associated with rhinosinusitis is a complex mix of elements derived from glands, goblet cells, plasma cells, and plasma exudate from capillaries, and the relative contribution from these different sources varies with the time course and the severity of the inflammatory response [22]. Rhinosinusitis may be associated with purulent posterior nasal discharge that is only slowly cleared from the nasopharynx and may be a cause of persistent throat clearing [23].

Many cases with CRS reported facial pain. While as two major CRS guidelines include presence of facial pain as part of the clinical diagnostic criteria for CRS [24, 25], the association of facial pain with CRS continues to be controversial, such that the EPOS guidelines highlight literature demonstrating that only a minority of subjects with CRS experience facial pain [24]. Prior investigations into facial pain and CRS have been limited by a lack of validated outcomes measures. Investigation of pain in the context of CRS has generally been undertaken by either reporting of 'facial pain' by patients [26, 27], or using a visual analog scale [28]. Moreover, the literature describing facial pain associated with CRS reports a wide range of prevalence. Unlike to our findings, earlier cross-sectional studies evaluating subjects with CRS upon presentation report pain in only a minority of patients with CRS [26, 29, 30]. Interestingly, these cross-sectional studies have been influential, and have shifted the perception that patients with CRS rarely have pain [23, 26] unless experiencing an acute exacerbation.

In the current study we did not find any correlation of symptoms based of LK scoring between cases controls. In our subjects, based on endoscopic findings, edema, nasal discharge and polyps were reported comparable in cases and controls. An earlier study from north India by Nanda et al 2017 reported polyps in 38% of CRS patients, while as nasal discharge was in 68% of subjects [31]. Mucus secretion is one of the signature features of CRS. The increase in mucous gland density occurs in severe CRS subjects without polyps, while as those with nasal polyps show a significant reduction in mucous gland density [32]. Glandular hypertrophy and mucous secretion in the airway mucosa MUC5AC and MUC5B are the main secreted mucins (proteins) in the human airway, with MUC5A produced primarily by goblet cells are likely to be mediated by the cytokines, tumor necrosis factor (TNF)-α, IL-8 and IL-13 [33]. Several inflammatory markers, including IL-1α, IL-1β, IL-6, IL-8, TNF-α, and granulocyte-macrophage colony-stimulating factor (GM-CSF), are engaged in this process[34], that lead to localized inflammatory responses as well.

We observed emphysema in ~51% and chronic bronchitis in ~49% of COPD. Emphysema, a progressive lung disease, is a form of COPD. It is caused by chronic and significant exposure to noxious gases, and cigarette smoking in a dose dependent manner [35]. Although identified as separate entities, most patients with COPD have features of both [36]. We also observed >2-fold risk of emphysema in CRS cases. While emphysema and COPD are hand in glove, the association observed in our study needs validation in further replicative studies with a larger sample size. Chronic bronchitis a long-term inflammatory disease of lower airways leads to an increased decline in lung function[37], a higher risk of cardiovascular disease [38], impaired quality of life [39] and increased mortality [38].

CRS and chronic bronchitis share several risk factors, such as tobacco smoking and occupational exposure [40]. While a recent large study [6], reported that CRS was associated with increased odds of developing chronic bronchitis during a five-year follow-up, The risk was not observed in our study. Moreover, in a small Danish clinical study from 2014, [41] reported that CB is more common in CRS patients with nasal polyps compared with controls. But nasal polyps were an uncommon presentation in our study. The difference in the

results can also be attributed to the ethnic difference and sample size variations.

Conclusion

In conclusion we observed that COPD and CRS can frequently co-exist. The presence of CRS should be assessed in COPD patients, especially in those with severe diseases. Further research is needed to disclose possible common immunopathological mechanisms in the pathogeneses of COPD and CRS.

References:

1. Bachert, C., et al., Adult chronic rhinosinusitis. Nature Reviews Disease Primers, 2020. 6(1): 86.
2. Viniol, C. and C.F. Vogelmeier, Exacerbations of COPD. Eur Respir Rev, 2018. 27(147).
3. Quaderi, S.A. and J.R. Hurst, The unmet global burden of COPD. Glob Health Epidemiol Genom, 2018. 3: p. e4.
4. Vogelmeier, C.F., et al., Global strategy for the diagnosis, management, and prevention of chronic obstructive lung disease 2017 report. GOLD executive summary. American journal of respiratory and critical care medicine, 2017; 195(5): 557-582.
5. Yii, A.C.A., et al., Precision medicine in united airways disease: A "treatable traits" approach. Allergy, 2018. 73(10): 1964-1978.
6. Arndal, E., et al., Chronic rhinosinusitis in COPD: A prevalent but unrecognized comorbidity impacting health related quality of life. Respiratory Medicine, 2020. 171: 106092.
7. Schiller, J.S., et al., Summary health statistics for U.S. adults: National Health Interview Survey, 2010. Vital Health Stat 10, 2012(252): 1-207.
8. Hastan, D., et al., Chronic rhinosinusitis in Europe--an underestimated disease. A GA²LEN study. Allergy, 2011. 66(9): 1216-23.
9. Collins, M., et al., Environmental risk factors and gender in nasal polyposis. Clinical Otolaryngology & Allied Sciences, 2002. 27(5): 314-317.
10. Barnes, P.J., Sex differences in chronic obstructive pulmonary disease mechanisms. 2016, American Thoracic Society. 813-814.
11. Stevens, W.W., R.P. Schleimer, and R.C. Kern, Chronic rhinosinusitis with nasal polyps. The journal of allergy and clinical immunology: In practice, 2016. 4(4): 565-572.
12. Arndal, E., et al., Chronic rhinosinusitis in COPD: A prevalent but unrecognized comorbidity impacting health related quality of life. Respir Med, 2020. 171: 106092.
13. Hasten, D., W. Fokkens, and C. Bachert, Chronic rhinosinusitis in Europe–an underestimated disease. Allergy, 2011. 66(9): 1216-23.
14. Karthik, L., et al., Protease inhibitors from marine actinobacteria as a potential source for antimalarial compound. PloS one, 2014. 9(3): e90972.
15. Irvin, C.G., Chronic Rhinosinusitis and Structural Remodeling. Am J Respir Cell Mol Biol, 2017. 57(3): 265-266.
16. 16. Bousquet, J., et al., Allergic Rhinitis and its Impact on Asthma (ARIA): achievements in 10 years and future needs. Journal of Allergy and Clinical Immunology, 2012. 130(5): 1049-1062.
17. Kelemence, A., et al., The frequency of chronic rhinosinusitis/nasal polyp in COPD and its effect on the severity of COPD. COPD: Journal of Chronic Obstructive Pulmonary Disease, 2011. 8(1): 8-12.
18. Fokkens, W., V. Lund, and J. Mullol, European position paper on rhinosinusitis and nasal polyps 2007. Rhinology. Supplement, 2007. 20: 1-136.
19. 19. Nathan, K., et al., The Role of Diagnostic Nasal Endoscopy and a Computed Tomography Scan (Nose and PNS) in the Assessment of Chronic Rhinosinusitis: A Comparative Evaluation of the Two Techniques. Sinusitis, 2021. 5(1): 59-66.
20. Shelkar, R., et al., Role of nasal endoscopy in sinonasal diseases. International Journal of Scientific Study, 2014. 2(1): 6-10.
21. Hirsch, A.G., et al., Nasal and sinus symptoms and chronic rhinosinusitis in a population-based sample. Allergy, 2017. 72(2): 274-281.
22. Eccles, R., Physiology of nasal secretion. Eur J Respir Dis, 1983. 62: p. 115-119.
23. 23. Eccles, R., Mechanisms of the symptoms of rhinosinusitis. Rhinology, 2011. 49(2): 131-8.
24. Fokkens, W.J., et al., EPOS 2012: European position paper on rhinosinusitis and nasal polyps 2012. A summary for otorhinolaryngologists. Rhinology, 2012. 50(1): 1-12.
25. Benninger, M.S., et al., Adult chronic rhinosinusitis: definitions, diagnosis, epidemiology, and pathophysiology. Otolaryngol Head Neck Surg, 2003. 129(3 Suppl): S1-32.
26. Clifton, N.J. and N.S. Jones, Prevalence of facial pain in 108 consecutive patients with paranasal mucopurulent discharge at endoscopy. J Laryngol Otol, 2007. 121(4): 345-8.
27. Fahy, C. and N.S. Jones, Nasal polyposis and facial pain. Clin Otolaryngol Allied Sci, 2001. 26(6): 510-3.
28. Ling, F.T. and S.E. Kountakis, Important clinical symptoms in patients undergoing functional endoscopic sinus surgery for

chronic rhinosinusitis. Laryngoscope, 2007. 117(6): 1090-3.
29. Eweiss, A.Z., et al., Do patients with chronic rhinosinusitis with nasal polyps suffer with facial pain? Rhinology, 2013. 51(3): 231-5.
30. West, B. and N.S. Jones, Endoscopy-negative, computed tomography-negative facial pain in a nasal clinic. The Laryngoscope, 2001. 111(4): 581-586.
31. Nanda, M.S., M. Kaur, and V. Gupta, Correlation between chronic rhinosinusitis and laryngopharyngeal reflux. National Journal of Physiology, Pharmacy and Pharmacology, 2018. 8(4): 544-549.
32. Martínez-Antón, A., J. Roca-Ferrer, and J. Mullol, Mucin gene expression in rhinitis syndromes. Curr Allergy Asthma Rep, 2006. 6(3): 189-97.
33. Shimizu, S., et al., Eosinophil-epithelial cell interactions stimulate the production of MUC5AC mucin and profibrotic cytokines involved in airway tissue remodeling. Am J Rhinol Allergy, 2014. 28(2): 103-9.
34. Cho, S.H., D.W. Kim, and P. Gevaert, Chronic Rhinosinusitis without Nasal Polyps. J Allergy Clin Immunol Pract, 2016. 4(4): 575-82.
35. Pahal, P., A. Avula, and S. Sharma, Emphysema. 2018.
36. Zhang, H., et al., Epidemiology of chronic airway disease: results from a cross-sectional survey in Beijing, China. J Thorac Dis, 2018. 10(11): 6168-6175.
37. Guerra, S., et al., Chronic bronchitis before age 50 years predicts incident airflow limitation and mortality risk. Thorax, 2009. 64(10): 894-900.
38. Puddu, P.E., et al., Chronic bronchitis in the 50-year follow-up of the European cohorts of the Seven Countries Study: prevalence, mortality and association with cardiovascular diseases. Respiratory Medicine, 2021; 181: 106385.
39. Kanervisto, M., et al., COPD, chronic bronchitis and capacity for day-to-day activities: negative impact of illness on the health-related quality of life. Chronic respiratory disease, 2010; 7(4): 207-215.
40. Doney, B., et al., Occupational risk factors for COPD phenotypes in the Multi-Ethnic Study of Atherosclerosis (MESA) lung study. COPD: Journal of Chronic Obstructive Pulmonary Disease, 2014; 11(4): 368-380.
41. Håkansson, K., et al., A comparative and descriptive study of asthma in chronic rhinosinusitis with nasal polyps. American journal of rhinology & allergy, 2014; 28(5): 383-387.