

## A Comprehensive Epidemiological and Clinical Study of Chronic Rhinosinusitis: First Report from an Iranian Sinusitis Registry Center

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### Abstract

**Background & Objective:** Chronic rhinosinusitis (CRS) is a high prevalent disease throughout the world. The aim of this study was to investigate the epidemiological and clinical characteristics of the CRS patients.

**Materials & Methods:** A total of 241 CRS patients aged 15-70 years were recruited. The prevalence of allergic diseases and its association with CRS, disease severity, and quality of life (QoL) were assessed using GA2LEN and SNOT-22 questionnaires, respectively. Patients' clinical diagnoses and allergic comorbidities were evaluated using paranasal sinus computed tomography (CT), nasal endoscopy, and paraclinical tests (smell identification test, fractional exhaled nitric oxide (FeNO), skin prick test (SPT), pulmonary function test (PFT)).

**Results:** The mean ( $\pm$ SD) age of all participants was 40.1 $\pm$ 11.1 years, with a gender distribution of 56% male and 44% female. Nasal polyps (NP) were diagnosed in 42.4% of patients. The total mean SNOT-22 scores and the mean scores of the nasal symptoms category were significantly higher in CRS patients with NP (CRSwNP) compared to CRS without NP (CRSsNP) (OR = 2.3, 95%CI = 9.6–0.55, P = 0.028). Furthermore, there was a significant association between CRSwNP and persistent allergic rhinitis comorbidity (P = 0.006). Finally, a significant association was found between CRSwNP and severe SPT reactivity to *Dermatophagoides farinae* and date palm pollen (P = 0.04 and P < 0.001, respectively).

**Conclusion:** This study suggests that higher SNOT-22 scores may impact QoL in CRSwNP patients. Additionally, a significant association was found between CRS and respiratory allergic diseases.

**Keywords:** Chronic rhinosinusitis, Allergic diseases, EPOS2020, GA2LEN, SNOT-22

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### Introduction

Chronic rhinosinusitis (CRS), an inflammation of the nose and paranasal sinuses, in adults is characterized by the presence of two or more symptoms, including nasal blockage (obstruction or congestion), anterior or posterior nasal

discharge, with or without facial pain (or pressure), and reduction or loss of smell for more than 12 weeks. Broadly, CRS, based on nasal endoscopic findings, is phenotypically classified as CRS with nasal polyps (CRSwNP) and without nasal polyps (CRSsNP) (1). Recently, studies have focused on endotyping of CRS based on the type of immune inflammation. Such endotyping may provide a new method for understanding the immunopathology of the disease and ultimately

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developing more efficient treatment approaches (2, 3).

The prevalence of CRS is 10.9–13.4% in the general population of Europe and the USA (4, 5). Our previous population-based study showed that the prevalence of CRS was 28.4% in Iran (6). Also, it was reported that CRSwNP was thought to be around 1.1% in the USA, and its prevalence in Europe was shown to be between 2.1% and 4.4% (7, 8). Moreover, a study revealed that the burden of CRS on the healthcare system in the US was in the range of 6.9 to 9.9 billion USD per year (9). The European direct and indirect economic burden of CRSwNP was reported as 1501€ and 5659 € per patient/year, respectively (10, 11).

In an international survey of clinical specialists from 50 countries, the most common symptoms of CRS were reported to be nasal obstruction, postnasal drip (PND), and headache. This study also found that the most common paraclinical investigation modalities for CRS assessment were paranasal sinus CT, fiberoptic endoscopy, and anterior rhinoscopy (12).

Based on the “one airway, one disease” theory, the association between local allergic inflammation in the nose, known as allergic rhinitis (AR), and CRS could be attributed to a shared underlying mechanism. This suggests that they may represent the coexistence of two or more chronic diseases. Consequently, local allergic inflammation of the nose has been proposed as a component of the pathophysiological mechanism that may lead to the development of CRS and may increase its severity, especially in CRSwNP (13, 14). Previous studies have strongly confirmed that CRS, particularly CRSwNP, is associated with AR and asthma, often resulting in comorbidity. Therefore, allergic inflammation in both the nasal mucosa and the lower airway are directly interrelated (6, 15, 16). Although 8–18% of the general population experience poor quality of life (QoL) and sleep problems, approximately 60–75% of CRS patients suffer from these conditions, with a significantly higher prevalence among CRS patients (17). Furthermore, QoL may be significantly

impaired in CRSwNP patients compared to CRSsNP patients, with CRSwNP patients exhibiting lower mental than physical health scores, indicating a greater impact on mental than physical health (18, 19). Additionally, sleep disorders in CRS patients have been attributed to multiple factors, including upper airway obstruction, nasal congestion, and the inflammatory process (17). Importantly, studies have shown that cigarette smoking is a well-known airway irritant that can induce airway inflammation and adversely affect the mucociliary clearance system. Active cigarette smoking has been linked to an increased prevalence of CRS and poor outcomes following sinus surgery (20, 21). Nasal endoscopy and CT scans were not feasible for all participants in large sample population-based studies. Given the high prevalence of CRS and the scarcity of valid epidemiological and clinical data in the region, the aim of this study was to investigate the epidemiological and clinical assessment of CRS patients using the criteria outlined in the European Position Paper on Rhinosinusitis and Nasal Polyps 2020 (EPOS2020) and the Global Allergy and Asthma European Network (GA2LEN) questionnaire. Moreover, the clinical diagnosis of patients was confirmed using paranasal sinus CT, nasal endoscopy, and paraclinical tests [(smell identification test, fractional exhaled nitric oxide (FeNO), skin prick test (SPT), pulmonary function test (PFT)]. Finally, we assessed the association between CRS and allergic diseases.

## **Materials and Methods**

### **Study design**

This observational, cross-sectional study recruited 241 adult patients (aged 15–70 years) with suspected CRS who referred to the Sinusitis Research Center of Bushehr (SRCB), affiliated with the Medical University of Bushehr, Iran, between June 2018 and June 2020. Eligible patients met the EPOS2020 diagnostic criteria for CRS, presenting with at least one major symptom (nasal blockage or obstruction,

congestion, anterior or posterior nasal discharge) and one minor symptom (facial pain or pressure) for more than 12 weeks. Patients with acute sinusitis, immunodeficiency, or cystic fibrosis were excluded. The study was approved by the Ethics Committee of the Bushehr University of Medical Sciences, Bushehr, Iran (ethical approval code: IR.BPUMS.REC.1399.176). Informed written consent for participation in the study protocol was obtained from all subjects.

### Chronic Rhinosinusitis Registry Center questionnaire

The Sinusitis Registry Center's questionnaire incorporates several standard questionnaires, including the Sino-Nasal Outcome Test (SNOT)-22, the GA2LEN, and socioeconomic and smoking status questionnaires. Trained staff administered the questionnaires, and patients completed the SNOT-22 questionnaire after receiving guidance. The SNOT-22 questionnaire measures the physical impairments, functional limitations, disability, and societal limitations caused by CRS and is designed to determine the severity of CRS. The questionnaire was translated into Persian and standardized through a pilot study prior to the main study. A trained interviewer administered the questionnaire to the participants. It is categorized into four sections: nasal, otologic, sleep, and emotional symptoms. Additionally, the severity of the CRS condition for the patients was registered using a visual analog scale (VAS) as mild (0-3), moderate (4-7), and severe (8-10). Furthermore, the GA2LEN questionnaire was used to assess patient-reported allergic comorbid conditions such as asthma, allergic rhinitis (AR), and atopic dermatitis (AD). The GA2LEN questionnaire includes four questions for evaluating the presence of AR (intermittent: IAR or persistent: PAR). Additionally, it contains ten questions for evaluating and assessing asthma and four more questions about having AD. Physician-diagnosed asthma and AD were also inquired about. Finally, participants were asked about aspirin-exacerbated respiratory disease (AERD) and gastroesophageal reflux disease (GERD).

### Clinical diagnosis of CRS

The clinical diagnostic criteria for CRS were defined based on the EPOS2020 guidelines (1). Symptoms were assessed by an immunologist and an otolaryngologist, and radiological findings were evaluated by a radiologist. To confirm the clinical diagnosis of CRS and comorbid conditions, we employed several paraclinical methods. Paranasal sinus computed tomography (PNS CT) scans were performed for all patients to assess mucosal changes within the ostiomeatal complex and sinuses and to identify the presence of nasal polyps (NPs). Otolaryngologists visually assessed the presence or absence of NPs, mucopurulent discharge, edema, and mucosal obstruction in the middle meatus using endoscopy. AR was defined as the presence of nasal symptoms such as itching, sneezing, and watery rhinorrhea, particularly during seasonal periods (as assessed by the GA2LEN questionnaire), along with moderate or severe reactivity to aeroallergens, a high level of total IgE ( $>100$  IU/mL), and eosinophilia. Pulmonary function tests (PFTs) were performed using a spirometer (Spirolab, MIR, Italy) to evaluate lower respiratory tract involvement related to CRS, such as asthma, and to clinically confirm these conditions.

### Smell Identification test

The presence or absence of an olfactory dysfunction was determined based on the patient's complaints. For this purpose, we employed the Iran Smell Identification Test (Saba Tajheez Sabalan CO, Tehran, Iran). This test has been standardized for the Iranian population and the kit contains 24 different types of odors categorized into eight groups: aromatic, fruity, mint, spicy, sweet, sour, woody, and nasty. The test result is reported as a range from 0 to 24 and indicates the function of the olfactory sense, with the following categories: normal (19-24), mild hyposmia (14-18), moderate hyposmia (10-13), and anosmia (0-9).

### Fractional exhaled Nitric Oxide (FeNO)

Nitric oxide (NO), a noninvasive biomarker for evaluating airway inflammation, aids in the diagnosis and monitoring of osteomeatal complex obstruction in paranasal sinus diseases, particularly in patients with CRSwNP. To measure the exhaled NO concentration for the patients, a chemiluminescent analyzer (NObreath, Bedfont Scientific Ltd, England) was employed. The measurement of FeNO was performed in accordance with the American Thoracic Society and European Respiratory Society recommendations (22).

### Skin Prick Test (SPT)

Skin Prick Test (SPT) was performed on all patients using regional common allergen extracts (Greer, USA). Allergens were selected for the study based on the types of plants grown in the area, as well as other allergens identified and introduced by the Agricultural Research Center, Bushehr, Iran. The allergens tested included trees that commonly spread pollen (date palm, mulberry red, oleaceae, and false acacia), grasses (Bermuda, couch, and meadow grass), weeds (Chenopodium album, Russian thistle, and sorrel), house dust mites (HDMs) (*Dermatophagoides farina* and *pteronyssinus*), molds (*Aspergillus fumigatus* and *Alternaria alternate*), animals' dander, and cockroach extracts. The SPT was performed according to international guidelines (23). A wheal size  $\geq 3$  mm was measured as a positive reaction. Histamine hydrochloride (10 mg/mL) and glycerin saline were used as positive and negative controls, respectively. All subjects analyzed had a positive reaction to histamine, and none reacted to the negative controls.

### Laboratory tests

To assess the allergic conditions of CRS patients, eosinophil counts and total serum IgE (IU/mL) were measured. Additionally, serum vitamin D3 (ng/mL) levels were evaluated to investigate the association between CRS and vitamin D deficiency.

### Statistical analysis

Descriptive statistics, including mean  $\pm$  SD of paraclinical, radiological, and laboratory findings, were calculated. The frequency distribution of age groups, gender, smoking status, and comorbid allergic conditions, AERD, and GERD in CRS patients was also determined. Chi-square tests were used to evaluate the association between demographic characteristics and clinical data of the patients. Additionally, Chi-square tests were used to assess the correlation between allergic diseases and CRS and its severity (based on VAS). Differences in laboratory findings were compared using two independent T-tests. P values less than 0.05 were considered statistically significant. Statistical analyses were performed using IBM SPSS Statistics for Windows, version 22 (IBM Corp., Armonk, NY, USA).

### Results

In this study, 241 patients (56% males and 44% females) with CRS were enrolled. The mean (SD) age of all patients was  $40.1 \pm 11.1$  years, with a range of 15 to 70 years. The most common symptom among the patients was posterior nasal discharge (PND) (90.9%). The positive family history, antibiotic use, and previous nasal polypectomy of the patients were 42.7%, 78.8%, and 12%, respectively. Demographic and clinical data of the patients are shown in Table 1.

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**Table 1.** Demographic and clinical data of the patients with CRS

Variable	All CRS patients 241 (100%)	CRSwNP 102 (42.4%)	CRSsNP 139 (57.6)	P value
Men Women	135 (56) 106 (44)	61 (59.9) 41 (40.1)	74 (53.2) 65 (56.7)	0.1
Age group -15- 25 -26- 50 -> 50	16 (6.6) 180 (74.8) 45 (18.7)	4 (3.9) 73 (71.5) 25 (24.5)	12 (8.6) 101 (72.6) 19 (13.7)	0.06
Smoking	38 (15.8)	16 (15.6)	22 (15.8)	0.5
Occupational status -Employed -Unemployed -Retired	145 (60.2) 70 (29) 22 (9.1)	64 (62.7) 24 (23.5) 12 (11.7)	81 (59.1) 46 (33.5) 10 (7.2)	0.1
Education level -Academic -Diploma and lower	137 (56.8) 104 (43.2)	57 (55.8) 45 (44.2)	80 (57.6) 59 (41.4)	0.3
Patients complaint: -Nasal blockage (obstruction) -Anterior nasal secretion -Posterior nasal discharge (PND) -Facial pain (pressure) -Reduction or loss of smell	199 (82.6) 173 (71.8) 219 (90.9) 196 (81.3) 135 (56)	94 (92.2) 79 (77.5) 95 (93.1) 83 (81.4) 78 (76.5)	100 (71.9) 89 (64) 118 (84.8) 107 (76.9) 55 (39.5)	0.001 0.03 0.1 0.1 0.001
Visual analog scale (VAS) -Mild -Moderate -Severe	58 (24) 116 (48.1) 67 (28.7)	8 (7.8) 46 (45) 48 (47)	47 (33.8) 73 (52.5) 19 (13.7)	0.001

Furthermore, a significant association was observed between the severity of SNOT-22 and the presence of PAR ( $P= 0.01$ ) and asthma ( $P< 0.001$ ). Additionally, SNOT-22 severity was significantly correlated with abnormal PFT results ( $P= 0.013$ ) but was not associated with higher levels of FeNO,

total serum IgE, eosinophil counts, or serum vitamin D3 ( $P>0.05$ ). Moreover, patients with academic education and employment had significantly higher SNOT-22 scores ( $P= 0.01$  and  $P< 0.001$ , respectively). The SNOT-22 test outcomes in patients with CRSwNP compared to CRSsNP are presented in Table 2.

**Table 2.** SNOT-22 test outcomes in the patients with CRSwNP in comparison with CRSsNP

Variable	All CRS patients (mean± SD)	CRSwNP (mean± SD)	CRSsNP (mean± SD)	P value
Nasal symptoms:	2.6± 1.6	3.0± 1.6	2.4± 1.6	0.003
-Need to blow your nose	2.1± 1.5	2.2± 1.5	1.9± 1.6	0.09
-Sneezing	2.1± 1.6	2.4± 1.5	1.9± 1.6	0.009
-Running nose	1.6± 1.6	1.9± 1.7	1.5± 1.5	0.05
-Cough	3.2± 1.4	3.3± 1.5	3.2± 1.4	0.5
-Post-nasal discharge	1.9± 1.7	2.5± 1.7	1.5± 1.5	0.001
-Thick nasal discharge	1.8± 1.8	2.7± 1.9	1.1± 1.4	0.001
-Difficulty to feel smells or tastes				
-Stuffed nose	2.9± 1.6	3.4± 1.2	2.5± 1.6	0.001
Otologic symptoms:	1.9± 1.7	2.1± 1.8	1.8± 1.6	0.2
-A feeling of full or stuffed ear				
-Dizziness or vertigo	1.6± 1.6	1.4± 1.6	1.7± 1.6	0.09
-Earache	1.3± 1.5	1.3± 1.6	1.4± 1.6	0.7
-Facial pain or pressure	2.9± 1.7	2.7± 1.7	3± 1.6	0.1
Sleep symptoms:	1.9± 1.9	2.1± 1.9	1.7± 1.9	0.05
-Difficulty sleeping	1.6± 1.7	1.8± 1.8	1.5± 1.6	0.2
-Wake up in the middle of the night	1.5± 1.7	1.7± 1.8	1.4± 1.7	0.1
-Lack of a good night's sleep				
-Wake up tired	2.3± 1.6	2.2± 1.6	2.4± 1.6	0.3
-Fatigued or tired during the day	2.5± 1.5	2.3± 1.6	2.6± 1.6	0.07
-Reduced productivity				
-Reduced concentration	2.2± 1.6	2.2± 1.7	2.3± 1.6	0.6
-Frustrated, restless or irritated	2.2± 1.7	2.2± 1.6	2.2± 1.7	0.8
	2.1± 1.7	2.0± 1.7	2.2± 1.7	0.5

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Emotional symptoms: -Sadness -A feeling of shame	1.7± 1.6 1.4± 1.6	1.5± 1.6 1.4± 1.7	1.9± 1.6 1.3± 1.6	0.06 0.5
Total SNOT-22 score (Mean± SD)	46.3± 17.6	49.2± 18.2	44.2± 17	0.028
SNOT-22 severity -Mild -Moderate -Severe	8 (3.3) 127 (52.7) 106 (44)	1 (0.9) 50 (49) 51 (50.1)	7 (5) 79 (56.8) 53 (38.2)	0.08

In addition, the prevalence of CRSwNP and CRSsNP was 42.4% and 57.6%, respectively. The self-reported prevalence of allergic comorbidities among the patients was as follows: AR: 65.6%, PAR: 48.5%, IAR: 17.8%, asthma: 32%, AD: 18.3%, AERD: 5.4%, and GERD: 50.6%.

Furthermore, a significant association was observed between

having CRSwNP and clinically diagnosed AR ( $P < 0.001$ ) and asthma ( $P = 0.048$ ). The frequency of allergic comorbidities in both CRSwNP and CRSsNP patients, based on epidemiological assessment, is shown in Table 3.

The results of radiological and endoscopic findings, PFT, FeNO, smell identification, and laboratory tests are shown in Table 3.

**Table 3.** The frequency of allergic comorbid diseases, paraclinical and laboratory findings in the patients with CRwNP and CRSsNP

Variable	All CRS patients 241 (100%)	CRSwNP 102 (100%)	CRSsNP 139 (100%)	P value
Allergic comorbid diseases (self-reported):				
-Allergic rhinitis (AR)	158 (65.6)	73 (71.5)	80 (57.5)	0.05
-Persistent AR	117 (48.5)	60 (58.8)	54 (38.8)	0.006
-Intermittent AR	43 (17.8)	27 (26.4)	14 (10)	0.1
-Asthma	77 (32)	39 (38.2)	37 (26.6)	0.06
-Atopic dermatitis	44 (18.3)	15 (14.7)	27 (19.4)	0.1
-AERD	13 (5.4)	7 (6.8)	6 (4.3)	0.3
-GERD	122 (50.6)	53 (51.9)	68 (46)	0.5

Endoscopic findings				
-Mucopurulent discharge from middle meatus	52 (21.4)	22 (21.5)	28 (20.1)	0.3
-Edema or mucosal obstruction in middle meatus	43 (17.8)	21 (20.5)	22 (15.8)	0.4
Endoscopic findings				
-Mucopurulent discharge from middle meatus	52 (21.4)	22 (21.5)	28 (20.1)	0.3
-Edema or mucosal obstruction in middle meatus	43 (17.8)	21 (20.5)	22 (15.8)	0.4
PNS CT scan finding				
-Mucosal changes within the osteomeatal complex and or sinuses	53 (22)	30 (29.4)	23 (16.5)	0.038
PFT findings				
-FEV1 (%)	86.0± 17.3	85.3± 19.0	86.3± 16.2	0.6
-PEF (%)	77.8± 20.1	77.9± 20.8	77.5± 19.7	0.9
-FVC (%)	78.4± 17.9	77.6± 17.7	78.0± 18.3	0.8
FeNO (ppb)	16.9± 14.1	18.2± 14.9	15.8± 13.6	0.2
Smell Identification Test findings				
-Normal	143 (59.3)	47 (46)	92 (66.1)	0.001
-Mild hyposmia	18 (7.5)	13 (12.7)	5 (3.5)	
-Moderate hyposmia	0 (0)	0 (0)	0 (0)	
-Anosmia	28 (11.6)	24 (23.5)	4 (2.8)	
Lab data findings				
-Eosinophil (%)	4.5± 1.2	6.7± 1.9	2.8± 1.6	0.3
-Neutrophil (%)	55.5± 8.7	50.8± 11.2	55.3± 6.0	0.003
-Total IgE (IU/mL)	172.2± 109.2	175.2± 201.9	169.7± 219.6	0.9
-Vit D3 (ng/dL)	26.6± 11.5	24.8± 12.2	27.9± 11	0.2

Aspirin exacerbated respiratory disease (AERD); Gastroesophageal reflux disease (GERD), PNS: Para Nasal Sinuses; PFT: Pulmonary Function Test; FeNO: Fractional exhaled Nitric Oxide



Moreover, the most frequent allergen reactivity in SPT was to HDM (48.4%), followed by Russian thistle (36.3%) and Lambs quarter (34.3%). Additionally, the most severe reactivity was observed with HDM and date palm pollen in both CRSwNP and CRSsNP patients (23.5% and 21.5% for CRSwNP versus 10.8% and 2.8% for CRSsNP patients, respectively). There was a significant association between having CRSwNP and severe reactivity to *Dermatophagoides farina* ( $P=0.04$ ) and date palm pollen ( $P<0.001$ ).

### Discussion

This study was conducted by the Sinusitis Registry Center of Bushehr (SRCB), Iran, involving 241 diagnosed CRS patients. The study provides valuable insights into the clinical and paraclinical characteristics of the patients, including related allergic comorbid conditions, CRS-specific QoL, and aeroallergen reactivity. To the best of our knowledge, this is the first study from Iran to utilize the EPOS2020 diagnostic criteria for evaluating CRS patients.

The most common CRS symptoms identified in this study were PND (90.9%), nasal blockage (82.6%), facial pain or pressure (81.3%), anterior nasal secretion (71.8%), and reduction or loss of smell (56%). Our data also revealed that PND, nasal blockage, anterior nasal secretion, and reduction or loss of smell were more prevalent in patients with CRSwNP than CRSsNP. This aligns with the findings of McNally et al., who reported that the most common symptoms associated with CRS were nasal congestion (73%), PND (69%), facial pressure (42%), and anosmia or hyposmia (39%) (24). A study conducted in Italy reported that the most common symptoms were nasal obstruction (86%), PND (82%), anterior rhinorrhea, and hyposmia (46%) (12, 24).

Interestingly, in the present study, PND was the most common symptom in CRS patients, while studies from the USA and Europe reported nasal congestion (or obstruction) as the most prevalent symptom. This suggests that climate and geographic conditions may influence the manifestation of CRS symptoms. The SNOT-22 standard questionnaire is used to assess the health status and health-related QoL of CRS patients through scoring (25). Our data indicated that a majority of patients fell within the moderate to severe category of SNOT-22. The mean SNOT-22 score for all patients was 46.3. Additionally, the mean scores for nasal symptoms such as 'need to blow your nose', 'running nose', 'thick nasal discharge', 'difficulty to feel smells or tastes', and 'stuffed nose' were significantly higher in CRSwNP patients compared to CRSsNP patients.

These patients also had significantly lower disease-related specific and generic QoL. Notably, other CRS symptoms in SNOT-22, such as otologic, sleep, and emotional symptoms, did not differ significantly between the two groups. Interestingly, the total mean SNOT-22 score was significantly higher in CRSwNP patients compared to CRSsNP patients. The mean SNOT-22 score in the study by Abdalla et al. was 41.5 and 44.4 ( $P<0.05$ ) in the CRSwNP and CRSsNP groups, respectively (26). The SNOT-22 score was lower (28.1) in CRSwNP patients in the study conducted by Lange et al. in Europe. However, other studies have shown that 75% of CRS patients had a SNOT-22 total score below 38 across the four categorized sections of SNOT-22 (nasal, otologic, sleep, and emotional symptoms) and reported that nasal symptoms were not the only concern for patients; it is also clear that CRS affects patients in multiple ways (27). Furthermore, studies have reported that the improvement of SNOT-22 score after

surgery and the higher rate of required revision surgeries were most evident in CRSwNP patients (28).

Importantly, nasal polyps (NPs) were the most common factor affecting the quality of life (QoL) of CRS patients. NPs cause nasal obstruction, hyposmia, and recurrent infections, leading to impaired QoL. Approximately 20–40% of all CRS patients present with NPs (12). Our data aligns with other studies, with 42.4% of all patients affected by NPs (59.9% men vs. 40.1% women) (29-31).

Allergic inflammation plays a central role in the pathogenesis of NPs. It has been reported that 10-64% of patients with NPs have allergic conditions (30). Our study revealed that 100% of CRSwNP patients had reactions to at least one aeroallergen in skin prick testing (SPT). However, patients had a significantly higher reactivity to house dust mites (HDM) and date palm pollen. The high temperature and humidity in the region provide favorable conditions for HDM growth, and palm trees are widely cultivated in such areas. In contrast, other studies have found that the percentage of positive SPT responses in patients ranged from 16 to 35%, highlighting the controversial nature of these findings among researchers (32, 33). Consistent with other studies, our results demonstrated a high prevalence of comorbid allergic diseases among CRS patients (65.5% had allergic rhinitis (AR) and 32% had asthma). Additionally, CRSwNP was associated with aspirin-exacerbated respiratory disease (PAR) comorbidity (29, 30). The prevalence of asthma in CRS patients has been reported to range from 23 to 50% (34, 35).

Furthermore, the relationship between CRS and respiratory allergies aligns with the concept of “one airway, one disease,” mirroring the association between AR and asthma (36).

associations have been attributed to the involvement of common inflammatory

mediators and cytokines, the recruitment of eosinophils in both upper and lower airways, and the production of local IgE, all of which contribute to the pathogenesis of these diseases (37, 38).

Olfactory dysfunction is another factor that impacts QoL in CRS patients. We observed that 56% of all patients and 76.5% of CRSwNP patients reported loss of smell. Additionally, 31.9% of patients had a high SNOT-22 score, which was significantly associated with the severity of the symptom. Olfactory dysfunction is caused by mechanical obstruction of the olfactory cleft by NPs, edema, and secretions (39). The severity of olfactory dysfunction is related to the direct and severe inflammation of the neuroepithelium (40). Consistent with other studies, we found a significant association between loss of smell in CRS patients and asthma (37).

A strength of this study was the comprehensive epidemiological and clinical assessment of CRS patients. Moreover, we employed several standardized questionnaires and paraclinical tests. However, given the high prevalence (28.4%) of CRS in the region (6), we anticipated a larger sample size.

### Conclusion

The results of this investigation revealed that posterior nasal discharge (PND) was the most prevalent complaint among patients with chronic rhinosinusitis (CRS). Additionally, we observed that the severity of SNOT-22 and impaired quality of life (QoL) were significantly higher in patients with CRS with nasal polyps (CRSwNP) compared to those with CRS without nasal polyps (CRSsNP). Conclusively, our findings suggest a high prevalence of comorbid allergic diseases such as allergic rhinitis (AR) and asthma in CRS patients and a significant association between CRS and respiratory allergic diseases.

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### **Conflict of interest**

The authors declare that they have no conflicts of interest.

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### **Ethical Considerations**

All patient information is confidential and is only accessible to the project manager.

### **Author Contributions**

AD, MZ, and AA drafted the manuscript, interpreted the findings, and participated in study design and conduction. MM participated in study design and performed data analysis. AM, RK, AG, and ZM participated in study design and reviewed the manuscript. SF conceived the study, helped draft the manuscript, and participated in study design and conduction.

### **Code of Ethics**

The study was approved by the Ethics Committee of Bushehr University of Medical Sciences, Bushehr, Iran (ethical approval code: IR.BPUMS.REC.1399.176).

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