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ORIGINAL ARTICLE

'Central Compartment Atopic Disease' and 'Other Subtypes of Chronic Rhinosinusitis with Nasal Polyps': A Prospective Observational Study

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Abstract

Background: Chronic rhinosinusitis with nasal polyps (CRSwNP) comprises heterogeneous inflammatory phenotypes. 'Central Compartment Atopic Disease' (CCAD) is a distinct subtype strongly connected with inhalant allergies. **Aim:** To assess the clinical characteristics, atopic profile, histopathology, treatment outcomes of CCAD and other CRSwNP subtypes in a tertiary care setting. **Methods:** A prospective study of 127 CRSwNP patients was conducted. Based on clinical, endoscopic, radiologic, and histologic criteria, patients were categorized as CRSwNP (NOS), CRSwNP with central compartment involvement (CRSwNP/CC), 'Aspirin-Exacerbated Respiratory Disease'(AERD), 'Allergic Fungal Rhinosinusitis' (AFRS), and 'CCAD'. 'Allergy testing'(skin prick/specific IgE) and eosinophil counts done. The 'Sino-Nasal Outcome Test'(SNOT-22) was utilised to record the pre and postoperative symptom scores. **Results:** Mean patient age was 45.2 ± 11.5 years; with 56.69% (72 patients) males and 43.3% (55 patients) females. CCAD (15.75%) and CRSwNP/CC (37.8%) subgroups demonstrated highest allergy prevalence (100% and 91.67%, respectively), with significantly lower asthma rates in CCAD (15%). Mean eosinophil count was 36/HPF. SNOT-22 improved from 54 to 8 postoperatively. Recurrence occurred in 20% of CRSwNP (NOS) but none in CCAD or CRSwNP/CC. **Conclusion:** 'CCAD' and 'CRSwNP/CC' are allergy-driven eosinophilic phenotypes showing excellent response to targeted therapy and surgery, emphasizing the importance of precise phenotyping in CRS.

Key Words

Central Compartment Atopic Disease, Chronic Rhinosinusitis with Nasal Polyps, Atopy, 'Eosinophilic Inflammation, 'Histopathological Endotype.

Introduction

Chronic rhinosinusitis (CRS) is a prevalent, persistent inflammatory disorder of the sinonasal mucosa which affects about 5% to 15% of the population. There are two main clinical phenotypes: 'CRS with nasal polyps'(CRSwNP) and 'CRS without nasal polyps'(CRSsNP), both with different patterns of inflammation[1,2]. CRSwNP includes a number of clinically relevant subtypes, including 'allergic fungal rhinosinusitis'(AFRS), 'aspirin-exacerbated respiratory disease'(AERD), 'cystic fibrosis-associated CRS', 'eosinophilic granulomatosis with polyangiitis', and the newly described 'CCAD'[3].

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'CCAD' is an atopic variant of CRSwNP, first formally illustrated by DelGaudio and colleagues in 2017[4]. It is distinguished by polypoid or edematous variations of central nasal structures like'middle turbinate'(MT), 'superior turbinate'(ST), and 'posterosuperior nasal septum' (PSNS)[5]. The pathogenesis of CCAD is closely connected to inhalant allergy, with allergen accumulation in these central compartments likely caused by nasal cavity airflow patterns[6].

The immunopathology of CRSwNP varies geographically, with eosinophilic inflammation more commonly discovered in Western populations, while Asian populations often exhibit neutrophilic or mixed inflammatory profiles[7]. These variations affect disease severity, recurrence, and therapeutic responsiveness. Eosinophilic endotypes are associated with worse olfactory dysfunction and higher recurrence, whereas neutrophilic inflammation tends to be less responsive to corticosteroids and is attached to poorer surgical outcomes[8].

Comprehensive evaluation of the cellular profile and associated comorbidities of CCAD is crucial for improving diagnostic accuracy, prognostication, and targeted therapeutic strategies.

Objective

Primary Objective: To assess the clinical characteristics, atopic profile, histopathology, treatment outcomes of 'CCAD' and other subtypes of CRSwNP in a tertiary care setting.

Secondary Objective:

1. To access symptom improvement with SNOT-22.
2. To find out the recurrence rates.

Materials and Methods

This prospective observational study was done at 'Shri Mata Vaishno Devi Institute of medical excellence' between september 2023 and august 2025 after approval by the Institutional Ethics board (ADM/23-24/105-21/08/23), and all participants gave written informed consent before the start of study.

Inclusion and Exclusion Criteria

Patients were included if nasal endoscopy revealed 'polypoid edema' or 'frank nasal polyps' involving the central compartment structures (MT, ST &/or PSNS). The diagnosis of CRSwNP was made according to the criteria outlined in the European Position Paper on Rhinosinusitis and Nasal Polyps 2020 (EPOS 2020).

Patients were excluded if they had 'antrochoanal polyps', 'cystic fibrosis', 'inverted papilloma', 'vasculitis', 'primary ciliary dyskinesia', or 'acute upper respiratory tract infections' at the time of evaluation[9].

Data Collection and Definitions

Age, gender, clinical parameters such as presenting symptoms, smoking history, and relevant medical history (± asthma and/or allergic rhinitis), were noted. Preoperative as well as post surgery '22-item Sino-Nasal Outcome Test' (SNOT-22) scores were collected.

'Asthma' was diagnosed based on 'Global Initiative for Asthma' i.e. GINA guidelines, defined by a supportive spirometry with bronchodilator or challenge testing, or ongoing use of inhaled bronchodilators or corticosteroids[10]. Smoking status was defined as current smoking or cessation within the past 12 months.

The diagnosis of allergic rhinitis was made in light of the positive atopy test and the clinical history (such as sneezing, rhinorrhea, nasal congestion, and itching)[11]. Additionally recorded were the outcomes of allergy tests and previous allergy treatments.

Disease Subtypes

- Eosinophilic CRSwNP was defined histologically, with tissue eosinophils exceeding 10% of total infiltrating cells[12].
- 'Central Compartment Atopic Disease'(CCAD) was diagnosed when polypoid changes involved the MT, ST, and PSNS, supported by both endoscopic and radiologic findings, along with a positive inhalant allergen test[13].
- Patients with sinonasal polyps not fulfilling criteria for eosinophilic CRSwNP, CCAD, AERD, or AFRS were grouped as CRSwNP Not Otherwise Specified (NOS)[13].

Patient Evaluation and Imaging

Diagnostic endoscopy of nose and non-contrast computed tomography (CT) of the paranasal sinuses was done in all of the patients. CT scans were qualitatively analyzed for mucosal changes, with attention to thickening of soft tissue in the central compartment of the nasal cavity— especially 'MT', 'ST', and 'PSNS'— as well as opacification patterns in the osteomeatal complex (OMC), sinus roofs, medial and lateral sinus walls. These features were assessed to identify patterns suggestive of 'central compartment atopic disease'(CCAD)[14].

Allergy Testing & Atopy Status

Sensitization with aeroallergens was assessed either by serologic testing or skin-prick testing, depending on patient history and availability. For serologic evaluation, specific IgE (sIgE) levels to airborne antigens were measured using a standardized allergy screening panel, with values >0.35 kU/L (or IU/mL) considered positive.

For skin-prick testing, allergens in '50% glycerin' solution were applied to the volar surface of forearm with appropriate positive and negative controls. Intradermal testing was performed selectively. Patients were advised to withhold antihistamines for not less than seven days prior to testing. Participants were regarded as 'atopic' or 'allergic' when either the serum-specific IgE test or the skin prick test yielded a positive result, whereas negative findings on both tests indicated a 'non-atopic'/'non-allergic' status[15].

Histopathological Analysis

Tissue samples were preserved in 10% neutral formalin, placed in paraffin, and cut into 4 micron sections for staining with hematoxylin and eosin. Whole slide imaging (WSI) was performed using a digital slide scanner. The digital slides were examined using an 'artificial intelligence-based chronic rhinosinusitis evaluation platform' (AICEP 2.0), which enabled automated quantification of 'eosinophils', 'neutrophils', 'lymphocytes', and 'plasma cells' in nasal mucosa. The cellular composition was recorded for further analysis[16].

Medical and Surgical Management

Initial medical therapy included intranasal corticosteroids, oral antihistamines, systemic corticosteroids, and antibiotics, depending on clinical indication. Immunotherapy (IT) was recommended in selected cases. If medical management failed, endoscopic sinus surgery was performed approximately 1–2 months after initial evaluation. Surgical intervention focused on removing polypoid tissue in the central compartment and restoring ventilation of paranasal sinuses. Postoperatively, patients received 'high-volume topical corticosteroid rinses' (budesonide 0.5–1.0/ mg/2/ mL, twice daily) and continued allergy-directed therapies as needed.

Statistical Analysis

Data analysis was carried out using SPSS version 20.0 (SPSS Inc., Chicago, IL, USA). Age was treated as a continuous variable and reported as the mean with its standard deviation. Categorical variables were summarized using counts and percentages. No comparative or inferential statistical tests were applied.

Results

Demographic details:

As shown in Table 1, 127 patients with 'chronic rhinosinusitis with nasal polyps' (CRSwNP) were included. The mean age of the cohort was 45.2 ± 11.5 years (range: 22–68), with 56.69% (72 patients) males and 43.3% (55 patients) females.

Table 2 showing types of nasal polyposis and their associations with causative factors.

As shown in table 2, Patients were stratified into subgroups based on clinical, radiological, and histological criteria:

Table 1: Showing Demographic Details.

Number of patients	Male	Female
127	72(56.69%)	55 (43.3%)
Mean age in years	45.2 ± 11.5 years (range: 22–68)	

Table 2: Subgroup Classification and Atopy Status.

	Patients (%)	Allergy	Allergic rhinitis	Asthma	Atopic dermatitis
CRSwNP (NOS)	25 (19.68%)	32%	32%	16%	none
CRSwNP/CC	48 (37.80%)	91.67%	95.83%	45.83%	16.67%
AFRS	29(22.83%)	86.20%	6.8%	17.24%	none
AERD	5 (3.94%)	100%	90%	100%	20%
CCAD	20(15.75%)	100%	100%	15%	25%

Table 3: Showing 'SNOT-22' Score pre and Post-treatment.

	Mean	Range
Pre- treatment SNOT-22 score	54± 8.5 years	38-72
Post treatment SNOT-22 score	8± 4.5 years	3-20

- CRSwNP (NOS) – 25 patients (19.68%)
- CRSwNP with Central Compartment involvement (CRSwNP/CC) – 48 patients (37.80%)
- Allergic Fungal Rhinosinusitis (AFRS) – 29 patients (22.83%)
- Aspirin-Exacerbated Respiratory Disease (AERD) – 5 patients (3.94%)
- Central Compartment Atopic Disease (CCAD) – 20 patients (15.75%)

As shown in table-2, The prevalence of allergy and associated atopic conditions was significantly higher in

the CRSwNP/CC and CCAD subgroups. Other observations were:

- In CCAD: 100% had allergy, allergic rhinitis, and 25% had atopic dermatitis. Asthma was present in 15%.
- In CRSwNP/CC: Allergy was present in 91.67%, allergic rhinitis in 95.83%, asthma in 45.83%, and atopic dermatitis in 16.67%.
- In AFRS: Allergy was seen in 86.2% and asthma in 17.24%.
- In AERD: All patients had allergy and asthma, with 90% having allergic rhinitis.
- In CRSwNP (NOS): Allergy and allergic rhinitis were observed in 32% each, asthma in 16%. No atopic dermatitis was observed.

Histopathological analysis of nasal polyp tissues showed:

- Eosinophil count ranged from 4 to 80 per high-power field (HPF)
- Mean eosinophil count: 36/HPF

SNOT-22 scores (Preoperative vs. Postoperative)

As shown in table 3, the 'Sino nasal Outcome Test'(SNOT-22) scores were recorded pre- and post-operatively:

- Preoperative SNOT-22: Range 38–72; mean score: 54 ± 8.5 years
- Postoperative SNOT-22: Range 3–20; mean score: 8 ± 4.5 years

These results reflect a significant symptomatic improvement following surgical and medical treatment.

Endoscopic Follow-Up Outcomes:

Postoperative follow-up endoscopy demonstrated:

- CCAD patients showed excellent outcomes with allergen immunotherapy and nasal steroid irrigations. No recurrences were observed.
- CRSwNP/CC patients also responded well to allergen immunotherapy and nasal douches, with no recurrences till date.
- In contrast, CRSwNP (NOS) patients without evidence of type 1 inflammation had a 20% recurrence rate. These cases were successfully managed with oral clarithromycin 250 mg and budesonide nasal rinses.

Discussion

Prevalence of Allergy and Asthma:

In our study, CCAD was seen in 20% patients(15.75%) with 100% prevalence of allergy and allergic rhinitis, 25% having atopic dermatitis and only 15% presenting with asthma. These findings align closely with the study by Sonya Marcus *et al.*, (2020), which identified CCAD as the CRSwNP subtype with 97.6% prevalence of allergy and 15% presenting with asthma[17].

The likelihood of allergy was notably greater in CCAD (90%) and CRSwNP (32%), in a study by Jung H et al., 2023, while our study showed highest allergy incidence in CCAD(100%) followed by CRSwNP (91.67%)[18].

Histopathological Findings:

Histological analysis of CRSwNP subtypes showed a wide eosinophil range (4–80/HPF; mean 36/HPF), supporting eosinophilic and non-eosinophilic phenotypes and their clinical correlation.

The average eosinophil count in nasal polyp tissue was reported as 50.6 ± 10.7 and 49.9 ± 43.8 eosinophils per high-power field respectively in a study by Huang SK *et al*., 2023[19] and Moreno luna R *et al.*, 2025[20].

SNOT-22 Outcomes:

Preoperative SNOT-22 scores were 54 ± 8.5 years, with significant improvement postoperatively (8 ± 4.5 years), reflecting effective symptom control. This improvement was particularly striking in CCAD and CRSwNP/CC patients. These groups had no observed recurrences during follow-up and showed excellent response to allergen-targeted therapies. These outcomes are in accord with the original research by DelGaudio et al. (2017), who emphasized CCAD's responsiveness to medical therapy when the allergic component is appropriately addressed. They proposed that allergen deposition on central structures i.e. the middle turbinate superior septum is central to CCAD pathogenesis, a theory our findings support[21].

Endoscopy on Follow-up

Postoperative endoscopic evaluation reinforced these observations. CCAD and CRSwNP/CC patients showed excellent mucosal healing with no recurrence, likely due to effective control of allergic triggers and inflammation. In contrast, 20% of CRSwNP (NOS) patients experienced polyp recurrence, necessitating oral macrolides and budesonide rinses.

In an earlier cohort study of 132 CRSwNP patients (including CCAD, CRSwNP subtypes), the polyp recurrence rate among CCAD was reported at 7.9%, and a re-operation was performed in 5.3%, both

significantly lower than in non-CCAD subtypes (e.g. in that study CRSwNP NOS had recurrence ~27%, revision ~29.7%) in a study by Davis C *et al.*, 2023[22].

Conclusion

Overall, this study reinforces that CCAD and CRSwNP/CC are distinct, allergy-driven subtypes of CRSwNP with favorable outcomes when treated with targeted anti-inflammatory and allergen-specific therapies. These findings align well with previous studies validating the clinical and pathological distinctiveness of CCAD and emphasizing the need for precise phenotyping in CRS to optimize management.

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Conflict of Interest: Nil

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