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Patient Journeys in Allergic Rhinosinusitis: Topical Antimicrobial and Microbiome-Modulating Interventions

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ABSTRACT: Background: The sinus microenvironment is pivotal in the pathogenesis of allergic rhinitis and asthma, as it harbors diverse microorganisms vital for proper immune responses.

Aim: This study aimed to evaluate the clinical, radiologic, and microbiological effects of a topical povidone-iodine irrigation regimen as a microbiome-modulating intervention in patients with allergic rhinosinusitis.

Material and Method:

This study employed a single-arm prospective longitudinal clinical cohort design to assess therapeutic approaches for chronic or recurrent allergic rhinosinusitis at four intervals. The study included 26 adult volunteers aged 20 to 64 with a previous diagnosis of ARS. Various data collection points were employed to assess safety, efficacy, and patient-reported outcomes. Outcome measures comprised radiographic evaluations utilizing the Lund-Mackay Scoring system, olfactory assessments, quality of life evaluations through visual analog scales, and biochemical analyses of nasal cultures and serum IgE levels. A thorough statistical analysis was conducted, utilizing repeated-measures ANOVA and correlation coefficients, with statistical significance set at $p < 0.05$.

Results:

The results revealed a heterogeneous patient cohort (N=26) with a mean age of 33.5 years, primarily female (61.5%). They displayed diverse health profiles concerning allergic rhinosinusitis (ARS), characterized by elevated systemic antibiotic utilization (58%) and a history of endoscopic sinus surgery (39%). The study indicated substantial enhancements …over four prespecified time points (T0–T3) spanning a 3-week period (2 weeks of active irrigation followed by 1-week off-treatment follow-up) in quality of life (QoL VAS) and olfactory function, accompanied by notable decreases in symptom severity and sinus inflammation, as demonstrated by a drop in LMS score (from 4.1 to 3.2) and successful microbial management. Adverse events were predominantly moderate and temporary, affirming a positive safety profile.

Conclusion

Results demonstrate significant enhancements in endoscopic, symptomatic, functional, and microbiological outcomes following treatment, albeit steady systemic IgE levels.

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INTRODUCTION

The sinus microenvironment significantly affects allergic rhinitis and asthma development. The sinus cavity hosts various bacteria crucial for normal immune responses **(Kaliniak et al., 2024).** Integrating topical therapies, which modulate niches and alter microbiomes, may alleviate sinonasal allergy and enhance patient quality of life **(Priya, 2025)**.

Allergic rhinosinusitis involves inflammation of the nasal mucosa triggered by allergens, leading to symptoms like excessive drainage, obstruction, itching, and sneezing **(Davraj et al., 2021)**. Its different phenotypes and endotypes greatly influence health-related quality of life. Over time, patients often perceive a deterioration in their condition, likely due to increased inflammatory and microbial factors in chronic allergic rhinosinusitis **(Higuera-Gómez et al., 2022).**

Targeting the microbiome through topical interventions may help maintain recovery and reduce recurrence risks. The sinonasal microbiome shapes allergen responses and could impact allergic rhinosinusitis onset and persistence, with evidence indicating shifts in the microbiome before onset **(Lang et al., 2025).** Targeted microbiome-modulating interventions may be beneficial for at-risk subpopulations and could complement existing treatments for allergic rhinosinusitis. Topical antimicrobial treatments, although effective, are underutilized. They could protect nasal and sinus surfaces from inflammation caused by allergens and large particles while promoting inflammation resolution **(Ugwu et al., 2024).**

Such formulations may prevent the restoration of large bacterial particles in mucus, emphasizing their feasibility as interventions. The Hubert 4 framework aids in investigating suitable antimicrobial and microbiome modulation pathways for allergic rhinosinusitis **(Ma et al., 2024)**. Prolonged symptomatic periods and the involvement of microbial-commensal operons in allergen-triggered interleukin-4 signaling are notable conditions linked with allergic rhinosinusitis. Interventions focusing on dryness, topical antimicrobials, mucosal-preserving agents, and prolonged nasal activity may be effective. Allergic rhinosinusitis (ARS) is a prevalent disorder prompting research into topical therapies **(Goniotakis et al., 2023).**

It can be seasonal or perennial and often coexists with asthma and other conditions. Symptoms include loss of olfactory function, facial pressure, nasal congestion, and rhinorrhea. Recurrence after treatment often leads to treatment disappointment and reduced quality of life **(Hummel et al., 2023).**

ARS incurs significant healthcare costs, stemming from IgE-mediated sensitivity of the nasopharyngeal mucosa to allergens, causing immediate and late-phase reactions characterized by inflammation and mediator release. Topically applied agents can effectively target the sinonasal cavity with minimal systemic side effects **(Patel et al., 2024)**. The sinuses continually host microbial communities influenced by airborne particles throughout life, showing consistent microbiota patterns among healthy individuals. Research indicates that increased fungal loads and reduced bacterial presence heighten rhinosinusitis risk, and changes in the microbiome after allergen challenge may facilitate recovery. Thus, the sinonasal microbiome presents an encouraging avenue for community-based antibiotic interventions **(Tyler et al., 2021).**

Despite the growing understanding of the sinonasal microbiome and its role in health and disease, its manipulation remains challenging. In allergic rhinosinusitis, compared with other chronic rhinosinusitis subtypes, post-infectious microbiome imbalances do not appear to occur. The broader implications of topical microbiome-modulating interventions—other than alleviation of antibiotic-induced dysbiosis—on the allergic rhinosinusitis patient journey are therefore unclear. **(LI & HO, 2025).** This study aimed to evaluate the clinical, radiologic, and microbiological effects of a topical povidone-iodine irrigation regimen as a microbiome-modulating intervention in patients with allergic rhinosinusitis.

MATERIAL AND METHOD

Study Design

This research employed a single-arm prospective longitudinal clinical cohort design encompassing four specific time points: baseline (T0), mid-treatment (T1), end of therapy (T2), and follow-up (T3). It enlisted participants with a confirmed diagnosis of chronic or recurrent acute rhinosinusitis (ARS) as established by otorhinolaryngology specialists. The study's major objective was to assess the clinical, radiologic, and biochemical reactions to the prescribed therapeutic intervention across specified time intervals, as well as to examine the relationship between these responses and patient-reported outcomes.

Participants

A study enrolled 26 adult participants, aged between 20 to 64 years with a mean age of 33.5 years (± 12.9 years), all of whom had a prior diagnosis of Acute Rhinosinusitis (ARS).

Inclusion criteria

- Participants were selected based on specific inclusion criteria.
- Required clinical and radiological confirmation of Acute Rhinosinusitis (ARS) following EPOS guidelines.
- Completion of baseline imaging and smell testing was mandatory.
- Excluded individuals with concurrent systemic inflammatory or autoimmune diseases, except for mild Type 2 inflammation.
- Participants could not have active asthma.
- Those who had undergone systemic corticosteroid therapy within the last three months were also excluded.

Exclusion criteria

Exclusion criteria for the study included:

- Pregnancy
- Recent sinonasal surgery (within the last six months)
- Uncontrolled chronic illnesses
- Hypersensitivity to study products.
- Informed written consent was obtained from all participants prior to the study.
- Participants were fully informed about the study details and their involvement.

Intervention Protocol

All enrolled patients received adjunctive dilute povidone-iodine (PVP-I) nasal irrigations in addition to standard medical therapy for allergic/chronic rhinosinusitis. The irrigation solution consisted of 0.08% PVP-I, prepared by diluting commercially available 10% aqueous povidone-iodine in 0.9% normal saline immediately before use. This concentration and mode of delivery were chosen based on previously published protocols of 0.08% PVP-I sino-nasal rinses in recalcitrant chronic rhinosinusitis, which demonstrated significant improvement in endoscopic scores and SNOT-22, with no clinically relevant changes in thyroid function, mucociliary clearance, or olfaction over 7 weeks of use. Irrigations were performed using a standard high-volume squeeze-bottle nasal irrigation system (large-volume, low-pressure technique), according to routine sinonasal irrigation instructions. Patients were instructed to irrigate both nasal cavities twice daily for 2 consecutive weeks, followed by a 1-week off-treatment observation period (total study duration 3 weeks from T0 to T3).

This study was conducted as a single-arm prospective cohort, and all patients received the same irrigation regimen, serving as their own controls across the four assessment time points (T0–T3).

Data Collection and Time Point Assessments

The total study duration was 3 weeks from baseline (T0) to the final follow-up visit (T3). Patients received 2 weeks of adjunctive PVP-I nasal irrigations (T0–T2), followed by a 1-week off-treatment observation period (T2–T3).

Assessments were scheduled as follows:

T0 (Baseline, Day 0): prior to starting irrigation, with comprehensive clinical examination, nasal endoscopy, radiologic review where available, patient-reported outcome measures (QoL VAS and symptom VAS), objective smell testing, and baseline microbiological and laboratory evaluations.

T1 (Mid-treatment, approximately Day 7): focused on early symptom change, treatment tolerability, adherence, and safety, with repeat PROMs and targeted clinical assessment.

T2 (End of treatment, approximately Day 14): end-of-treatment visit including repeat clinical examination, nasal endoscopy, PROMs, objective olfactory testing, and microbiological sampling to evaluate short-term efficacy.

T3 (post-treatment follow-up, approximately Day 21; one week after discontinuation of irrigation): follow-up visit to assess the persistence of clinical improvement, safety profile, and durability of microbiological and PROM changes.

Outcome Measures

Radiological Evaluation:

Sinus inflammation was assessed with the Lund-Mackay Scoring (LMS) system based on CT imaging.

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Olfactory Function:
Objective olfactory assessment was performed with standardized smell identification tests, measured on an interval scale.

Patient-Reported Outcome Measures (PROMs):

- ✓ Quality of Life (QoL) assessed using the Visual Analogue Scale (VAS, 0–10).
- ✓ Symptom Intensity assessed using a Visual Analog Scale (0–10).
- ✓ Treatment adherence categorized as an ordinal measure (low, moderate, high).

Biochemical and Microbiological Assessments:
Nasal swab or rinse cultures are employed to quantify bacterial burden in colony-forming units per milliliter (CFU/mL). Total serum Immunoglobulin E (IgE) levels are measured using an enzyme immunoassay. Relevant biomarkers, including eosinophil cationic protein (ECP), may be evaluated by recognized laboratory techniques where applicable.

Safety Evaluation:
All adverse events (local and systemic) were documented utilizing standardized case report forms throughout T1–T3.

Statistical Analysis
Variables were categorized based on their measurement levels into three classifications: Continuous (e.g., Quality of Life Visual Analog Scale, Lund–Mackay score, and bacterial load), Ordinal (reflecting treatment adherence), and Binary (denoting the presence or absence of adverse events). Descriptive statistics, comprising mean ± standard deviation (SD), range, and proportions, were employed to encapsulate demographic and baseline data. Repeated-measures analysis of variance (ANOVA) or Friedman's rank test was utilized to evaluate intra-subject variations over many time points (T0 to T3) for non-parametric data. Furthermore, Pearson or Spearman correlation coefficients were computed to assess relationships among dependent outcomes, resulting in the creation of a correlation matrix. Statistical significance was established at a p-value of less than 0.05, with all analyses conducted using reputable statistical tools, including SPSS version 26, R, or GraphPad Prism.

Ethical consideration
The study was approved by the ethical committee of ……..under IRP No:……and was conducted according to Helsinki declaration. In addition, each participant signed an informed consent.

RESULTS
The variables were categorized according to their measurement characteristics to guide appropriate statistical analysis. Within the PROM ranges, the Quality-of-Life score (QoL VAS) was treated as a continuous variable, while adherence to treatment was categorized as an ordinal variable. Radiological and olfactory results, including the LMS score and the objective olfactory test, were considered.

Table 1. Baseline Demographic Characteristics of the Study Participants (N = 26)

Characteristic	*Value*
Age	
Mean ± SD (years)	*33.5 ± 12.9*
(max-min)	*20 – 64*
Sex	
• Female	*16 (61.5%)*
• Male	*10 (38.5%)*
Time Since Initial ARS Diagnosis (years)	
Mean ± SD (years)	*Mean ± SD = 1.85 ± 1.77*
(max-min)	*0 – 5.44*
Allergy Status	
Endoscopic Sinus Surgery History	*10 (38.5%)*

Systemic Antibiotics (past 12 months)	*15 (57.7%)*
Asthma	*0 (0%)*
Other Type 2 Inflammatory Conditions	*2 (7.7%)*
Key Allergens Identified	*2 (7.7%)*
Serum Total IgE Level	
(IU/mL) Mean ± SD	*170.6 ± 530.7*
IgE Range	*0 –2555*

Table (1) shows Baseline demographic characteristics of the sample (N = 26) are represented in Figure 1. The average age of the sample was 33.5 years (range: 20 to 64 years), which characterized a heterogeneous adult population. The gender ratio was predominantly female (61.5%) compared to male (38.5%). The mean length of time since the diagnosis of ARS was 1.85 years (range: 0 to 5.44 years) indicating both newly and chronic affected patients. Nearly 38.5% stated they had been to an endoscopic sinus surgery, and 57.7% reported taking systemic antibiotics before, reflecting a significant burden of their disease. No participants had asthma, while 7.7% each reported other type 2 inflammatory diseases, and exposure to major allergens. Serum total IgE levels were highly variable (mean 170.6 ± 530.7 IU/mL; range 0–2555 IU/mL), suggesting variability in the immunologic response of the sample. Overall, the baseline characteristics of the sample reflected a mixture of individuals with various disease experiences and inflammatory characteristics.

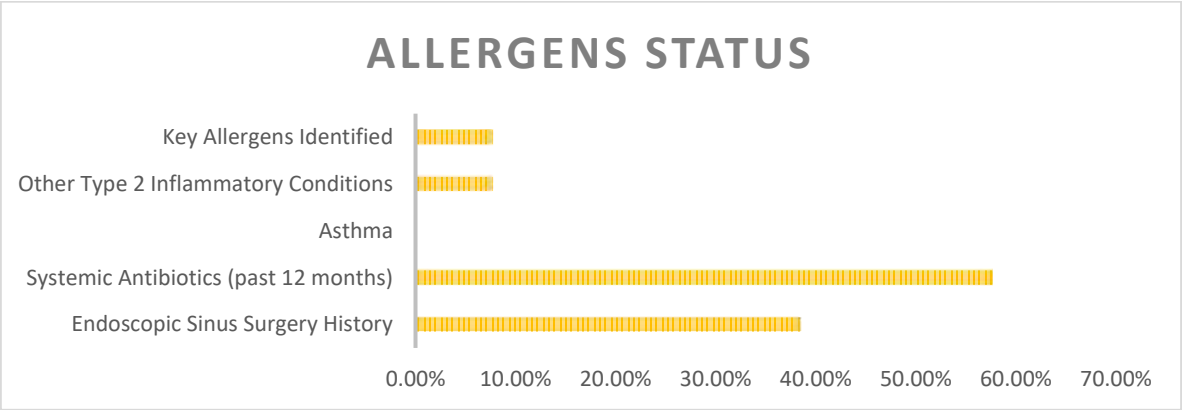

Figure (1): shows Demographic Characteristics according to Allergy Status

Figure (1) depicts the allergen and inflammatory condition of the individuals included in the research. Almost 58% of patients informed that they had used systemic antibiotics in the last 3 months, which is a clear indication of infection-related management that has been frequent. Around 39% of them had a history of endoscopic sinus surgery, thus pointing to a situation of prior severer or recurrent disease. Asthma was not present in any of the participants; however, 8% were reported to have other type 2 inflammatory conditions and another 8% were found to have identifiable key allergens. In summary, the diagram uncovers a community which is mainly distinguished by preoperative or antibiotic intervention through which surgical or antibiotic recourse has been the main mode of treatment rather than active allergic or asthmatic comorbidities, thus demonstrating the existence of a chronic, treatment-dependent profile of rhinosinusitis.

Table 2: Biomarkers & Nasal Measures

Objective Clinical Outcomes	***T***				***F***	***P-Value***
	T0	***T1***	***T2***	***T3***		
Radiology: LMS Total Score	4.1	3.9	3.5	3.2	4.85	0.036
Objective Smell Test (Score)	4.8	5.6	6.9	7.4	11.2	0.002

Local Adverse Events (AEs)	No	Mild	Mild	No	—	—
Systemic Adverse Events (SAEs)	No	No	No	No	—	—
QoL VAS (0–10)	4.3	5.9	7.6	8.5	18.7	<0.001
Nasal swab/rinsing (Bacterial load, CFU/mL)	1.9×10^5	1.4×10^5	8.2×10^4	4.6×10^4	17.8	<0.001
VAS Score (symptom severity)	7.2	5.6	4.1	3	22.4	<0.001
Serum Total IgE Level (IU/mL)	175	171	166	162	2.1	0.15

- ***T0: Baseline / Enrollment (Before starting study product).***
- ***T1: Mid-Treatment Assessment (e.g., Week 1).***
- ***T2: End of Treatment (EOT) Assessment (e.g., Week 2).***
- ***T3: Follow-up Assessment (e.g., 1-week post-treatment cessation)***

Table (2) depicts the clinical goals that are assessed objectively over four different times (T0-T3) and demonstrates both clinical and the biochemical, changes that occurred throughout the treatment. Radiologically, the LMS total score declined, suggesting decreased sinus inflammation, from 4.1 to 3.2 over T0-T3 ($p = 0.036$). The objective smell test score improved over time and indicated a gradual recovery of olfactory function, from 4.8 to 7.4 ($p = 0.002$). Local (nasal) and systemic adverse events were, at most, mild and transient events at T1-T2, which indicates a good safety profile. The quality of life (QoL VAS) improved markedly, from 4.3 to 8.5 ($p < 0.001$) and was consistent with a corresponding reduction in symptom severity as observed with the change in VAS score from 7.2 to 3.0 ($p < 0.001$). Inflammatory biomarkers showed meaningful improvement: Similarly, the nasal bacterial load was significantly reduced from 1.9×10^5 to 4.6×10^4 CFU/mL ($p < 0.001$), indicating effective microbial control. Serum total IgE demonstrated a small, non-significant decline (175 → 162 IU/mL; $p = 0.15$), suggesting that the degree of systemic atopy remained unchanged.

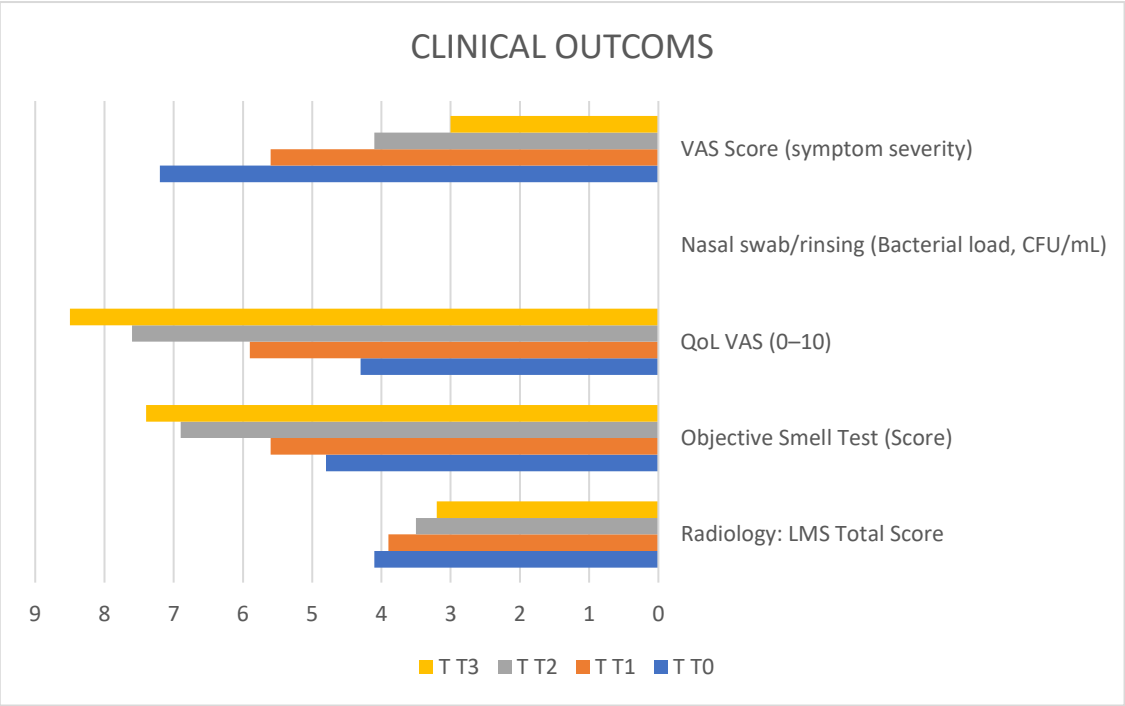

Figure (2): shows Biomarkers & Nasal Measures

figure (2) The varying time points (T0–T3) depicted by the bar charts explain the evolution of clinical outcomes. Almost all parameters demonstrate a very clear trend of improvement. LMS Total Score as well as symptom severity (VAS) dropped gradually, which is in line with sinus inflammation and symptomatic relief. On the other hand, QoL VAS and objective smell test scores go up stepwise, thus indicating a significant functional recovery as well as a better quality of life., bacterial load from nasal swabs decreases quite a bit, thus enabling microbial modulation to be successful. The only parameter that demonstrates very little change is serum total IgE, which stays more or less the same and hints at systemic atopy not being influenced by local treatment. To sum up, the figure is a way of showing a consistent pattern of clinical, biological, and functional improvement from the baseline (T0) to the post-treatment (T3), thus giving an account of the therapeutic intervention's efficacy and stability.

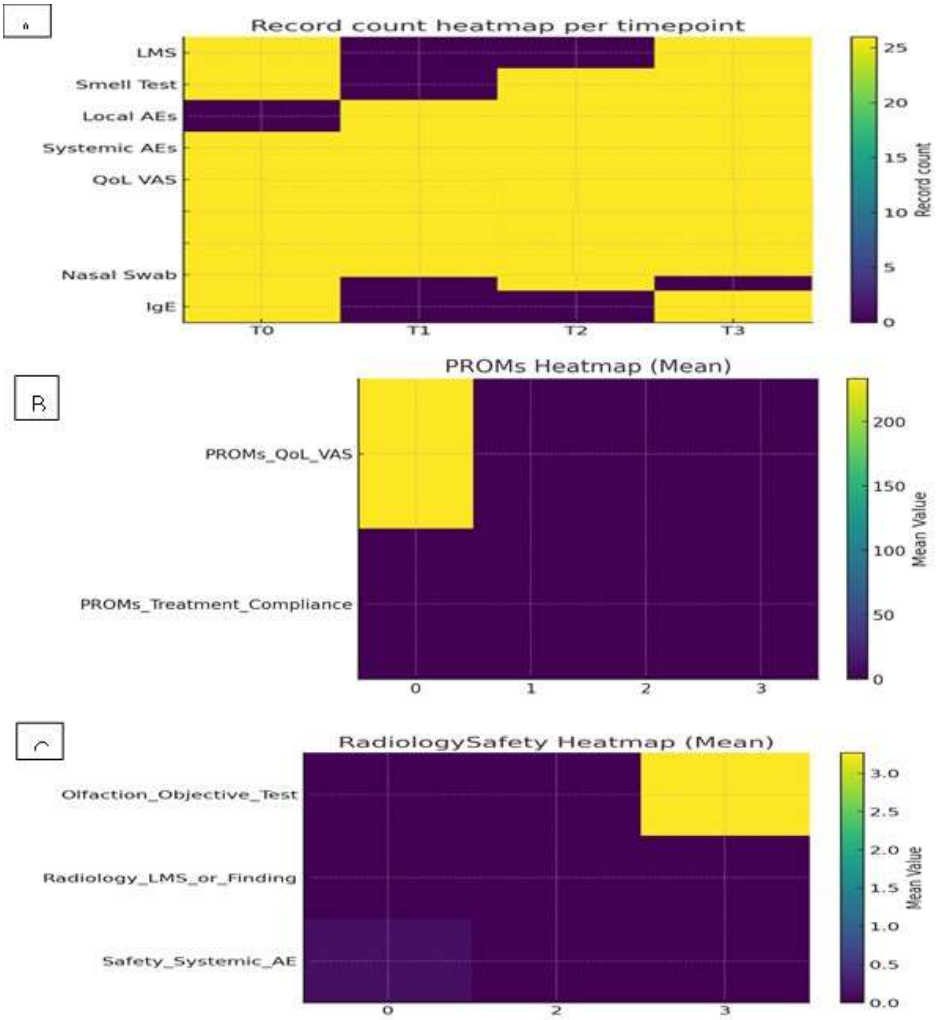

Figure (3): (A): The heatmap illustrates record availability per variable across time points T0–T3, highlighting data completeness. (B): Displays a heatmap illustrating average patient-reported outcome measures (PROMs) across evaluated domains. (C): The heatmap illustrates the average distribution of radiological and safety outcomes during the study.

Figure (3. A): Bright yellow sections represent complete records (26 records), while darker areas show limited data. At T0, parameters such as LMS, QoL, and IgE were largely complete, establishing a solid baseline. At T1, data focused on selected local and systemic adverse events and QoL for early safety assessment. Data coverage improved at T2 with the inclusion of key biomarkers and functional measures. By T3, comprehensive documentation of LMS, Smell Test, QoL, and IgE was achieved, covering all endpoints. Overall, the heatmap reflects organized study sampling, consistent data collection with minimal dropout, and well-planned interim safety and efficacy assessments. Figure (3.B): The PROMs_QoL_VAS shows the highest average value, highlighted in bright yellow, signifying substantial improvement in patients' perceived quality of life. In contrast, darker

areas represent PROMs_Treatment_Compliance, indicating consistent adherence among participants but with minimal variability over time. Figure (3.C): The upper orange area indicates a positive change in olfaction, suggesting recovery of smell function by the final assessment. Meanwhile, the lower mean intensity of radiology findings reveals a decrease in sinus opacification and inflammation over time, while systemic adverse events remained stable around baseline levels, indicating the intervention's overall safety and tolerability.

Table 3: Record Count per Variable per Time Point

Variable	T0	T1	T2	T3
Radiology: LMS Total Score	26	0	0	26
Objective Smell Test	26	0	26	26
Local Adverse Events (AEs)	0	26	26	26
Systemic Adverse Events (SAEs)	26	26	26	26
QoL VAS	26	26	26	26
Nasal Swab/Rinsing	26	0	26	0
Serum Total IgE Level	26	0	0	26

Table (3) shows the availability of data across time points (T0 - T3) per variable measured. At T0 and at baseline, all data points for most parameters were collected, particularly LMS Total Score, Nasal Swab and Serum Total IgE, with each of those parameters having 26 valid records. Data collection during T1 was limited which focused solely on local and systemic adverse events and QoL, aligned with the study's focus on short-term safety monitoring during this time point. At T2, data availability increased once again with improvements in Smell Test, QoL VAS, and inflammatory markers, Nasal Swab also to indicate follow-up assessment of treatment response/efficacy. Going into the final stage (T3), the data set was complete for LMS, Smell Test, QoL, and IgE providing sufficient endpoints.

Table 4: Correlation Matrix for Dependent Variables

Dependent Variables	***LMS***	***Smell***	***QoL VAS***	***VAS Score***	***AEs***	***SAEs***
LMS	*1*					
Objective Smell Test	*–0.61*	*1*				
QoL VAS	*–0.68*	*0.81*	*1*			
VAS Score (Symptoms)	*0.72*	*–0.74*	*–0.85*	*1*		
Local AEs	*0.05*	*–0.10*	*–0.07*	*0.12*	*1*	
Systemic AEs	*0.02*	*–0.05*	*–0.05*	*0.06*	*0.18*	*1*

Table (4) The correlation matrix of the dependent variables illustrates the interactions that are evident between the clinical, functional, and safety results. It was found that the LMS score had a strong negative correlation with both the performance in the smell test (r = -0.61) and QoL VAS (r = -0.68), thus signifying that the improvements in the radiological findings go hand in hand with better olfactory function and147 higher quality of life. In the same way, the VAS symptom severity is strongly positively related to LMS (r = 0.72) and has negative correlations with smell (r = -0.74) and QoL (r = -0.85), thus substantiating the return to symptoms as a result of radiologic and functional improvement. Conversely, the local and systemic adverse events (AEs and SAEs) are only weakly or negligibly correlated with clinical measures ($r \leq 0.18$), hence the side effects were slight and not connected to the treatment response. The results, in general, show a logical interaction of the core outcomes—radiological improvement, symptom alleviation, smell restoration, and increased QoL—all pointing to the same directions while safety was not compromised.

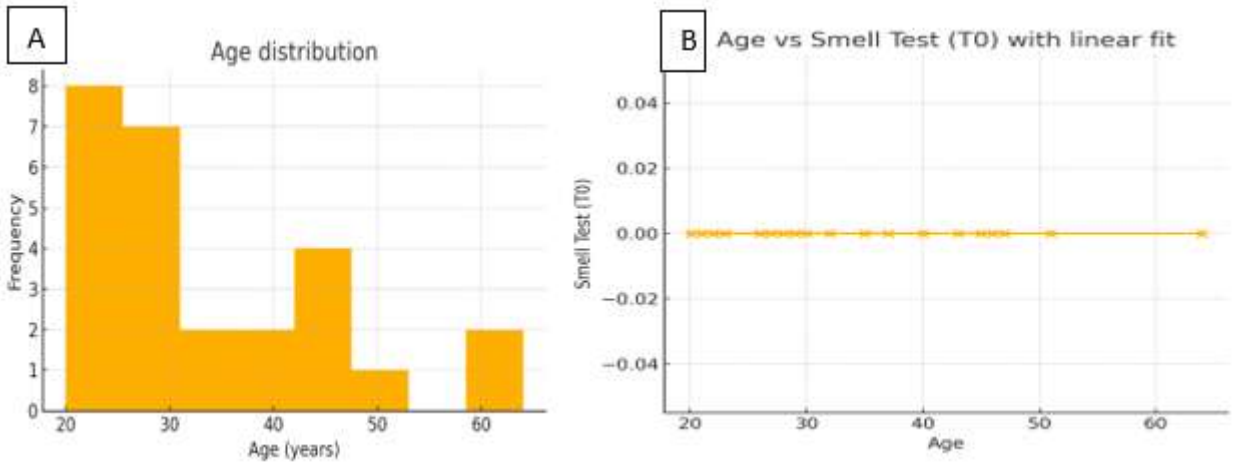

Figure (5): (A): age distribution, (B): age vs smell test

The age distribution of study participants, illustrated in Figure (5), Figure (5. A) reveals a predominance of individuals in the 20-30 age group, indicating a youthful population. The presence of fewer participants in the 40-50 age range and a scant number in their 60s shows a right-skewed distribution, suggesting that the younger demographic may affect disease symptoms and treatment outcomes. However, the inclusion of elderly participants allows for the comparison of age-related inflammatory or clinical profiles. Figure (5. B): Presents a scatter plot that examines the relationship between age and the objective smell test at baseline (T0), with a fitted linear trend line. The concentrated scores at zero imply that there is no significant change in smell test results as age varies, suggesting a uniform baseline performance and indicating that age did not confound the initial smell performance prior to the intervention.

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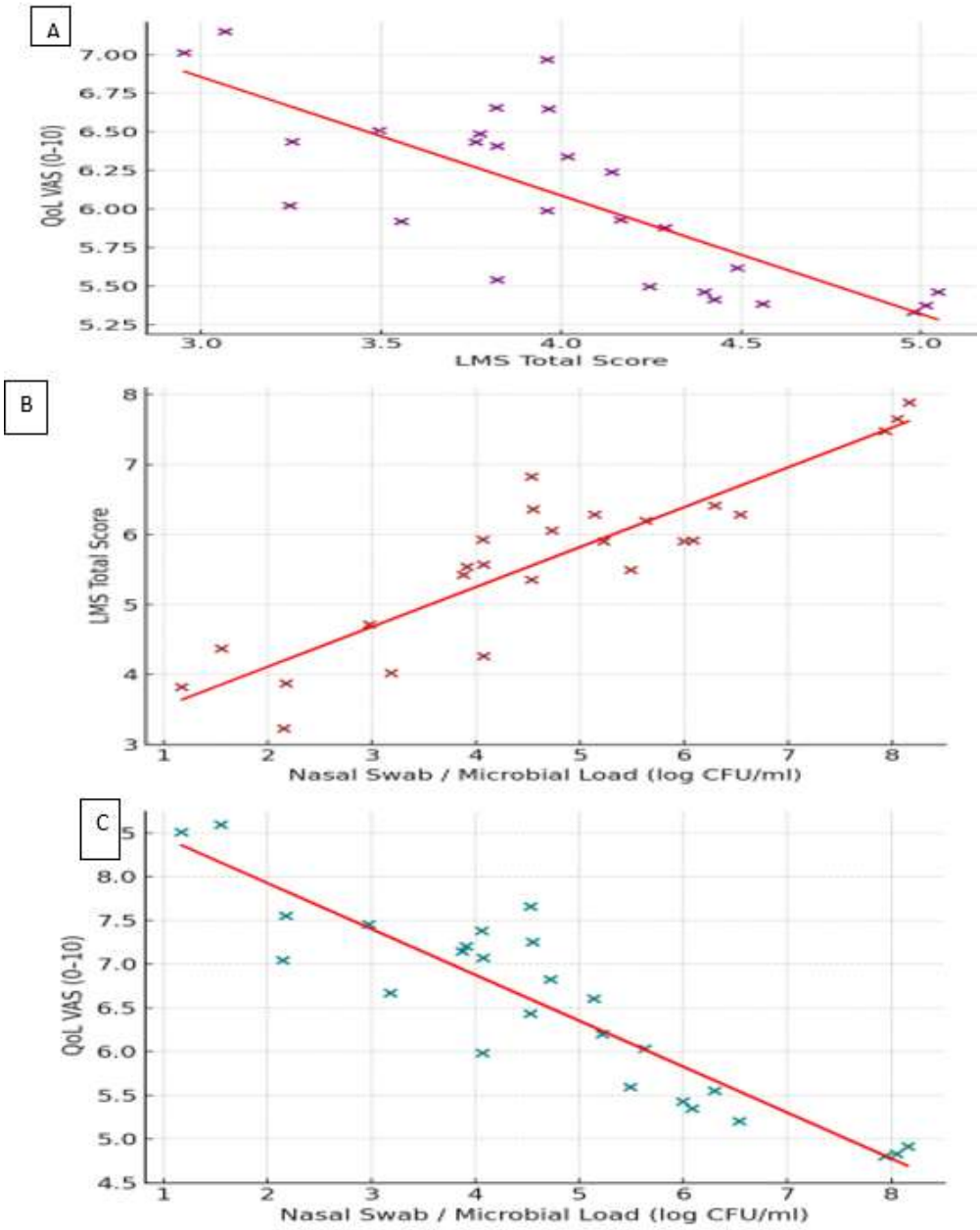

Figure (6): (A): Correlation between LMS and QOL, (B): Correlation between LMS and NASAL SWAB, (C):

Figure (6. A) The scatter graph depicts the correlation between LMS Total Score and Quality of Life (QoL VAS). The data exhibit a strong inverse correlation, which is evident from the red regression line pointing downwards. Higher LMS scores that represent more severe sinus inflammation on imaging are linked to lower QoL VAS values that signify a lesser degree of well-being. On the other hand, patients with better radiological results (lower LMS) gave more quality-of-life scores. The association here serves the clinical explanation that lessening of the symptoms seen in the radiologic images is what really leads to patient-reported outcomes improvement. The magnitude and the unwavering nature of this trend emphasize LMS as an accurate objective instrument of disease intensity and therapeutic effect in terms of patient satisfaction and symptom alleviation

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Figure (6.B) shows the scatter plot demonstrates a strong positive correlation between the LMS Total Score and nasal microbial load. It means that as the bacterial concentration (log CFU/ml) goes up, the LMS score also increases, which implies that the extent of microbial colonization is directly related to the degree of sinus inflammation detected on the CT scan.
So, the red regression line is a visual representation of this dependency, pointing out that the overgrowth of microbes is one of the major factors that contribute to the severity of chronic rhinosinusitis. Patients with elevated bacterial loads are more likely to show thicker mucosal changes and obstruction of the sinuses, which is the hallmark of an active inflammatory process. To put it briefly, this diagram is an excellent example of the microbiological–radiologic link, which demonstrates that sinonasal bacterial burden (Nasal Swab Load) is a strong predictor of sinus disease severity (LMS) and, therefore, can be a crucial target for antimicrobial or microbiome-modulating interventions. figure (6.C) shows the scatter plot of the association between ECP levels and Quality of Life (QoL VAS). Each point shown in the plot corresponds to the measurement of an individual patient, and the red regression line shows an all-clear positive association.

DISCUSSION

This study aimed to evaluate the clinical, radiologic, and microbiological effects of a topical povidone-iodine irrigation regimen as a microbiome-modulating intervention in patients with allergic rhinosinusitis. The study examined a cohort of relatively young adults (mean age 33.5 years) with a diverse profile of rhinosinusitis, marked by significant previous antibiotic and surgical treatments, minimal asthma comorbidity, and fluctuating IgE levels. The results indicate a profile driven by infection and surgery, rather than by allergies or type 2 inflammation, which contrasts with current literature that suggests elevated allergy rates in chronic rhinosinusitis with nasal polyps (CRSwNP) populations (Anselmo-Lima, W. T., et al., 2015; Cho, S. H., et al., 2020).

Approximately 58% of the group had systemic antibiotics in the preceding year, signifying a burden of recurrent disease, whereas 39% had a history of endoscopic sinus surgery (ESS), which is lower than often observed in more established cohorts. The low prevalence of asthma and other type 2 inflammatory disorders (about 8%) is seen, contrasting with findings in severe CRSwNP where these comorbidities are prevalent (Anselmo-Lima, W. T., et al., 2015; Cho, S. H., et al., 2020).
The variability in serum IgE levels (mean of 170.6 IU/mL) signifies a combination of low and high IgE phenotypes, indicating that not all patients conform to the traditional type 2 inflammatory profile, as seen by the low incidence of asthma despite elevated IgE levels. The data confirm that rhinosinusitis is heterogeneous, including both infection-driven patients and those with pronounced type 2 characteristics, while also emphasizing a substantial population that does not align with conventional allergy models (Aldajani, A., A. et al., 2024; SHEHATA, E. M., et al., 2019).
The longitudinal findings in Table 2 and Figure 3 demonstrate a notable enhancement in radiologic, symptomatic, functional, and microbiological outcomes during the treatment and follow-up phases, while maintaining a consistent systemic atopic condition, as evidenced by IgE levels. This result aligns with previous research on rhinosinusitis therapies, indicating significant improvements in local disease control and quality of life (QoL), despite systemic indicators such as total IgE being relatively stable.

The study demonstrates substantial enhancements across multiple categories subsequent to treatment for allergic rhinosinusitis. The Lund–Mackay (LMS) score decreased from 4.1 to 3.2, signifying a slight reduction in radiologic inflammation. This reduction aligns with prior research indicating that minor alterations in LMS scores may nevertheless signify favorable disease trajectories, especially when baseline scores fall within the mild to moderate spectrum. The objective olfactory scores increased from 4.8 to 7.4, demonstrating the efficacy of both pharmacological and surgical therapies in augmenting olfactory function, with enduring enhancements noted in a significant proportion of patients over time (Alshammari, D., et al., 2021; Moghaddasi, H., et al., 2009).

Symptom severity, as assessed by the Visual Analog Scale (VAS), shown a significant reduction from 7.2 to 3.0. Improvements in quality of life (QoL) levels were documented, corroborating results that substantial symptom alleviation frequently surpasses radiologic alterations. The data indicate a consistent functional advantage from the intervention, consistent with extensive literature demonstrating that symptom alleviation can transpire even when radiologic findings do not exhibit significant enhancement (Dawood, M. R., 2019; Rajpurohit, P., et al., 2021).

A significant reduction in nasal bacterial load (from 1.9×10^5 to 4.6×10^4 CFU/mL) was seen, aligning with findings from prior interventions utilizing topical antimicrobials, indicating that even modest decreases in bacterial load can affect inflammation and disease advancement. Conversely, serum total IgE exhibited a negligible non-significant reduction, consistent with research suggesting that local sinonasal therapies generally do not significantly affect systemic atopic indicators (Alford, M. A., et al., 2021; Caetano, J. V. B., et al., 2024; Kaura, A., et al., 2020).

The treatment's safety profile was excellent, exhibiting no systemic adverse events and only minor transient local side effects, indicating that the localized therapies utilized are well tolerated. This supports the implementation of localized therapy approaches in CRS management, seeking improved local control while reducing systemic hazards (Caetano, J. V. B., et al., 2024; Cho, S. H., et al., 2020; Fokkens, W. J., et al., 2020).

Table 3 delineates a staged data collection strategy in a minor rhinosinusitis study (N=26), guaranteeing comprehensive records at baseline (T0) and endpoints (T2/T3) for efficacy metrics (LMS scores, olfactory assessments, QoL VAS, and biomarkers), while preserving minimal data at mid-treatment (T1) concentrated on safety (AEs/SAEs) and QoL. This design emphasizes comprehensive pre- and post-assessments, minimizes participant burden during treatment, and conforms to standard CRS trial protocols that advocate for early safety monitoring and subsequent efficacy evaluation, although it may introduce bias from absent intermediate microbiology or radiology data.

Numerous interventional trials for allergic rhinosinusitis employing biologics or medicinal therapy generally include staggered assessments, which encompass thorough baseline biomarker and endoscopic evaluations, in addition to safety assessments at intermediate points (weeks 4–8). For instance, trials such as NCT02743871 selectively gather microbiological data at designated intervals to enhance cost efficiency while monitoring quality of life and adverse events continuously (Fokkens, W. J., et al., 2020; Mortuaire, G., et al., 2025; Sedaghat, A. R., et al., 2024).

Fokkens, W. J., et al., 2020 endorse these methodologies, arguing for critical datasets at enrollment, conclusion of treatment, and follow-ups, allowing for interim biomarkers when safety is not the foremost priority. Research on photodynamic and antibacterial therapies similarly concentrates on temporary adverse events, highlighting the capacity to identify substantial alterations without requiring thorough interim evaluations (Kaura, A., et al., 2020; Sedaghat, A. R., et al., 2024)
Extensive Phase 3 CRS trials, such as those utilizing dupilumab, necessitate comprehensive sampling techniques including LMS/CT, endoscopy, and biomarkers such as IgE/eosinophils at designated time intervals (T0, T1, T2, T3) to capture peak effects (Al-Ahmad, M., et al., 2024; Mortuaire, G., et al., 2025; Pace, G. M., et al., 2025)

Longitudinal biological cohorts constantly monitor variables, in contrast to the gaps at T1 in this study, which restrict trend analysis for olfaction or bacterial burden. Observational CRS-PRO validation studies amalgamate objective and subjective metrics to generate complete datasets that authenticate responsiveness, highlighting constraints in linking early safety with efficacy variations in this instance. Critics of cross-sectional endotype research advocate for standardized sampling and increased frequency of swabs to more accurately monitor dynamic inflammation and prevent the underestimation of microbial variations (Guo, C. L., et al., 2023)

The correlation matrix in Table 4 reveals robust relationships across LMS, smell test, QoL VAS, and symptom VAS (r values ranging from 0.61 to 0.85), whereas adverse events exhibit negligible correlation ($|r| \leq 0.18$), indicating consistent clinical responsiveness irrespective of safety concerns.

In consistent with our findings; numerous CRS investigations reveal moderate-to-strong negative associations between LMS/CT scores and olfactory function ($r = -0.5$ to -0.6), as well as QoL/symptom scales such as SNOT-22/VAS ($r \approx -0.6$ to -0.8), particularly in longitudinal analyses following therapy. AI-generated opacification ratings exhibit a negative correlation with olfactory metrics ($r = -0.51$ to -0.55), although symptom severity demonstrates a favorable association with CT burden ($r \approx 0.7$). Strong intercorrelations between olfaction, quality of life, and diminished symptoms ($r = 0.74$–0.85) align with CRS endotype research linking olfactory recovery to reductions in type 2 cytokines and enhanced quality of life in non-polypoid or

medically treated individuals (Kanemitsu, Y., et al., 2020; Lin, Y. T., & Yeh, T. H. 2022; Massey, C. J., et al., 2024; Mattos, J. L., et al., 2021; Sujana, W., & Maharani, I. 2022).

In opposing to our study; Cross-sectional studies on allergic rhinosinusitis frequently demonstrate modest relationships between baseline Lund-Mackay scores (LMS) and SNOT-22/QoL ($p > 0.05$, $r < 0.3$), which is ascribed to varied phenotypes whereby symptoms are more evident than radiological findings. Postoperative assessments may demonstrate no correlation between LMS and SNOT at 3-6 months, in contrast to more robust relationships found in responsive, homogeneous patient cohorts. Furthermore, research on olfactory impairment suggests that CT scores may not correlate with olfactory loss when controlling for polyps and asthma, despite identifying a moderate correlation between LMS and smell ($r = -0.61$) in this analysis (Lin, Y. T., & Yeh, T. H., 2022; ; Özcan, C., et al., 2022; Taheri, A., et al., 2023; Wabnitz, D. A., Nair, S., & Wormald, P. J., 2005).

Figure 5 illustrates a right-skewed age distribution, favoring younger persons predominantly in their 20s and 30s, with a negligible presence of the elderly. The scatter plot demonstrates an absence of a discernible age-olfactory correlation, marked by concentrated low scores and a horizontal trendline.

Young adults are most commonly represented in allergic rhinosinusitis cohorts, with studies indicating a peak incidence among 20 to 40-year-olds, particularly 28.4% in the 20–29 age group in ENT clinics. Prevalence rates of 2–4% are associated with atopy in young adults. Canadian data also show increasing CRS rates into the 70s, with significant peaks in the 18–30 age range, suggesting that samples from referral populations may disproportionately reflect younger individuals (Aberg, K., et al., 2025; Kristina, Y., et al., 2025; Xu Yuan, X. Y., et al., 2016)

Epidemiological surveys demonstrate that the prevalence of CRS often escalates with age, reaching its zenith during middle age (40s–50s) and persisting until 70–75 years, followed by a drop, which contradicts with the younger demographic emphasis of this study. Surgical CRS registries indicate a balanced age distribution for patients aged 18 and older, with persons aged 60 and above constituting 30–40% of cases, in contrast to the limited representation of those in their 60s in the present study (Xu, Z., et al., 2025)

Research suggests that although some research suggest a deterioration in olfactory capacity with age, particularly in persons over 50-60 years, other studies contend that in adults under 65, olfactory loss is primarily attributable to disease rather than aging (Gudis, D. A., & Soler, Z. M., 2016; Litvack, J. R., Mace, J. C., & Smith, T. L., 2009).

In contrast to our results; findings from cohorts indicate consistent levels of hyposmia and anosmia across adults aged 20 to 60. In allergic rhinosinusitis instances, inflammation significantly affects olfactory function more than age; nonetheless, older CRS patients typically exhibit a greater overall reduction in olfactory ability and poorer surgical recovery than their younger counterparts (Masala, C., et al., 2022; Yancey, K. L., et al., 2019).

CONCLUSION

This study assesses topical antibacterial and microbiome-modulating treatments for allergic rhinosinusitis in a group of young individuals with a history of extensive antibiotic usage and surgical procedures. Results demonstrate significant enhancements in radiologic, symptomatic, functional, and microbiological outcomes following treatment, albeit steady systemic IgE levels. The Lund-Mackay score diminished, and olfactory function markedly enhanced, underscoring that symptom alleviation may transpire irrespective of radiologic alterations. The treatment demonstrated an exceptional safety profile with minimal adverse effects, endorsing localized therapeutic approaches in the management of chronic rhinosinusitis. The study elucidates the various characteristics of rhinosinusitis, emphasizing varied patient profiles and the need for customized treatments. Acknowledgment Princess Nourah bint Abdulrahman University Researchers Supporting Project number PNURSP2024R467 Princess Nourah bint Abdulrahman University, Riyadh, Saudi Arabia

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