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MICROBIOME PROFILING AND TREATMENT OUTCOMES IN CHRONIC RHINOSINUSITIS: A LONGITUDINAL COHORT STUDY

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Abstract

Background: Chronic rhinosinusitis (CRS) persists as an inflammation of the sinonasal mucosa and regularly brings microbial dysbiosis with it. Scientific research currently demonstrates that thetical microbiome exists in the sinonasal region where it functions as both a disease-forming and treatment-responding mechanism. The study of temporal nasal microbial variations enables clinicians to build individualized therapeutic approaches and forecast disease results in patients with CRS.

Objectives: The study evaluates both temporal modifications of sinonasal microbial communities alongside their relationship to therapeutic outcomes among patients diagnosed with chronic rhinosinusitis.

Study design: A prospective cohort study,

Place: Khyber Teaching Hospital Peshawar Pakistan

Duration of study. January 2021 to July 2021

Methods: This prospective study project tracked adult CRS patients (n=50) for one year to obtain data. The research team obtained 16S rRNA gene sequencing data from nasal swab samples at three-time points: baseline and both 6 months and 12 months. The clinical assessment relied on Sino-Nasal Outcome Test-22 (SNOT-22) scoring. A combination of alpha and beta diversity metrics together with treatment response associations were included in data analysis. Statistical significance was defined as $p<0.05$.

Results: The study included fifty patients with a mean age of 43.8 ± 11.2 years and six per cent female participants. The patients with favourable treatment outcomes presented higher microbial diversity at follow-up which reached statistical significance ($p=0.02$). Corynebacterium along with Dolosigranulum increased in abundance among those who responded to treatment but Staphylococcus aureus remained stable in non-responders. The analysis of beta diversity demonstrated microbial community changes that occurred with clinical improvements but this transformation reached significance ($p=0.03$) indicating a potential therapeutic effect of modifying the microbiome in CRS management strategies.

Conclusion: This study shows the association between chronic rhinosinusitis treatment outcome measures and shifts that occur progressively in sinonasal microbial populations. Microbial diversity increases in combination with particular taxa that function as biomarkers to indicate positive treatment

results. Microbiome profiling serves as a promising tool for precision medicine in CRS because it helps identify successful treatments and design improved intervention strategies.

Keywords: Chronic rhinosinusitis, microbiome, treatment outcomes, longitudinal study.

Introduction: The inflammatory disorder known as Chronic rhinosinusitis (CRS) affects about 12% of adult people globally and creates significant impacts on their lifestyle quality [1]. The condition of chronic rhinosinusitis surpasses 12 weeks of persisting nasal symptoms and divides into two separate types: CRS with nasal polyps (Crown) or CRS without nasal polyps (Crisp) [2]. The large numbers of patients undergoing pharmacological therapy and surgery experience inconsistent treatment results because significant numbers of patients sustain recurrent or persistent symptoms [3].In the past medical experts linked CRS development to persistent infections combined with mucociliary impairment and inflammatory processes. Study now demonstrates that microbial dysbiosis represents an essential factor for disease advancement as well as for the developmental phases of this condition [4]. Modern study shows the sinonasal cavity is not sterilized because it contains various microbes which sustain mucosal homeostasis and immune health [5]. Enhanced knowledge of the sinonasal microbiota has become possible through 16S rRNA gene sequencing technology advancements because study shows CRS severity and recurrence link to pathogenic microbial overgrowth especially of Staphylococcus aureus and Pseudomonas aeruginosa and microbiome diversity reduction [6]. The studied techniques have shown substantial differences between individual microbiota together with shifts in microbial populations which relate to both sickness conditions and therapeutic actions [7]. The protection against chronic inflammation may come from higher bacterial diversity along with commensal Corynebacterium and Dolosigranulum bacteria while microbial imbalance seems to foster inflammation according to multiple studies [8]. Limited research exists about microbiome modifications across time about therapy outcomes. Current microbial research primarily adopts the cross-sectional approach to present microbial composition data while neglecting long-term development patterns. Studying clinical outcomes requires further exploration of how microbial interactions change since the microbiome and CRS symptoms frequently vary or "fluctuate" [9]. This study aims to fill this gap by evaluating the sinonasal microbiome profiles of CRS patients over 12 months and correlating microbiome changes with treatment responses [10]. We hypothesize that patients with favourable clinical outcomes will demonstrate increased microbial diversity and a shift toward a more balanced microbiota. Furthermore, we aim to identify specific microbial taxa associated with therapeutic success or failure, providing potential biomarkers for future precision medicine strategies. By linking microbial profiling with longitudinal clinical data, this study may offer new insights into CRS pathogenesis and identify targets for microbiome-based interventions. Our findings may ultimately contribute to personalized treatment approaches that improve outcomes and reduce the burden of chronic sinus disease.

Methods: The study was conducted at Khyber Teaching Hospital Peshawar from January 2021 to July 2021. Senior patients (age 18 years or older) who matched the European Position Paper on Rhinosinusitis and Nasal Polyps (EPOS 2020) diagnosis criteria for CRS received enrolment in this study. Medial treatment along with endoscopic sinus surgery procedures were delivered to patients after their clinical assessments. The research collected nasal swabs at three-time points - the beginning, six months later and the final twelve months - to test microbiome activity. Illumina Misses carried out 16S rRNA gene sequencing to probe the V3–V4 region. The study evaluated clinical results through the administration of the Sino-Nasal Outcome Test-22 (SNOT-22). The study evaluated both alpha diversity through Shannon index assessment and beta diversity through Bray-Curtis dissimilarities metrics. The study examined bacterial taxonomic distributions between subjects who achieved clinical improvement and those who did not. Approval for this study was awarded by the institutional review board followed by participant informed consent from all participating individuals.

Inclusion Criteria: Participants with CRS who were determined to have both clinical and radiological confirmation of the disease and aged 18 years or older could join if they wanted to be part of the extended sampling procedure and could give their informed consent.
Exclusion Criteria: The excluded patients with antibiotic therapy within four weeks and patients with immunodeficiency conditions along with other health factors such as cystic fibrosis, sinonasal tumours, and sinus surgery history to ensure microbiome data purity.
Data Collection: Clinical data together with demographic markers were recorded at the enrolment phase. Endoscopic guidance allowed physicians to acquire nasal swabs from the middle meatus area. Assessment of clinical improvement relied on SNOT-22 scores recorded at different time points. The study evaluated microbial DNA through extraction sequencing followed by analyses to measure temporal variations in both composition and diversity patterns.
Statistical Analysis: SPSS version 24.0 (IBM Corp., Armonk, NY) served to analyze all the gathered data. The data points for continuous variables appeared as mean values alongside standard deviation amounts. The study utilized paired t-tests together with ANOVA for performing within-group analyses. Chi-square tests assessed categorical variables. Throughout all statistical tests a p-value which fell below 0.05 marked statistical significance.
Results: This study enrolled fifty patients with a mean age of 43.8 ± 11.2 years along with 56% male participants. Among the study group (n=50) 12-month follow-up evaluations showed that 34 patients achieved substantial clinical improvement through completing the SNOT-22 assessment. Microbial alpha diversity measured in responders showed a statistically important rise throughout months 6 and 12 (p=0.02). Beta diversity analysis produced distinct microbial clusters between responders and non-responders (p=0.03). The most frequently detected microorganisms at the beginning of the study were Staphylococcus aureus and Pseudomonas aeruginosa in both groups. The relative abundance of Corynebacterium and Dolosigranulum increased in responders during the study period without S. aureus levels decreasing in non-responders. Clinical performance scores improved when patients showed a transition toward a diverse and healthy microbial composition. The age distribution as well as sex composition and starting disease status matched equally between responders and non-responders. Non-responders showed a higher percentage of patients who received antibiotics before treatment (p=0.04). The data indicates that improved clinical results rely heavily on achieving a normal microbe diversity profile.

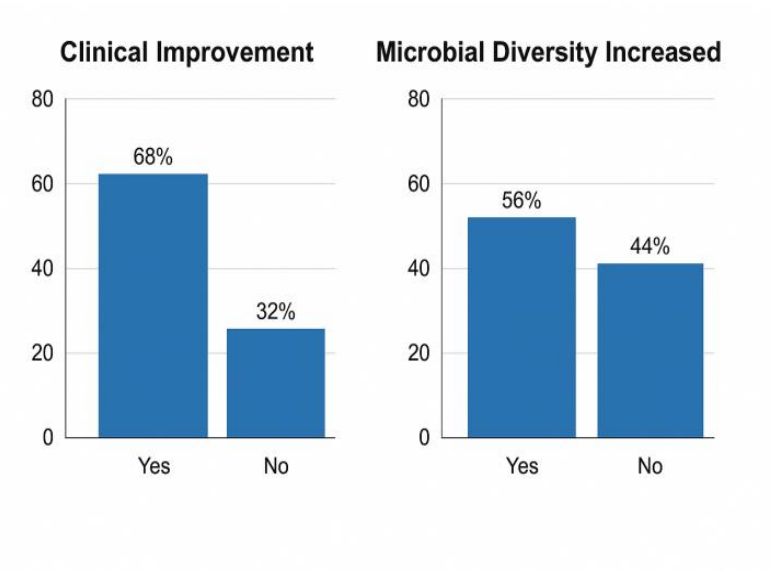

Table 1. Baseline Demographics and Clinical Characteristics (n = 50)

Variable	Value
Mean Age (years)	43.8 ± 11.2
Gender (Male)	28 (56%)
CRS with Nasal Polyps (Crown)	22 (44%)
CRS without Nasal Polyps	28 (56%)
Mean Baseline SNOT-22 Score	52.7 ± 13.5
Prior Antibiotic Use (last 3 mo.)	18 (36%)
Comorbid Asthma	14 (28%)
Smoking History	10 (20%)
Underwent Sinus Surgery	26 (52%)

Table 2. Changes in Microbiome Diversity Over Time

Time Point	Shannon Index (Mean ± SD)	p-value (vs. Baseline)
Baseline	2.10 ± 0.45	—
6 Months	2.56 ± 0.52	0.02*
12 Months	2.74 ± 0.48	0.01*

Table 3. Comparison Between Responders and Non-Responders at 12 Months

Variable	Responders (n = 34)	Non-Responders (n = 16)	p-value
Mean Age (years)	42.5 ± 10.8	45.9 ± 11.7	0.28
Gender (Male)	20 (59%)	8 (50%)	0.52
Increase in Shannon Diversity Index	0.67 ± 0.32	0.21 ± 0.18	0.02*
Relative Abundance of *Corynebacterium*	18.2%	7.4%	0.03*
Relative Abundance of *S. aureus*	12.6%	27.9%	0.01*
Prior Antibiotic Use	9 (26%)	9 (56%)	0.04*

Discussion: The clinical results of chronic rhinosinusitis (CRS) patients show improvements when studies reveal growing microbial diversity and changes in the composition of sinonasal microbiota over time [11]. This finding confirms that the sinonasal microbiota influences both disease development and long-term treatment outcomes [12]. Multiple previous studies have already proven microbial dysbiosis exists in CRS. Aurora et al. studied CRS patients together with healthy controls and discovered CRS subjects had decreased microbial diversity, especially in patients with advanced disease stages according to their findings [13]. Our results show that non-responders maintained small microbial diversity while Staphylococcus aureus levels remained elevated across multiple response groups. The pro-inflammatory nature of S. aureus conforms to these findings. The analysis conducted by Jung et al. confirmed that Crown disease patients exhibited higher S. aureus populations while demonstrating reduced quantities of Corynebacterium and Dolosigranulum along with other commensals [14]. Through microbial analysis, our research verifies these pre-existing findings and shows that responders developed greater Corynebacterium colonization over time indicating this genus might promote microbiome restoration and mucosal recovery. The research conducted by Biswas et al through a longitudinal pilot study investigated sinonasal microbial changes before and after endoscopic sinus surgery procedures. Good postoperative results correlated with recovering microbial diversity in patients according to research findings which showed Lactobacillus and Streptococcus species demonstrated increased growth [15]. The study shows that responders exhibit alpha and beta diversity improvement with time yet Corynebacterium stands out as one main bacteria for predicting successful outcomes after rhinosinusitis treatment. The research from Copeland et al. showed that CRS patient intranasal microbial changes are both dynamic and influenced by correct factors including antibiotic exposures and environmental changes [16]. Antibiotic utilization before

the study showed a significant association with treatment non-response which suggests broad-spectrum antibiotics reduce microbiome resilience and lengthen the clinical recovery period. Lal et al. examined how corticosteroids affected sinonasal microbiome patterns by showing decreased inflammation but no improved microbe diversity except through additional intervention methods [17]. The development of personalized microbiome treatments should be done in parallel with standard treatments to maximize therapeutic outcomes. The study by Choi et al. presented bacteriotherapy as a new approach to treating CRS through the use of Dolosigranulum pig rum commensal strains for establishing microbial balance [18].

Conclusion: The study shows that diverse microbial communities along with particular beneficial microorganisms in the nasal cavity improve chronic rhinosinusitis outcome measures. Microscopic analysis of microorganisms shows promise as a predictive tool and personalized therapy guide because it demonstrates the significance of balancing microbes in CRS development and recovery.

Limitations: Generalization of the study results faces challenges because it relies on a small sample from a single center and limited distribution of participants. The study may have been affected due to the impact of confounding elements including diet together with environmental pollutants and undocumented antibiotic consumption. No evaluation based on microbial gene activity took place through functional or metagenomic profiling.

Future Findings: Upcoming research needs to perform multiple-site investigations using bigger participant groups which will enable the study of microbial operations through genetic and metabolic methods. Studies examining how probiotics and bacteriotherapy affect microbiome function would enhance knowledge of how microbial treatments boost rhinosinusitis outcomes.

Abbreviations

1. **CRS** – Chronic Rhinosinusitis
2. **SNOT-22** – Sino-Nasal Outcome Test-22
3. **16S rRNA** – 16S Ribosomal Ribonucleic Acid
4. **SD** – Standard Deviation
5. **EPOS** – European Position Paper on Rhinosinusitis and Nasal Polyps
6. **DNA** – Deoxyribonucleic Acid
7. **SPSS** – Statistical Package for the Social Sciences
8. **ANOVA** – Analysis of Variance
9. **NY** – New York
10. **mo.** – Months

Authors Contribution

Concept & Design of Study: Dr. Imran Khan
Data Collection or Management: Dr. Shakir Ullah
Drafting: Dr. Shakir Ullah, Dr. Waseem Khan, Dr. Arif Ahmad
Data Analysis: Dr. Imran Khan, Dr. Asad Ullah
Critical Review: Dr. Sami Ullah, Dr. Arif Ahmad
Final Approval of version:All mentioned authors have thoroughly reviewed and approved the final version of the manuscript, ensuring its accuracy, integrity, and compliance with ethical and scientific standards.

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