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Variability of the Microbiota in Chronic Rhinosinusitis: A Scoping Review

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Abstract

Objective. Chronic rhinosinusitis (CRS) is characterized by a persistent inflammation of the nasal and paranasal sinus mucosa that could be potentially linked to a dysregulation between the microbiota and the immune system. We aim to explore general, methodological, and microbiological aspects of microbiota research in CRS compared to disease-free individuals.

Data Sources. Embase, Ovid MEDLINE, PubMed, Scopus, and Web of Science.

Review Methods. All studies comparing the composition of the resident microbiota of the sinonasal cavities in 2 groups: CRS and normal participants. We conducted systematic study selection, data extraction, and analysis first using the title and abstract, and then the full texts based on predefined inclusion and exclusion criteria. Compiled and presented findings include sampling site and technique, and microbiological results such as the relative abundance and the variability of the composition of the microbiota in both groups.

Results. Twenty-seven studies, using genomic identification with 16s RNA were analyzed. Case definitions primarily followed EPOS or AAO-HNS guidelines, with endoscopic swabs (82%), and middle meatus sampling (74%) being prevalent techniques. Despite relative abundance variability, patterns emerged across studies, indicating an increase in *Haemophilus* (19%) and *Pseudomonas* (11%), and decrease in *Propionibacterium* (15%) and *Anaerococcus* (11%). Another pattern was observed, showing a decreased alpha diversity (6/19; 22%) in CRS compared to normal individuals.

Conclusion. While variations exist among studies, analysis of CRS microbiota suggests an association with dysbiosis, potentially contributing to chronic inflammation. Future research must prioritize standardized criteria for diagnostics and patient selection, fostering a more comprehensive understanding of CRS microbiota.

Keywords

Biodiversity, chronic disease, host-pathogen interaction, microbial genetics, RNA, ribosomal, 16 s

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Chronic rhinosinusitis (CRS) is defined by persistent inflammation of the nasal and paranasal sinus mucosa for a minimum of 12 weeks. Clinically, the chronic inflammation of the mucosa is characterized by the presence of at least 2 of the following symptoms: nasal obstruction, nasal discharge with facial pain/pressure, or smell disorders.[1] This prevalent condition affects approximately 12% of the population in the United States, and 10% in Europe,[2,3] and negatively affect the quality of life. Moreover, CRS imposes a substantial socioeconomic burden on health systems due to direct costs incurred by repeated outpatient visits, medical therapy, and surgery. Additionally, there are indirect costs resulting from losses in work productivity that are proportional to the disease severity, especially in refractory cases. A review study reported that direct and indirect costs to the health system of the United States could be around $12.5 billion and $20 billion per year for direct and indirect cost respectively.[2]

Two types of CRS could be characterized: without and with nasal polyps. These conditions can be triggered by various factors, including genetic factors, smoking, occupational exposures, and air pollution.[4] These factors could result on the disturbance of the normal microbial population and may trigger an immune disbalance with chronic immune activation, and could potentially play a role in the development and maintenance of the inflammatory condition associated with CRS.[5] Some

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studies have suggested that the alteration of the composition of the microbiota in patients with CRS, including changes in diversity, increased bacterial load, and less stable bacterial networks.[6] Therefore, it is hypothesized that any disruption of the microbiological equilibrium of the resident microorganisms could initiate or sustain the disease.[7]

By definition, the microbiota represents the collection of living microorganisms present in a specific environment in a specific period of time. Otherwise, the microbiome describes the dynamic interrelation between the microbiota and their interaction with the environment, facilitated by a spectrum of molecules produced by these microorganisms, and the host.[8] As a dynamic entity, a delicate balance is maintained between the microbiome and the host and various factors can contribute to its alterations such as environmental conditions (temperature, humidity, and climate), or host-related factors (anatomical and immunological).[5,9]

The intricate organization of these communities and their connection with the environment is not well understood.[10] Several notable challenges hinder understanding of this subject, including (a) the complex nature of the sinonasal microbiota, (b) the variability of its composition among individuals, (c) the interactions among different microorganisms, (d) the use of different sampling methodologies, and (e) the limited availability of longitudinal and functional studies. The study of these factors should be necessary to acquire a more comprehensive understanding of how the microbiota evolves alongside the disease.[9]

It is essential to assess the current state of research regarding the relationship between the microbiota and CRS. Analyzing the variability in the methodological and microbiological characteristics used in different studies may elucidate the various forms of association between microbiota and CRS. This review aimed to examine the general, methodological, and microbiological aspects of microbiota research in CRS compared to patients without this disease.

Material and Methods

This review was reported following the recommendations of the Preferred Reporting Items for Systematic and Meta-Analysis Extension for Scoping Reviews (PRISMA-ScR),[11] and the methodological criteria of the Joana Briggs Institute.[12]

Eligibility Criteria

The analysis included clinical case-control and longitudinal studies, written in English, that compared the bacterial composition of the sinonasal microbiota in healthy patients with those having CRS. The included studies were conducted on adults aged over 18. Letters to the editor, editorials, studies including animal models, and review articles were excluded from the analysis.

Information Sources and Search Strategy

The following databases and search engines were used to retrieve related studies: PubMed, Scopus, Web of Science (Core collection), Embase, and Ovid/MEDLINE. The following keywords were used such as "chronic sinusitis," "chronic rhinosinusitis," "microbiota," and "microbiome". The comprehensive search strategy for each database is detailed in Supplemental Material S1, available online.

Study Selection

Three investigators (FBC, FCB, ZOB) created a database through electronic searches on December 19, 2022. Duplicates were subsequently removed using Rayyan software on December 26, 2022.[13] Then, they conducted the screening process by: (1) analyzing the titles and abstracts independently, (2) selecting those meeting the inclusion criteria, and (3) evaluating the full text if necessary. If case of disagreement, the researchers discussed until a consensus was reached; if a dispute arose, a fourth researcher joined the discussion to help resolve it. The selection of full-text articles began on January 8, 2023. The authors (FBC, FCB, and ZOB) reviewed the full-text reports according to the inclusion criteria to include the selected studies in the final database.

Data Extraction

Each of the 3 investigators independently extracted data from the selected studies into a Microsoft Excel spreadsheet. The general characteristics of the study were extracted and included: the first author, the year of publication, study country, study design, CRS case and control definitions, and the number of cases and controls. Methodological characteristics were collected including: the anatomical sampling site, sampling technique, sample access, and sample analysis technique. Microbiological results encompassed the variability of relative abundance (at phylum and genera level), alfa diversity (the variety and abundance of microorganisms within a localized area), beta diversity (variation in microorganisms among different spatial units), richness (variety of microorganisms present in a localized area), and evenness (relative abundance of different microorganisms within a localized area). There was reviewed the list of articles and data extractions to ensure that there were no duplicate articles or redundant information, and resolving discrepancies about study inclusion. The results are summarized in narrative form and tables.

Results

Study Selection

Initially, 1445 titles and abstracts were identified. After eliminating duplicates, the titles and abstracts of 553 articles were evaluated. Among these, 60 studies underwent a full-text review, and ultimately, 27 individual studies were included (**Figure 1**).[14–40]

Studies Characteristics

Of the 27 studies, 25 employed a cross-sectional design,[14–21,23–32,34–40] and 2 employed a longitudinal design[22,33] (**Table 1**). Most studies were conducted in the United States (n = 5; 18%) and Australia (n = 5; 18%). The rest were made in Belgium, China, Germany, Korea, New Zealand, and Sudan. One study was multicentric (Australia, New Zealand, Thailand, India, Chile, Brazil, USA, the Netherlands, and Canada). Regarding case definition methods, the 2012 European Position Paper on Rhinosinusitis and Nasal Polyps (EPOS) criteria[1] were most commonly utilized (n = 17; 63%), followed by the American Academy of Otolaryngology Head and Neck Surgery (AAO-HNS) guideline criteria (n = 8; 30%).[41] One study[38] utilizes the 2016 International Consensus Statement on Allergy and Rhinology,[42] and 1 study defines the CRS cases as overexpression of the MUC5A gene.[15] Controls were defined as patients undergoing nasal endoscopic surgery for other etiologies such as pituitary surgery, medial orbital decompression or septoplasty (n = 15; 56%), and the remaining studies considered patients healthy based on the guidelines applied in the study. The mean number of patients in the cases group was 58 patients, and the mean in the control group was 28 patients. The most commonly used exclusion criteria in the reviewed studies were immunodeficiency (n = 16; 59%), and the use of corticosteroids or antibiotics, ranging from 1 week to 1 year at the time of sampling (n = 15; 56%).

Regarding the sampling technique, swabs were mostly used (n = 22, 81.5%), followed by biopsy or swab combined (n = 5, 18.5%). In all studies, the microbiologic samples were obtained by an endoscopic approach of the nasal cavity, except for De Boeck et al, which was the only study that used endoscopic sinus surgery for cases, and nasal sampling for controls.[25] Samples were obtained from the middle meatus (n = 20, 74.1%), followed by the ethmoidal sinus (n = 8, 29.6%). Lastly, all studies were based on genomic identification using 16 s RNA (**Table 2**).

Microbiota Variability

Relative Abundance

Twenty-two studies (82%) revealed variations in the relative abundance of bacteria CRS groups and the normal group. Among these studies, differences at the genera level were observed: *Corynebacterium* and *Staphylococcus* were each found in 7 studies (26%), *Prevotella* in 6 (22%), *Haemophilus* in 5 (19%), *Propionibacterium* in 4 (15%). Additionally, 4

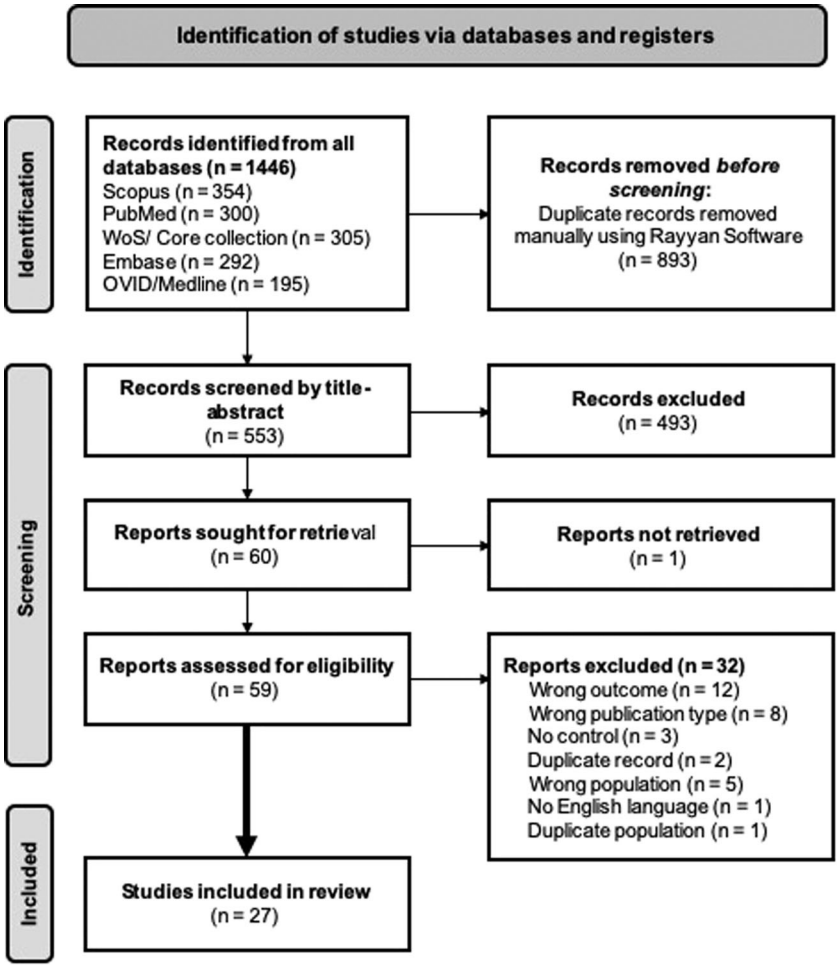

Figure 1. Flow diagram summarizing the process of literature search and selection.

Table 1. General Characteristics of the Included Studies (N = 27)

		Inclusion criteria				Exclusion criteria
Author (ref.)	Country	CRS cases	N	Controls	N	
Abbas[14]	Sudan	EPOS 2012 CRSwNP	46	Sinus healthy patients	12	Fungal CRS, immunodeficiency, malignancies, cystic fibrosis, autoimmune diseases, corticosteroid, or antibiotics 1 month before sampling
Abreu[15]	USA	Overexpression of the MUC5A gene	10	Surgery for non-CRS complaints (e.g. obstructive sleep apnea or post-traumatic malocclusion)	10	NR
Aurora[16]	USA	AAO-HNS 2003 Patients undergoing endoscopic sinus surgery	30	Endoscopic nasal surgery (pituitary, orbital, and septoplasty)	12	NR
Biswas[17]	New Zealand	EPOS 2012	23	Endoscopic nasal surgery (pituitary, orbital decompression) without clinical or radiological signs of CRS	8	Immunodeficiency, another comorbidity, corticosteroids, antibiotics within 1 month before sampling, and pregnancy
Boase[18]	Australia	AAO-HNS 2003	38	Clinical or radiological absence of sinus pathology	6	Immunodeficiency, decreased ciliary function, corticosteroids, or antibiotics within 3 weeks before sampling
Chalermwatanachai[19]	Belgium	EPOS 2012	41	Clinically healthy patients without symptoms of sinusitis, asthma, or atopy	17	Immunodeficiency or autoimmune disease, without cystic fibrosis, corticosteroids, or antibiotics within 3 months before sampling
Choi[20]	Korea	AAO-HNS 2003	5	Patients with septal deviation with normal endoscopic or radiologic findings	3	Pregnancy, immunodeficiency, any sinonasal diseases, corticosteroids, or antibiotics 1 month before sampling
Cho[21]	Korea	EPOS 2012	14	Endoscopic nasal surgery for septal deviation	8	Unilateral sinus disease, fungal disease, cystic fibrosis, primary ciliary dyskinesia, nasal tumors
Cleland[22]	Australia	AAO-HNS 2003	23	Transsphenoidal endoscopic approach of the anterior skull base without sinus disease	11	Immunodeficiency, primary mucociliary disease, corticosteroids, or antibiotics within 2 weeks before sampling
Cope[23]	USA	AAO-HNS 2007	59	Transnasal endoscopic surgery	10	NR
Copeland[24]	Australia	EPOS 2012	21	Endoscopic nasal surgery for other etiologies without clinical or radiological signs of CRS	12	Corticosteroids or antibiotics within 1 month before sampling
De Boeck[25]	Belgium	EPOS 2012	190	NR	100	Antibiotics or suffered acute or chronic airway infections within 1 year before sampling, ciliary dyskinesia, inverted papilloma, or aspirin intolerance
Feazel[26]	USA	AAO-HNS 2007	15	NR	5	NR
Feng[27]	Belgium	EPOS 2012	34	Endoscopic nasal surgery for other etiologies	39	Immunodeficiency, co-morbidities (cystic fibrosis, ciliary immobile syndrome, aspirin-exacerbated respiratory disease, allergic fungal sinusitis, and inverted papilloma, corticosteroids, or antibiotics within 4 weeks before sampling

Author (ref.)	Country	Inclusion criteria				Exclusion criteria
		CRS cases	N	Controls	N	
Gan[28]	China	EPOS 2012 CRSwNP	89	Endoscopic nasal surgery for other etiologies without signs of sinus pathology	33	Immunodeficiency, corticosteroids, or antibiotics within 1 month before sampling, cystic fibrosis, or autoimmune disease
Gan[29]	China	EPOS 2012 CRSwNP	59	Endoscopic nasal surgery for other etiologies without signs of sinus pathology	27	Immunodeficiency, corticosteroids, or antibiotics within 1 month before sampling, cystic fibrosis, or autoimmune disease
Goggin[30]	Australia	AAO-HNS 2015	72	Endoscopic nasal surgery of pituitary, septum, or inferior turbinate without clinical or radiological signs of CRS	10	Immunodeficiency, corticosteroids, or antibiotics within 2 months before sampling
Hoggard[31]	New Zealand	EPOS 2012	94	Endoscopic nasal surgery for pituitary or dacryocystorhinostomy	29	Immunodeficiency, sinonasal vasculitis
Hoggard[32]	New Zealand	EPOS 2012	14	Endoscopic nasal surgery for orbital or skull base pathologies without CRS	12	Immunodeficiency, ciliary dysfunction, autoimmune disease, cystic fibrosis
Kim[33]	Korea	EPOS 2012 CRSwNP	31	Endoscopic nasal surgery without CRS	6	Immunodeficiency, corticosteroids, or antibiotics within 1 month before sampling, cystic fibrosis, or autoimmune disease, and did not have medical comorbidities
Kim[34]	Korea	EPOS 2012	70	Endoscopic nasal surgery without CRS	29	Unilateral rhinosinusitis, antrochoanal polyps, allergic fungal sinusitis, cystic fibrosis, or immotile ciliary disease
Koeller[35]	Germany	EPOS 2012 CRSsNP	18	Orbital decompression, orbital tumor or mucocele	3	Antibiotics within 1 month before sampling
Paramasivan[36]	Multic.[a]	2016 International Consensus statement on Allergy and Rhinology	271	Other otolaryngological procedures (tonsillectomy, septoplasty, or skull base tumors) without clinical or radiological CRS	139	NR
Ramakrishnan[37]	USA	AAO-HNS 2007	31	Endoscopic nasal surgery without clinical or radiological CRS	70	Immunodeficiency, autoimmune disease, cystic fibrosis.
Rom[38]	Australia	EPOS 2012	37	Endoscopic transnasal surgery without clinical or radiological CRS	52	Immunodeficiency, coagulation disorder, Churg-Strauss syndrome, or cystic fibrosis
Wei[39]	China	EPOS 2012	202	Patients with nasal congestion and snoring without CRS	49	Immunodeficiency, corticosteroids, or antibiotics within 1 month before sampling, immotile-cilia syndrome, cystic fibrosis
Wos-Oxley[40]	Germany	EPOS 2012	42	No clinical or radiological signs of CRS	37	Corticosteroids or antibiotics within 1 month at the time of sampling, melanoma, papilloma

Abbreviations: AAO-HNS, American Academy of Otolaryngology–Head and Neck Surgery; CS, Cross-sectional; & Longitudinal; CRSwNP, chronic rhinosinusitis patients with polyps; CRS, Chronic rhinosinusitis; CRSsNP, chronic rhinosinusitis patients without polyps; EPOS, European position paper on rhinosinusitis and nasal polyps; ESS, Endoscopic sinus surgery; NR, not reported; USA, United States of America.
[a]Multicentric study: Australia, Brazil, Canada, Chile, India, The Netherlands, New Zealand, Thailand, USA.

Table 2. Methodology Characteristics of the Included Studies (N = 27)

Author (ref.)	Anatomical sampling site	Sample access	Sampling technique
Abbas[14]	Middle meatus	Endoscopic	Biopsy and swab
Abreu[15]	Maxillary sinus	Open nasal or endoscopic	Sinus brushings
Aurora[16]	Middle and superior meatus	Endoscopic	Lavage and suction
Biswas[17]	Ethmoidal sinus	Endoscopic	Biopsy
Boase[18]	Case: ethmoid sinus Control: ethmoid and sphenoid mucosa	Endoscopic	Biopsy and swab
Chalermwatanachai[19]	Middle meatus	Endoscopic	Swab
Choi[20]	Nasal cavity	Open nasal or endoscopic	Nasal lavage and suction
Cho[21]	Swab: middle meatus. Biopsy: uncinate tissue and ethmoidal sinus	Endoscopic	Biopsy and swab
Cleland[22]	Middle meatus and/or anterior ethmoid cavity	Endoscopic	Swab
Cope[23]	Diseased sinus	Endoscopic	Sinus brushings
Copeland[24]	Case: middle meatus, maxillary sinus, ethmoid sinus, sphenoid sinus, and frontal sinus Control: Right nostril, right and left middle meatus and each sinus opened at surgery	Endoscopic	Swab
De Boeck[25a]	Maxillary and ethmoid sinus	Open nasal or endoscopic	Swab
Feazel[26a]	Middle meatus	Endoscopic	Swab
Feng[27]	Middle meatus	Endoscopic	Biopsy and swab
Gan[28]	Middle meatus	Endoscopic	Swab
Gan[29]	Middle meatus	Endoscopic	Swab
Goggin[30]	Middle meatus	Endoscopic	Swab
Hoggard[31]	Middle meatus	Endoscopic	Swab
Hoggard[32]	Middle meatus	Endoscopic	Swab
Kim[33]	Middle meatus	Endoscopic	Swab
Kim[34b]	Middle meatus	Endoscopic	Swab
Koeller[35a]	Middle meatus, anterior ethmoid, and maxillary sinus	Endoscopic	Biopsy and swab
Paramasivan[36]	Middle meatus	Endoscopic	Swab
Ramakrishnan[37]	Ethmoid region	Endoscopic	Swab
Rom[38]	Middle meatus	Endoscopic	Swab
Wei[39a]	Middle meatus	Endoscopic	Swab
Wos-Oxley[40]	Inferior and middle meatus	Endoscopic	Swab

[a]With microbiological culture.
[b]With proteomic analysis.

genera exhibited distinct patterns: *Haemophilus* and *Pseudomonas* showed increases, while *Propionibacterium* and *Anaerococcus* showed decreases.

At phylum level, 8 studies (30%) showed variations in relative abundance. Among the analyzed phyla, Proteobacteria (n = 5; 19%) and Firmicutes (n = 3; 11%) exhibited an increase in relative abundance in more than 3 studies.

Variation of Microbiota Composition

Regarding the microbiota composition, the variation in microbial community was assessed by comparing normal and CRS groups. Alpha diversity was reported in 19 studies (70%), with a decrease observed in the CRS group in 6 studies (6/19; 32%), and no difference in 13 studies (13/19; 68%). Richness was reported in 16 studies (59%), indicating a decrease in richness in the CRS group compared to the normal group in 6 studies (6/16; 38%), with no difference in 10 studies (10/16; 62%). Beta diversity was reported in 8 studies (30%), revealing a decrease in the CRS group compared with the normal group in 3 studies (3/8; 38%), and no significant difference in 5 studies (5/8; 62%). Evenness was reported in only 6 studies (22%), with a decrease observed in the CRS group compared to the normal group in 3 studies (3/6; 50%) and no significant difference in 3 studies (3/6; 50%) (**Table 3**).

Table 3. Statistically Significant Differences Between the Relative Abundance of the Nasosinusal Microbiota of Patients With Chronic Rhinosinusitis (CRS) with Respect to Healthy Individuals

First author (ref.)	Relative abundance																										Microbiota			
	At genera level																									At phylum				CRS vs control			
	Corynebacterium	Staphylococcus	Prevotella	**Haemophilus**	**Propionibacterium**	**Anaerococcus**	Bacteroides	Moraxella	Porphyromona	**Pseudomona**	Dolosigranullum	Peptoniphilus	Ruminococcus	Streptococcus	Stentrophomonas	Acinetobacter	Ackermansia	Citrobacter	Desulfovibrio	Escherichia	Lactobacillus	Lawsonella	Neisseria	Rotia	Ruminoclostridium	Tissierella	**Proteobacteria**	**Firmicutes**	Actinobacteria	Verrucomicrobia	Alfa diversity	Richness	Beta diversity	Evenness
Abbas (14)			↓			↓		↑					↓				↓		↓			↓			↓					↓	-	-	ND	-
Hoggard (31)	↓		↓		↓				↓			↓											↓			↑	↑			↓	↓	-	-
Kim (34)		↓	↑		↓		↑	↓																			↑			↓	-	↓	-
De Boeck (25)	↑	↑	↑	↑							↓																			ND	ND	-	-
Cleland (22)*	↓	↑								↑						↓									↓	↑				ND	ND	-	-
Biswas (17)				↑				↑		↑					↑															ND	-	-	-
Cope (23)	↑			↑										↑										↑						-	↓	↓	↓
Choi (20)		↑	↓				↓																			↑	↑			↓	-	-	-
Chalermwatanachai (19)				↑	↓		↓																			↑				↓	ND	-	↓
Koeller (35)									↑	↑					↑															-	ND	-	-
Gan (29)	↓										↓																	↓		ND	↓	-	-
Boase (18)		↑			↓																									-	-	-	-
Cho (21)			↓										↓																	-	-	-	-
Feng (27)		↓		↑																										↓	↓	↓	-
Ramakrishnan (37)									↓			↓																		ND	ND	ND	ND
Abreu (15)	↑																				↓									↓	↓	-	↓
Paramasivan (36)	↓													↑																ND	ND	ND	-
Copeland (24)																				↑						↑				ND	-	-	-
Feazel (26)		↑																												-	ND	-	ND
Hoggard (32)						↓																								ND	ND	-	-
Kim (33)						↓																								ND	-	-	-
Wei (39)																		↓												-	-	-	-
Aurora (16)																														-	-	ND	-
Gan (28)																														ND	ND	ND	-
Goggin (30)																														ND	-	-	-
Rom (38)																														ND	↓	-	-
Wos-Oxley (40)																														ND	ND	-	ND
N	7	7	6	5	4	3	3	3	3	3	2	2	2	2	2	1	1	1	1	1	1	1	1	1	1	5	3	1	1	6	6	3	3

↓, a statistically significant decrease in patients with CRS compared to healthy patients; ↑, a statistically significant increase in patients with CRS compared to healthy patients. ND: No significant difference; "–", The study did not evaluate this factor; N, Number of studies that found a difference between CRS vs healthy individuals.

Discussion

Chronic rhinosinusitis is a condition characterized by a persistent inflammation of the nasal and the paranasal sinus mucosa for more than 12 weeks. It is hypothetized that the disruption of the microbiological equilibrium of the normal microbiota could be source of chronic inflammation. Here, we examine different aspects of microbiota research works that compared CRS microbiota to those without disease. Despite of the variability among works, a pattern of an increase of the relative abundance in CRS compared to normal patients was observed for *Haemophilus* (19%), and *Pseudomonas* (11%), whereas a decrease was observed for *Propionilbacterium* (15%), and *Anaerococcus* (11%). Regarding the variation of the microbiological composition, a pattern of a decrease of alpha diversity in patients with CRS was observed in 32% of studies.

Regarding patient selection, almost all the studies were based on the diagnostic criteria of the EPOS 2012 or AAO-HNS 2007 guidelines. While both guidelines are based on similar clinical criteria, the EPOS guidelines, in addition, include objective evidence for CRS diagnosis, including endoscopic and radiological findings. In 2 studies, there was used the International Consensus Statement on Allergy and Rhinology that is another validated guideline for the diagnosis of CRS which is focused on clinical criteria and requires an additional radiological confirmation.[42] Only 1 study used the overexpression of the MUC5A and B genes that was associated with CRS compared to normal subjects.[43] Despite the variability in the use of different guidelines for

diagnosing CRS, all of them are validated tools for the determination of CRS, and the choice of different criteria may not significantly affect the variability the microbiological results.

There were notable differences in the criteria for inclusion and exclusion of patients, some studies excluded patients who took antibiotics within a range from 1 week[22] to 1 year before sampling.[25] Others works did not consider the prior use of antibiotics,[21,31,32,34,38,43] and other studies did not reported this factor.[15,16,23,36] Previous studies focusing on gut microbiome show that the restoration of bacterial population after a short-term administration of antibiotics (less than 10 days), the restoration of bacterial populations to pre-antibiotic levels is more important the first month,[44] and remained perturbed 2 years posttreatment.[45] Therefore, in patients undergoing prolonged treatments, the microbiological recovery time could be highly variable, potentially accounting for heterogeneity in the selection of this criterion.[45] In the case of the nasal and paranasal microbiota, the mucosa of these sites could be colonized by antibiotic-resistant bacteria after the use of antibiotics.[46]

Sampling techniques and sample type vary across studies, ranging from guarded swabs and/or brushings, unguarded endoscopically guided swabs, mucosal biopsy, and nasal lavage. Guarded or carefully performed endoscopically guided swabs may reduce the risk of anterior nares contamination, which is particularly important in studies of a specific sinonasal niche, where contamination may influence the interpretation of results. A study comparing mucosal biopsy samples and mucosal swabs from patients with CRS demonstrated similar bacterial diversity and compositional profiles between the 2 sample types; once again, interpersonal variation was a stronger driver of bacterial composition.[47] The best sampling protocol depends on the question being addressed. A mucus swab of the middle meatus compared with other locations such as the ethmoid cavity may be the simplest approach for the longitudinal study of the sinus microbiome, considering that it can be obtained from a wide range of subjects and does not require invasive procedures. These potential confounding factors could be influence on the variability of the results of the microbiota analysis.

Regarding the relative abundance of the genera and phyla of CRS compared to normal subjects, an important variability on the genera isolated was observed among different studies. No consensus regarding the increase or decrease in the relative abundance was evidenced, with most studies lacking agreement with these observations. However, 4 genera exhibited consistent variations in relative abundance across more than 3 studies. *Haemophilus* showed an increase in relative abundance in 4 studies, with only 2 studies specifying the insolated species: *H. influenzae*,[19,25] and *H. aegyptius*.[25] This genus could be a part of the sinus microbiota or act as a pathogen causing upper respiratory tract infections, such as *H. influenzae*.[48] *Pseudomonas*, identified in 3 studies,[17,22,35] is not considered a part of the commensal microbiota in humans, and is recognized as an opportunistic bacterium associated with nosocomial infections.[49] Two genera exhibited a decrease in relative abundance in 3 studies: *Propionibacterium* and *Anaerococcus*. Both genera are commensal in humans, with *Propionibacterium* being more abundant on the skin but also found in gut and oral cavity and it could be an opportunistic pathogen.[50] *Anaerococcus* is also part of commensal microbiota, found in skin, vagina, gut, and oral cavity, and may be associated with polymicrobial infections.[51] Regarding the composition of the microbiota, studies reported discrepancies, with some noting a decrease in alpha diversity, while others found no difference between normal and CRS subjects. The same pattern was observed for beta diversity, richness, and evenness.

Despite the described patterns, the important variability among studies may be potentially attributed to various factors. Individual exposure to specific environments, lifestyle choices, dietary habits, and their interaction with the genetic factors could account for individual variations.[4,5] Additionally, observed geographical and population differences among the included studies further contribute to this variability. Despite the differences in sampling techniques, such as the use of swabs, nasal lavage, or biopsies, as well as variations in the approach to the nasal or paranasal cavity—whether endoscopic with a wake patient or during surgery, there was no observed intrastudy variability, and the samples were taken at the same anatomic sites and using the same sampling technique in both healthy and CRS individuals. Clinical heterogeneity within the included patients, presenting with CRS of varying severity, including cases with or without nasal polyps, may influence the composition of the nasal and paranasal microbiota. Furthermore, the use of antibiotics emerged as another influencing factor capable of impacting microbiota composition. Collectively, these multifaceted factors render the comparison of microbiota studies challenging across different research endeavors.

All these finding suggest that CRS could be associated with a dysbiosis of the microbiota of the nasal and paranasal sinus and the maintain of the chronic inflammation. Despite the variability observed in the relative abundance and the composition of the microbiota among the studies due to the multiple factors associated with the nasal microbiota, an increase of potential pathogen microorganisms and a decrease of the non-pathogen bacteria could produce the chronic inflammation. Additionally, the dysbiosis associated with changes in relative abundance of 1 microorganism could produce a diminished diversity of the nasal and paranasal microbiota.

This scoping review has certain limitations including the inclusion of only English studies and the lack of a formal assessment of methodological quality. Nevertheless, this review represents an attempt to synthesize and provide an overview of the literature in this study area.

Conclusion

Despite the inherent variation among studies, the analysis of CRS microbiota reveals some findings that suggest that CRS may be associated with dysbiosis of the nasal microbiota, potentially leading to chronic inflammation. Despite the variability in microbiota composition, the increase of potential pathogen microorganisms and decrease of non-pathogen bacteria could contribute to chronic inflammation. The dysbiosis associated with changes in the relative abundance of microorganisms may result in diminished diversity of nasal and paranasal microbiota without be conclusive. Future research should prioritize standardized diagnostic and patient selection criteria, fostering a more comprehensive understanding of CRS microbiota.

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Fabricio Ccami-Bernal, conception, design of the work, acquisition, analysis, interpretation of data, drafting the manuscript; **Fernanda Barriga-Chambi**, acquisition, analysis, interpretation of data, drafting the manuscript; **Zhamanda N. Ortiz-Benique**, acquisition, analysis, interpretation of data, drafting the manuscript; **Evelyne Ferrary**, analysis, interpretation of data, revise critically, final approval; **Renato Torres**, conception, design of the work, interpretation of data, revise critically, final approval.

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Supplemental Material

Additional supporting information is available in the online version of the article.

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