



## Role of Microorganisms in Acute and Chronic Rhinosinusitis: A Review

Muhammad Ali<sup>1\*</sup> and Muhammad S. Abdallah<sup>2</sup>

<sup>1</sup>Department of Microbiology, Federal University Gusau, Nigeria

<sup>2</sup> Desert Research Monitoring and Control Centre, Yobe State University Damaturu, Nigeria

\*Corresponding author: Muhammad Ali, Department of Microbiology, Federal University Gusau.

Email: alimuhd4real@gmail.com

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### Abstract

*Rhinosinusitis (RS) is an inflammation of the mucous membrane that lines the paranasal sinuses. It is a common disorder related to inflammation of your nasal passages and sinus cavities. Most cases of rhinosinusitis are caused by allergies or infection. Rhinosinusitis is divided into four categories based on duration of symptoms and frequency of onset into: Acute rhinosinusitis, sub-acute rhinosinusitis, chronic rhinosinusitis and recurrent rhinosinusitis. Several respiratory viruses may infect the upper respiratory tract and cause Acute and chronic rhinosinusitis. These include, for example, human rhinovirus, respiratory syncytial virus (RSV), influenza, parainfluenza viruses, coronavirus and adenovirus. Some bacteria are also found to cause rhinosinusitis such as Pseudomonas spp., Corynebacterium spp certain Streptococcus spp., Staphylococcus aureus and Haemophilus influenza. Common symptoms of rhinosinusitis include thick nasal mucus, a plugged nose, and pain in the face. Other signs and symptoms may include fever, headaches, poor sense of smell, sore throat, and cough. The paper aimed at reviewing the role microorganisms played in acute and chronic rhinosinusitis.*

**Keywords:** Rhinosinusitis, Bacteria, Virus, infection, chronic, acute.

### Introduction

Rhinosinusitis (RS) is an inflammation of the mucous membrane that lines the paranasal sinuses [1]. It is a common disorder related to inflammation of your nasal passages and sinus cavities [2]. About 1 out of every 8 people experience rhino sinusitis every year, so you will likely experience this; particularly if you have any of the risk factors which includes: smoking, elderly, air travel or other activities that changes air pressure (like scuba diving), swimming, asthma, allergies, dental problems, or a weakened immune system [3]. Rhino sinusitis (RS) is characterized by inflammation of nasal and paranasal sinuses mucosa, which is one of the most prevalent upper airways affections. Rhinosinusitis is as result of infectious viral, bacterial or fungal processes and may be associated with allergy, nasosinus polyposis and mucosa vasomotor

A bacterial infection may be present if symptoms last more than ten days or if a person worsens after starting to improve [6]. Recurrent episodes are more likely in people with asthma, cystic fibrosis, and poor immune function [6]. Rhinosinusitis is considered as common condition which generally occurs when viruses or bacteria infect the sinuses

dysfunction [4]. Viral Rhinosinusitis is the most prevalent form. It is estimated that adults have on average 2 to 5 episodes of cold per year and children have 6 to 10 years [3]. However, it is difficult to precisely define this prevalence because most patients who have flu or cold do not go to the doctor. Out of viral episodes, about 0.5% to 10% progress to bacterial infections, which explains the high prevalence of this affection in the general population [5].

The most common symptoms of Rhinosinusitis include thick nasal mucus, a plugged nose, and pain in the face [6]. Other signs and symptoms may include fever, headaches, poor sense of smell, sore throat, and cough [7,8]. The cough is often worse at night and serious complications are rare [8]. It is defined as acute rhinosinusitis (ARS) if it lasts less than four weeks and as chronic rhinosinusitis (CRS) if it lasts for more than 12 weeks [6]. Sinusitis can be caused by infection, allergies, air pollution, or structural problems in the nose [7]. Most cases are caused by a viral infection [7].

and begin to multiply and this often happens during a cold. The body's reaction to the infection causes the sinus lining to swell, blocking the channels that drain the sinuses [8]. This causes mucus and pus to build up in the sinus cavities. This build-up and the associated symptoms can become more severe. Allergies and other medical conditions can worsen the course of infection, though the acute infection is usually

caused by a virus or bacteria. An acute infection lasts usually days but can last for up to four weeks. Chronic rhinosinusitis sees symptoms last for more than twelve weeks and is usually caused by prolonged inflammation, rather than a persistent infection. Chronic rhinosinusitis can present with or without polyps and may be associated with other medical conditions [7].

### Classification of Rhinosinusitis

Rhinosinusitis cases are mostly caused by infections or allergy. Rhinosinusitis is divided into four categories based on duration of symptoms and frequency of onset as follows;

- Acute rhinosinusitis: In acute rhinosinusitis, the symptoms last less than four weeks
- Sub-acute rhinosinusitis: In sub-acute rhinosinusitis, the symptoms last between four and twelve weeks
- Chronic rhinosinusitis: Chronic rhinosinusitis is the one with symptoms last longer than twelve weeks
- Recurrent rhinosinusitis: Recurrent rhinosinusitis is the one with frequent episodes of rhino sinusitis throughout the year i.e. four or more episodes per year [9].

### Signs and symptoms

Headache, facial pain or pressure of a dull, constant, or aching sort over the affected sinuses is common with both acute and chronic stages of sinusitis. This pain is typically localized to the involved sinus and may worsen when the affected person bends over or when lying down. Pain often starts on one side of the head and progresses to both sides [10]. Acute sinusitis may be accompanied by thick nasal discharge that is usually green in color and may contain pus (purulent) and/or blood [11]. Often a localized headache or toothache is present, and it is these symptoms that distinguish a sinus-related headache from other types of headaches, such as tension and migraine headaches. Another way to distinguish between toothache and sinusitis is that the pain in sinusitis is usually worsened by tilting the head forwards and with valsalva maneuvers [12].

In addition, Infection of the eye socket is possible in Rhinosinusitis, which may result in the loss of sight and is accompanied by fever and severe illness. Another possible

complication in Rhinosinusitis is the infection of the bones (osteomyelitis) of the forehead and other facial bones – Pott's puffy tumor [10]. Sinus infections can also cause middle ear problems due to the congestion of the nasal passages. This can be demonstrated by dizziness, "a pressurized or heavy head", or vibrating sensations in the head. Post-nasal drip is also a symptom of chronic rhinosinusitis. Halitosis (bad breath) is often stated to be a symptom of chronic rhinosinusitis; however, gold standard breath analysis techniques have not been applied. Theoretically, there are several possible mechanisms of both objective and subjective halitosis that may be involved [12].

A 2004 study suggested that up to 90% of "sinus headaches" are actually migraines [13]. The confusion occurs in part because migraine involves activation of the trigeminal nerves, which innervate both the sinus region and the meninges surrounding the brain. As a result, it is difficult to accurately determine the site from which the pain originates. People with migraines do not typically have the thick nasal discharge that is a common symptom of a sinus infection [14].

### Acute Rhinosinusitis (ARS)

Acute sinusitis is usually precipitated by an earlier upper respiratory tract infection, generally of viral origin, mostly caused by rhinoviruses, coronaviruses, and influenza viruses, others caused by adenoviruses, human parainfluenza viruses, human respiratory syncytial virus, enteroviruses other than rhinoviruses, and metapneumovirus. If the infection is of bacterial origin, the most common three causative agents are *Streptococcus pneumoniae*, *Haemophilus influenzae* and *Moraxella catarrhalis* [15]. Until recently, *Haemophilus influenzae* was the most common bacterial agent to cause sinus infections.

However, introduction of the *H. influenzae* type B (Hib) vaccine has dramatically decreased *H. influenzae* type B infections and now non-typable *H. influenzae* (NTHI) are predominantly seen in clinics. Other sinusitis-causing bacteria pathogens include *Staphylococcus aureus* and other *Streptococci species*, anaerobic bacteria and, less commonly, gram negative bacteria. Viral sinusitis typically lasts for 7 to 10 days [15], whereas bacterial sinusitis is more persistent. Approximately, about 0.5% to 2% of viral sinusitis results in subsequent bacterial sinusitis. It is thought that nasal irritation from nose blowing leads to the secondary bacterial infection [16]. Acute episodes of sinusitis can also result from fungal invasion. These infections are typically seen in patients with diabetes or other immune deficiencies (such as AIDS or transplant patients on immunosuppressive anti-rejection medications) and can be life-threatening. In type I diabetics, ketoacidosis can be associated with sinusitis due to mucormycosis [9]. Chemical irritation can also trigger sinusitis, commonly from cigarette smoke and chlorine fumes [1]. Rarely, it may be caused by a tooth infection [15].

## Acute Rhinosinusitis and Microorganisms

Several respiratory viruses may infect the upper respiratory tract and cause Acute Rhinosinusitis (ARS). These include, for example, human rhinovirus, respiratory syncytial virus (RSV), influenza and parainfluenza viruses, coronavirus, adenovirus, and less frequently, enteroviruses, bocavirus, Ebstein-Barr virus, and human metapneumovirus (hMPV) [17,18]. The most common viral pathogen causing ARS is human rhinovirus, which is the pathogen in most of the cases during ARS episodes. [17,18] The relative proportions of different viral pathogens depend on the time of year, the age and location of the patient, and the method used to identify the pathogen. According to [19], the viral cause of ARS includes; Rhinovirus 30-50%, Respiratory Syncytial Virus 5-10%, Influenza A 5-22%, Influenza B 0-13%, Para-influenza 5-10%, Corona 2-15%, Adenovirus 1-9% and Bocavirus 2-19%.

Bacteria are believed to co-infect or complicate ARS in a small proportion of patients. The nasopharynx has been suggested to be the reservoir of bacterial pathogens for the nasal cavity and middle meatus [20]. Debate on whether the paranasal sinuses are sterile in the absence of sinus abnormalities continues [1]. Studies pro and con exist, however, most of the studies suggesting non-sterility report findings of other bacteria than the ones currently considered as ARS pathogens [21,22]. This raises the question of whether these findings are of clinical relevance. Bacterial ARS is estimated to complicate 0.5–2% of ARS. These numbers can be traced back to two separate original articles. Dingle et al. [23] reported that 53 (0.5%) of 11 134 patients with a common cold had sinusitis based on clinical criteria. Berg et al. [24] did a maxillary sinus aspiration to 100 patients with respiratory tract infection symptoms and found that 2 (2%) of the patients had purulent secretion in the aspiration. However, the study by Dingle et al. [25] is over 50 years old and Berg et al excluded patients with local paranasal symptoms or purulent discharge. In a review by Smith et al. [1] a higher percentage of bacterial cause than 0.5–2% was suggested in clinically diagnosed ARS, but exact percentages were not given.

The most common bacteria isolated from the maxillary sinuses during Acute Rhinosinusitis are traditionally *Streptococcus pneumoniae*, *Haemophilus influenza*, and *Moraxella catarrhalis*, but *Staphylococcus aureus* has also been reported as a possible pathogen in ARS [17]. Similar findings have been reported concerning other paranasal sinuses, also. Earlier, *Staphylococcus aureus* was considered mostly a contamination, [17] but its prevalence in ARS seems to have increased during recent years [17,26]. Earlier, *Streptococcus pyogenes*, anaerobic bacteria, and gram negative bacteria have also been reported to be possible pathogens in bacterial ARS [27]. Anaerobic bacteria may be of dental origin and contamination might explain some of the changes in the proportions of bacterial pathogens in previous reviews compared with recent ones. The proportions of the most common bacterial pathogens

found in the maxillary sinuses during ARS according to recent meta-analysis [17] are *Streptococcus pneumoniae* 33%, *Haemophilus influenza* 32%, *Moraxella catarrhalis* 09% and *Staphylococcus aureus* (10%).

Bacterial biofilm has a role in chronic rhinosinusitis. Bacterial biofilm is a complex, organized community of live bacteria forming a multilayer matrix on the nasal or paranasal mucosa with the capability to resist host defense mechanisms and antibiotic treatment [28]. Theoretically, bacterial biofilm could work as a reservoir for pathogens, resulting in recurrent acute infections, but so far, its role in Acute Rhinosinusitis is unknown [28].

## Chronic rhinosinusitis

Based on duration, chronic sinusitis lasts longer than twelve weeks and can be caused by many different diseases that share chronic inflammation of the sinuses as a common symptom [10]. Symptoms of chronic sinusitis may include any combination of the following: nasal congestion, facial pain, headache, night-time coughing, an increase in previously minor or controlled asthma symptoms, general malaise, thick green or yellow discharge, feeling of facial 'fullness' or 'tightness' that may worsen when bending over, dizziness, aching teeth, and/or bad breath [29]. Each of these symptoms has multiple other possible causes, which should be considered and investigated as well. Often chronic sinusitis can lead to anosmia, the inability to smell objects [29]. In a small number of cases, acute or chronic maxillary sinusitis is associated with a dental infection. Vertigo, lightheadedness, and blurred vision are not typical in chronic sinusitis and other causes should be investigated [10].

Chronic sinusitis cases are subdivided into cases with polyps and cases without polyps. When polyps are present, the condition is called chronic hyperplastic sinusitis; however, the causes are poorly understood [15] and may include allergy, environmental factors such as dust or pollution, bacterial infection, or fungus (allergic, infective, or reactive). Chronic rhinosinusitis represents a multifactorial inflammatory disorder, rather than simply a persistent bacterial infection [15]. The medical management of chronic rhinosinusitis is now focused upon controlling the inflammation that predisposes patients to obstruction, reducing the incidence of infections [29]. However, all forms of chronic rhinosinusitis are associated with impaired sinus drainage and secondary bacterial infections. Most individuals require initial antibiotics to clear any infection and intermittently afterwards to treat acute exacerbations of chronic rhinosinusitis [10].

## Chronic Rhinosinusitis and Microorganisms

Compared to healthy sinuses, CRS sinuses have decreased bacterial diversity and evenness [30,31], in other words, healthy sinuses have many different types of bacteria present in similar numbers, while CRS sinuses have few types of bacteria present, and of those some are

overabundant while others are barely present. In ecology terms, these decreases are mainly due to selective enrichment of certain 'disease-producing' species and depletion of other 'protective' species. Mostly commensal taxa are depleted in CRS patients; notably, decreases in *Bacteroidetes* spp., *Prevotella* spp [31], *Lactobacillus* spp. [32], *Peptoniphilus* spp., *Propionibacterium acnes*, *Acinetobacter johnsonii* and *Corynebacterium confusum* have been observed [33].

Other bacterial taxa are found to be enriched in CRS microbiomes. Increases in *Pseudomonas* spp. [34], *Corynebacterium* spp. [32,34] certain *Streptococcus* spp., *Staphylococcus aureus*, *Propionibacterium acnes* and *Haemophilus influenza* [34] have been reported in CRS. Abreu et al. [32] notably found enrichment of a novel sinopathogen *Corynebacterium tuberculostearicum*, typically a commensal when present on skin. Of particular importance to CRS is *S. aureus*. Most microbiome studies found that *S. aureus* was enriched in CRS patients; some even found it to be the most abundant organism in CRS sinuses [33,34] With particular regard to *S. aureus*, no study has been carried out to explicitly determine whether or not an increased sinus level of *S. aureus* will cause CRS. However, current research on *S. aureus* in CRS [35,36] indicates that *S. aureus* increases the severity of CRS, and is at the very least involved in CRS development.

## Conclusion

Rhinosinusitis is an inflammation of the mucous membrane that lines the paranasal sinuses. Most cases of rhinosinusitis are caused by allergies or infection. Several respiratory viruses may infect the upper respiratory tract and cause Acute and chronic rhinosinusitis. These include, for example, human rhinovirus, respiratory syncytial virus (RSV), influenza, parainfluenza viruses, coronavirus and adenovirus. Some bacteria are also found to cause rhinosinusitis such as *Pseudomonas* spp., *Corynebacterium* spp certain *Streptococcus* spp., *Staphylococcus aureus* and *Haemophilus influenza*.

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