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Review Article

Chronic rhinosinusitis - clinico microbiological profile: a review

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ABSTRACT

The inhaled air at extremes of temperature or sometimes laden with animate aero-pathogens or maybe inanimate aero-allergens, induces a mechanical, thermal or infective trauma respectively, on the nasal and the sinus mucosa. The rhino-sinusitis acute or chronic has multiple underlying aetiologies and presentations. The aetiological factors and primarily the microorganisms show a shift with time. Viruses, aerobic and anerobic bacteria are cultured in individuals with varying levels of immunity.

Keywords: Bacteria, Drug resistance, Rhinosinusitis

INTRODUCTION

"Sinusitis" and rhinitis are conventionally diagnostic terminologies related to clinical features of the effected paranasal sinus and the nose.[1] Histopathologically sinusitis and rhinitis are "the inflammation of mucosa of paranasal sinus and the nose respectively.[1] Clinically there is a co -existence of rhinitis and sinusitis .Even so of the inflammatory response of both regions due to a similar mucosal lining to a lesser or greater extent. Thus, the term sinusitis is pre- fixed and captioned rhinosinusitis to represent the inflammatory symptom complex.[1,2] An exception to the wide application of the coding rhinosinusitis often particular type of rhinitis is categorised as a clinical entity, the allergic rhinitis.[1]

Chronic rhinosinusitis is ideally defined as the inflammation of mucosa of nose and paranasal sinus for at least twelve consecutive weeks of duration.[3] Rhinosinusitis task force by American Academy of Otorhinolaryngology and Head and Neck Surgery defines rhinosinusitis as the presence of two major symptoms or one major and two minor symptoms. Major symptoms are facial pain/pressure, facial congestion/fullness, nasal obstruction/blockage, nasal discharge/ purulence, postnasal drip, hyposmia/anosmia or purulence on nasal examination. Minor symptoms are headache, fever (non-acute), halitosis, fatigue, dental pain, cough, ear pain/ pressure/fullness.[4] Rhinosinusitis is classified on the basis of duration of symptoms too. Acute rhinosinusitis (ARS) is disease lasting less than or equal to 4 weeks, sub-acute lasting 4 to 12 weeks and chronic (CRS) for more than 12 weeks. Recurrent acute sinusitis includes attacks of more than 4 episodes of acute rhinosinusitis per year and acute exacerbation of chronic sinusitis includes sudden worsening of chronic rhinosinusitis with return to baseline.[3,4]

Rhinosinusitis is a common health issue worldwide. Usually patients present to the primary family physician with symptoms of upper respiratory tract infection. 83% approximately have an acute upper respiratory tract infection subsequent to bacterial rhinosinusitis.[3] An extrapolated data shows that in India 136,657,953 individuals out of 1,065,070,607 have chronic rhinosinusitis.[5]

Underlying factors in chronic rhinosinusitis are ostiomeatal obstruction, allergies, polypi, dental diseases and occult or subtle immunodeficiency states, which lead to inflammation of nose and paranasal sinus. Two broad groups are seen, A predominantly eosinophilic group (allergic rhinitis, nasal polypi, especially aspirin sensitive polypi) and the neutrophilic group (immune deficiency, chronic infection, polypi in cystic fibrosis). Microorganisms, i.e. the bacteria and the fungi are the secondary invaders on the sinus and nasal mucous membranes. Moreover, structural abnormalities, conchae bullosae, Haller (infraorbital) cells, and septal deviations aggravate the situation, any disease process or toxin that affects ciliary motility of the mucosa has a negative effect on chronic rhinosinusitis.[6]

The infection leads to mucosal swelling with consequent occlusion or obstruction of the sinus ostia. Thereby leading to reduction in oxygen tension, which can impair mucociliary transport and transudation of fluid into the sinuses.[7] The inflammation also results in changes in the mucous that become more viscid and often alterations in ciliary beat frequency occur. These shifts in the environment of the nose and the sinuses, lead to stasis of the mucous and thereby bacterial colonization.[6]

The diagnosis of chronic rhinosinusitis is made by existence of symptoms, eneumerated by the Rhinosinusitis task force along with either endoscopic signs of oedema, mucosal congestion, mucopurulent discharge or polypi extruding into the middle meatus and/or on computed tomographic fearures like mucosal thickness within the ostiomeatal complex and in the sinuses.[3,4]

Predominantly isolated organisms from subjects of acute bacterial rhinosinusitis are S*treptococcus pneumoniae, Haemophilus influenzae* and *Moraxella catarrhalis*. Pathogenesis of chronic rhinosinusitis is controversial with multiple aetiologies. Mixed flora of bacteria, fungi or viruses may co-exist in some while in others there are no identifiable pathogenic organisms. In patients of chronic rhinosinusitis the potential pathogenic bacteria, are *Staphylococcusspecies* (55%) and out of those, *Staphylococcus aureus* is the major organism (20%). Studies even document a high prevalence of Enterobacteriaceae, anaerobes, Gram-negative bacteria and fungi.[8-12]

Therapeutics in chronic rhinosinusitis incorporates medical, surgical or a combined sequential modality. Medical includes, use of antibiotics. Antibiotic resistance is an emerging vital issue now-a-days. The US, Rujuvanej et al13 study of 10387 positive intranasal culture samples over a period of two decades from 1990 to 2010 reported *Staphylococcus aureus* in 800 (7.7%) and out of which 110 (1.06%) were methicillin resistant *Staphylococcus aureus* (MRSA) and there was a statistically significant increasing trend for MRSA sinusitis.

Resistance of microorganisms to the present day drugs is seen which varies with time. This antimicrobial resistance is increasing nowadays due to non-judicial use of antibiotics. It is increasing in common pathogens of chronic rhinosinusitis. Resistance mechanism is due to antibiotic inactivating enzymes, alterations in the target site of antibiotics and changes in the influx/efflux process.

PATHOPHYSIOLOGY OF SINUSITIS

The host factors include

genetic factors like immotile ciliary syndrome and cystic fibrosis. Anatomical abnormalities like concha bullosa, septal spur or a paradoxical middle turbinate. Allergic and Immunologic disorders, systemic disease or medical therapeutics which predisposes the individual to infection.

Among the environmental factors are

Viral, bacterial or fungal infections, trauma, primary or secondary tobacco smoke exposure, chronic or acute irritants, noxious chemical fumes, prior surgery, nasal packings and indwelling naso-gastric tubes.

Acute sinusitis is usually preceded by acute viral respiratory tract infection, which leads to mucosal edema causing obstruction of sinus ostia. Ostial obstruction leads to reduction in oxygen tension, which causes reduction in mucociliary transport and leads to transudation of fluid into sinuses. Inflammation also causes an increase in mucus consistency. All these changes lead to mucostasis and bacterial colonization and lead to bacterial infection.[6]

There is strong suspicion of the role of allergy. Antigen-antibody reactions result in the release of histamine and other mediators of inflammation, which cause changes in vascular permeability, destabilization of lysosomal membranes causing inflammation, mucosal swelling and ostia obstruction. Other factors leading to chronic rhinosinusitis are biofilms, superantigens and osteitis.[6]

Organisms responsible for acute or chronic rhinosinusitis are different. Since the pathogenesis of chronic rhinosinusitis is not well defined and there are multiple etiological factors. Pathogenesis of chronic rhinosinusitis is ill well defined, with various hypotheses. . Inflammation of nose and paranasal sinuses mucosa result in sinus ostial obstruction and leads to infection.

Many factors predispose an individual to chronic rhinosinusitis, namely. It is difficult to identify causative organisms. Chronic rhinosinusitis is regarded as an inflammatory disease, which may or may not contain causative organisms. Most common causative organisms are *Staphylococcus* species (55%) of which *Staphylococcus aureus* (20%) is most common. High prevalence of *Enterobacteriaceae species*, anaerobes, gram-negative bacteria and fungi is also seen at times.

HISTORICAL REVIEW

Doyle et al conducted a study in 1991 by taking a biopsy of ethmoid sinus mucosa and found that *Staphylococcus aureus* (32%) and *Enterobacteriaceae* (19%) were the commonest pathogenic isolates. Coagulase negative staphylococci were the most common pathogen overall (71 %).[14]

A study about middle meatal commensal flora, done by Klosek et al, in 1996, included 139 subjects irrespective of sex and over 16 years of age.[15] They found out that 359 samples yielded a single organism in culture. One hundred and thirteen samples contained at least one aerobic or anaerobic bacterium. They showed that the adult middle meatus contained mixed commensal flora and it is useful in interpreting endonasal swab cultures during acute and chronic sinus infection.

James et al in 2006 studied 83 patients and they managed to isolate pathogens in 59 of these patients (71%). Approximately 12% of the 83 patients cultured positive for multiple organisms.[16] The most common were coagulase-negative staphylococci (31% of isolates). Distributions of other pathogens were *Haemophilus influenzae* (25%), *Streptococcus pneumoniae* (12%), *Moraxella catarrhalis* (10%), *Pseudomonas aeruginosa* (7%), *alpha-hemolytic streptococci* (5%) and *Staphylococcus aureus* (3%). Approximately 39% of the coagulase-negative staphylococciisolates were resistant to penicillin. 20% of the *Haemophilus influenzae* isolates were beta-lactamase-positive, and 14% of all isolates were resistant to multiple antibiotics.

A retrospective study done by Bhattacharya et al, in 2008, reviewed the microbiological data of all endoscopically obtained paranasal sinus cultures from 2001 to 2005 in adult patients with chronic rhinosinusitis.[17] They took 392 culture samples and they got 701 bacterial isolates. In their study *Staphylococcus aureus* was the most commonly isolated organism (19.0%). Nineteen percent of *Staphylococcus aureus* species were found to be methicillin resistant *Staphylococcus aureus* but *methicillin resistant Staphylococcus aureus*-specific antibiotic resistance rates did not change over the course of the study (all $p \geq 0.222$). They concluded that methicillin resistant *Staphylococcus aureus* exhibited statistically significant higher rates of resistance to each antibiotic tested than did methicillin sensitive *Staphylococcus aureus* (MSSA).

In 2009, Neiderfuhr et al studied 31 patients having sinusitis with polyposis and 13 patients without polyposis and 21 control patients.[18] The study showed mixed cultures of aerobes and anaerobes. Most common aerobes found in biopsy specimens were coagulase negative staphylococci and alpha haemolytic *Streptococci*. *Propionibacterium* and *Peptostreptococcus* were the most common anaerobes. Pathogenic bacteria were *Staphylococcus aureus, Enterobacteriaceae and Haemophilus influenzae*.

Genoway et al conducted a retrospective study in 2011 to evaluate the isolated pathogens and their resistance pattern.[19] They found out that the most common organisms seen in isolates were *Staphylococcus aureus* (39%) followed by *Haemophilus influenzae* (29%), *Pseudomonas aeruginosa* (15%), *Streptococcus pneumoniae* (12%) and *Moraxella catarrhalis* (11%). In their study they got only 3 cases of methicillin resistant *Staphylococcus aureus*.

A study was published by Xio et al in 2011 about microbiological profile and antibiotic susceptibility in chronic rhinosinusitis, where 51 patients were taken. 41 patients showed bacteria in culture.[20] Most sensitive antibiotics against bacteria were vancomycin and moxifloxacin (100%) followed by levofloxacin (92.31%), rifampin (90.91%). Sensitivity of other antibiotics was ciprofloxacin (81.58%), sulfamethoxazole-trimethoprim (67.65%), azithromycin (47.62%), clarithromycin (45%), ampicillin sodium and sulbactam (35.90%), ceftriaxone (39.39%), cefuroxime sodium (30.43%). Least sensitive antibiotic was penicillin, which showed 8.33% sensitivity.

A study done by Brook et al in 2011 found out that most sinus infections are viral. The most common viruses responsible for sinus infection are Rhinoviruses, Influenza viruses, and Parainfluenza viruses. Small proportion of them developed super infections and showed bacteria. *Streptococcus pneumoniae, Haemophilus influenzae, Moraxella catarrhalis,* and Streptococcus pyogenes are the most common isolates in acute purulent sinusitis. *Staphylococcus aureus* and anaerobic bacteria like *Prevotella* and *Porphyromonas*, *Fusobacterium* and *Peptostreptococcus* spp. are the main isolates in chronic sinusitis. In patients with nosocomial sinusitis, immunocompromised host, HIV infections and in cystic fibrosis *Pseudomonas aeruginosa* and other aerobic and facultative gram-negative rods are commonly isolated. Fungi and *Pseudomonas aeruginosa* are the most common isolates in neutropenic patients. They stated that the microbiology of sinusitis is influenced by the previous antimicrobial therapy, vaccinations, and the presence of normal flora capable of interfering with the growth of pathogens.

Faezel et al compared microbiological culture-based and culture-independent (16S rRNA gene sequencing) methodologies for pathogen identification in chronic rhinosinusitis patients in 2012.[22] A total of 21 swab samples from 15 chronic rhinosinusitis patients and 5 non-chronic rhinosinusitis controls were analysed. All subjects had positive bacterial cultures, with a mean of 2.8 isolates per subject. The most prevalent cultivars were coagulase- negative *Staphylococci* (15/20 specimens, 75%), *Staphylococcus aureus* (10/20, 50%) and *Propionibacterium acnes* (6/20, 30%). Among 57,407 pyro sequences generated, the most prevalent were from

coagulase-negative *Staphylococci* (21/21specimens, 100%), *Corynebacterium* (18/21, 85.7%), *Propionibacterium acnes* (16/21, 76.2%), and *Staphylococcus aureus* (14/21, 66.7%). Chronic rhinosinusitis patients were characterized by altered microbial composition (p=0.02), and greater abundance of Staphylococcus aureus (p=0.03).[29] The study indicated that bacterial culture and 16S rRNA gene pyrosequencing of specimens from CRS patients and controls yield largely consistent results. There was, however, significantly more diversity regarding the anaerobic groups as seen by sequencing than by culture. In addition, it was also observed that chronic rhinosinusitis patients have significantly different microbial communities from non-chronic rhinosinusitis controls, with more abundant occurrence of *Staphylococcus aureus*.

Boase et al performed a study in 2014 to find out the causative middle meatal organisms.[23] They evaluated 38 chronic rhinosinusitis patients and 6 controls. They concluded that the healthy sinus is not sterile and it appears that not only prevalence but also abundance of organisms is critical in determining the disease state. *Staphylococcus aureus* was the most common organism (23/38) 61% followed by *Staphylococcus epidermidis* (21/38) 55%.[24] *Staphylococcus aureus* was found in 15 (16%) of 97 patients with chronic sinusitis between 2001 and 2003, and 4 (27%) were MRSA. *Staphylococcus aureus* was recovered from 23 (20%) of 117 patients with chronic sinusitis between 2004 and 2006, and 14 (61%) were MRSA (p<0.05).

Farhani et al did a study in Iran in 2014 about antibiotic resistant patterns of aerobic organisms in chronic rhinosinusitis.[24] Samples were taken from maxillary sinus aspirate, meatus and oropharynx. Study was performed on 216 patients of which 62.1% were males and 37.1% were females. In their study 56.4% of patients were from urban areas. More than half of the participants aged between 30 and 39 years. The most frequent isolated strains from oropharynx and meatus were alpha-hemolytic Streptococcus (15.4%), followed by coagulase negative Staphylococcus (14.6%), and *Branhamella catarrhalis* (13.2%). The most prevalent isolated strains from sinus aspiration were *Staphylococcus aureus* (19.1%), *Klebsiella pneumonia* (16.4%) and *Branhamella catarrhalis* (15.6%).

DISCUSSION

The highest antibiotic susceptibility was detected to ciprofloxacin and ceftriaxone in most of the strains. *Escherichia coli* and *Haemophilus influenza* showed 100% sensitivity to ciprofloxacin and least sensitive was *Pseudomonas aeruginosa* with 76.7% sensitivity. Susceptibility to ceftriaxone ranged from 71.4 to 100%. *Streptococcus pneumonia*, *Corynebacterium diphtheria*, and *H. influenzae* showed 100% sensitivity to ceftriaxone and least sensitive was *Acinetobacter baumannii* showed 71.4%. The highest resistance was mostly detected to penicillin (ranging from 33.3% to 91.7%), and to ampicillin (ranging from 38.4% to 83.7%) regardless of strain.[24]

CONCLUSION

As the microbiological organisms show emergence of drug resistance, therefore, periodical fresh study is needed to detect the most common pathologic organisms and the most effective drugs against them. Thus, we conducted this study to find out the microbiological profile in chronic rhinosinusitis and their sensitivity pattern.

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