**Original Research Paper**

**Association of Staphylococcus aureus with Etiopathogenesis, severity of symptoms and extent of Rhino sinusitis in the patients of Barabanki District, Uttar Pradesh, India**

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**ABSTRACT**

Rhinosinusitis (RS) is inflammation of the nasal cavity and paranasal sinuses.  The term “rhinosinusitis” is preferred over “sinusitis” because inflammation of the sinus cavities is almost always accompanied by inflammation of the nasal cavities. Rhinosinusitis is associated with a significant negative impact on the quality of life and has high healthcare costs due to medical visits, prescriptions and over the counter medications, sinus surgeries, and missed days from work and school. Most Acute RS are viral in origin and improve on their own.  It is important to distinguish viral from bacterial RS to avoid prescribing unnecessary antibiotics that are not effective for viral infections.

The study was conducted with the objectives to determine the association of S. aureus in rhino sinusitis patients; to determine the relationship of S. aureus and severity of rhino sinusitis; to determine the relationship of S. aureus and extent of rhino sinusitis – involvement of more than one sinus or pan sinusitis, spread of disease beyond sinuses like pharynx, ear, chest, and its association with complications of sinusitis as nasal polyposis, abscess formation, intracranial complications etc.; to suggest a treatment protocol of patients of rhino sinusitis with or without infestation with S. aureus. The study was a cross-sectional, prospective, observational study carried out in Barabanki district and Microbiology laboratory of Mayo Institute of Medical Sciences, Barabanki

In the study we found that staphylococcal aureus should be included as an important causative agent in rhino sinusitis as out of 200 patients that met our inclusion criteria 25% of the cases were culture positive for S. aureus. Hence an appropriate antibiotic coverage must be included in the patients so as to treat the disease and prevent its complications although a study with bigger patient numbers is needed to validate our research.

**Keywords:** Staphylococcus aureus, Rhino sinusites, etiopathogenesis

**INTRODUCTION**

Rhino sinusitis refers to the inflammation of sinuses resulting in symptoms such as nasal congestion, nasal discharge, fever, headache, toothache, decreased sensation of smell, sore throat, halitosis; post nasal drip and cough that usually worsens at night [1, 2, 3].Women are generally affected more than men [4]. Risk factors include smoking, elderly age group, activities such as scuba diving, swimming, asthma, allergies, dental problems or weakened immune system [1]. Rhino sinusitis may be acute (<4weeks), subacute (4weeks-12weeks), chronic (>12weeks) and recurrent( four or more episodes per year) [1]. It may affect any of the four sinuses i.e. maxillary, ethmoid, frontal or sphenoid [1]. Organisms commonly affected are Streptococcus pneumoniae, Haemophilus influenzae, and Moraxella catarrhalis, the latter being more common in children. Other streptococcal species, anaerobic bacteria, and Staphylococcus aureus cause a small percentage of cases [5]

Numerous studies, using varying culture techniques, have researched the culture rates of these specific bacteria in an attempt to determine the exact prevalence of these bacteria. However, deep nasal swab cultures or nasopharyngeal cultures have traditionally been thought to be associated with a high rate of contamination, and the results of these tests have been unreliable[6],often casting doubt on the prevalence of S. aureus as a true pathogen in acute disease. Recent studies highlighting S. aureus as a major pathogen in acute rhino sinusitis should be interpreted cautiously. The range of reported results for the incidence of S. aureus as a cause of acute rhino sinusitis in adults is similar to the results reported for staphylococcal colonization of the middle meatus in healthy adults.(7)

In addition, because of the increasing presence of community-acquired methicillin-resistant S. aureus (MRSA) infection [8], determining the rate of S. aureus in Rhino sinusitis has become an even more important factor in treating the disease.

The purpose of this study was to determine the association of S. aureus with rhino sinusitis, with respect to etio-pathogenesis, severity of symptoms and extent of Rhino sinusitis.

**AIMS AND OBJECTIVES**

The study had following objectives

1. To determine the association of S. aureus in rhino sinusitis patients.

2. To determine the relationship of S. aureus and severity of rhino sinusitis

3. To determine the relationship of S. aureus and extent of rhino sinusitis – involvement of more than one sinus or pan sinusitis, spread of disease beyond sinuses like pharynx, ear, chest, and its association with complications of sinusitis as nasal polyposis, abscess formation, intracranial complications etc.

4. To suggest a treatment protocol of patients of rhino sinusitis with or without infestation with S. aureus

MATERIAL AND METHODS

**Study design**: The study was a cross-sectional, prospective, observational study carried out in Barabanki district and Microbiology laboratory of Mayo Institute of Medical Sciences, Barabanki .

**Study population:** Included patients suffering from rhino sinusitis in all the socioeconomic status categories including both Rural and urban population in Barabanki district.

**Sample size**: 200 patients

**Sélection Criterias:**

A. Inclusion criteria: All the patients suffering from Rhino sinusitis were taken up in the study. The diagnostic criteria’s was both clinical and radiological.

1. **Clinically**: patients suffering from symptoms such as nasal obstruction due to congestion, nasal discharge, headache, decreased sensation of smell, fever, sore throat, halitosis, post nasal drip and cough that usually worsens at night and sinus tenderness were taken up for study. Symptoms were graded according to the SINO-NASAL OUTCOME TEST (SNOT-20) - by Jay F. Piccirillo, M.D., Washington University School of Medicine, St. Louis, Missouri (9)
2. **Radiologically:** Classification system of Gliklich and Metson was used

**B. Exclusion criterias:** There was no exclusion criteria and all the patients suffering from Rhino sinusitis and fulfilling the above criteria were considered in the study.

**Data collection**: After proper enrolment of subjects, information was noted in a preformed questionnaire that included identification, demographic details, medical history and physical examination.

**Sample collection**: Standard protocol of sample collection method was followed

**Detection of MRSA-** was done by Cefoxitin disc diffusion test

**OBSERVATION AND RESULTS**

**CHART 1:**

**Severity wise number of patients in various age groups**

Out of 200 patients that met our inclusion criteria, severity wise mild category included 12 patients which were of the age group 0-20, 46 in the age group 20-40 and 10 in age group 40-60. In moderate category there were 16 patients in the age group of 0-20, 44 patients in the age group of 20-40, 8 patients in the age group of 40-60 and 4 patients were more than 60 years old. In severe category 18 patients were of 0-20 age group, 34 patients of 20-40 age group and 8 patients in the age group of 40-60. (Chart 1)

**Table 1-**

**Radiologically Number of Patients**

|  |  |  |
| --- | --- | --- |
| **MILD** | **STAGE 1** | **n=68 (34%)** |
| MODERATE | STAGE 2 AND 3 | n=72 (36%) |
| **SEVERE** | **STAGE 4** | **n=60 (30%)** |

In radiological evaluation, according to Gliklich and Metson classification system stage 1 was considered as mild that included 68 patients i.e.(34%), stage 2 and 3 was considered as moderate and included 72 patients i.e. (36%) ,stage 4 was considered as severe and included 60 patients i.e. (30%). Hence in the study radiologically most number of patients were of moderate severity followed by mild severity and least number of patients were in the severe category. (Table 1)

**Chart 2:**

**Severity wise number of patients on the basis of gender**

On the basis of gender out of 200 patients 128 patients were male and 72 were female. Among the males 50(25%) were mild, 40(20%) were moderate and 38(19%) were severe. Among the females 18 patients (9%) were of mild severity, 32(16%) were of moderate and 22(11%) were of the severe category. (Chart 2)

**Chart 3:**

**Number of patients who were culture positive in various age groups**

According to culture positivity, in mild category 6 (3%) patients were culture positive of the age group 20-40 and 2(1%) in the age group of 40-60.In moderate category 2(1%) patients were culture positive of age group 0-20,14(7%) of age group 20-40 and 2 (1%)of age group >60.In severe category 12(6%) patients were culture positive of age group 0-20,10(5%) of age group 20-40and 2(1%) were of the age group 40-60. (Table 2)

**Chart 4:**

According to culture reports we observed that out of 200 patients, 50 patients were S. aureus positive (25%) and 150 were patients were S. aureus negative (75%). (Chart 4)

**Table 3: Correlation with Severity (n=number of patients)**

|  |  |  |
| --- | --- | --- |
|  | **Staphylococcus aureus Positive** | **Staphylococcus aureus Negative** |
| **Mild** | n=8 (4%) | n=60 (30%) |
| **Moderate** | n=18 (9%) | n=54 (27%) |
| **Severe** | n=24 (12%) | n=36 (18%) |

When we correlate the culture results with the severity of the disease we found that out of 50 patients that were positive for Staphylococcus aureus culture, 8(4%) patients were of mild category,18 (9%) of moderate and 24(12%) of the severe category.(Table 3)

**Table 4: Results of coagulase test in culture positive patients with Staphylococcus aureus. (n=number of patients = 50)**

|  |  |  |
| --- | --- | --- |
|  | **Coagulase Positive (46/50=92%)** | **Coagulase Negative (4/50=8%)** |
| **MILD (n=8)** | n=8 (100%) | n=0 (0%) |
| **MODERATE(n=18)** | n=14 (77%) | n=4 (23%) |
| **SEVERE (n=24)** | n=24 (100%) | n=0 (0%) |

When we compare the results of coagulase test in culture positive patients with Staphylococcus aureus we found that out of total 50 patients, 46 i.e. (92%) patients were Staphylococcal positive and coagulase positive and 4 i.e. 8% patients were Staphylococcal positive and coagulase negative. When correlating the severity of sinusitis with coagulase positive test we found that 8 patients (16%) were positive in mild category, 14 (28%) patients were positive in moderate category and 24(28%) patients were positive in severe category. Hence we found a direct correlation between severity of sinusitis and coagulase test in culture positive patients i.e. more severe the disease more are the chances of Staphylococcus aureus to be coagulase positive. (Table 4)

**Table 5: Sensitivity Report** (n=50)

|  |  |  |
| --- | --- | --- |
|  | **Sensitivity** | **Resistance** |
| **Penicillin** | n=22 | n=28 |
| **Ciprofloxacin** | n=40 | n=10 |
| **Teicoplanin** | n=50 | n=0 |
| **Linezolid** | n=50 | n=0 |
| **Vancomycin** | n=50 | n=0 |

When we analyse the Culture sensitivity report we found that 22 patients were found to be Penicillin sensitive and 28 patients were found to be resistant to it. In case of Ciprofloxacin 40 patients were found to be sensitive to it and 10 patients were found to be resistant. In case of Teicoplanin, Linezolid and Vancomycin all patients were sensitive to it. (Table 5)

**DISCUSSION**

There were limited number of studies that were available in literature to validate or rule out the role of Staphylococcus aureus in etiopathogenesis and severity of Sinusitis.

In our study we found that staphylococcus aureus was involved in etiopathogenesis of Sinusitis in as high as 25% of cases as found in the culture report.

Most number of cases was in the age group of 20-40 years, in which most cases were mild then moderate and least were severe cases, this was followed by the age group of 0-20 years in which most cases was severe category suggesting that disease was more severe in younger age group, then the age group of 40-60 years in which again most cases was in the mild category. We observed disease of only moderate severity in the age group of >60 years. Hence we must be careful and start the therapy of Staphylococcus aureus in all cases of sinusitis more so in children and the elderly where even moderate infection can flair up to complications.

We also observed that the disease was more severe in the males as compared to females in all the three grades of severity; this should also be kept in mind while treating these patients.

While correlating the severity of sinusitis with S. aureus we observed that most number of Staphylococcus aureus culture positive patients was in the severe sinusitis category followed by moderate category and the least positivity was found in the mild category. Hence we found a direct correlation between severity of the disease and Staphylococcus aureus culture positivity. Since most severe cases was of Pansinusitis hence we also concluded that S. aureus was also associated with extent of rhino sinusitis – i.e involvement of more than one sinus or pan sinusitis, spread of disease beyond sinuses like pharynx, ear, chest as was found in our series.

Since 92% patients in our series who gave a positive culture response to S. aureus were Coagulase positive, we suggest that antibiotic coverage with this fact in mind must be initiated in all cases of sinusitis.

Dam etal (10) conducted a similar study and concluded that nasal colonization with Staphylococcus aureus is not associated with the severity of symptoms or the extent of the disease in chronic rhino sinusitis and found that S. aureus carriage rate was 25.5% in chronic rhinosisnsitis, these results was very similar to our study but we thought that 25% was a very high percentage and we must consider this in the management of these patients.

Lin A etal (11) states that review of recent literature shows a high incidence of positive cultures for Staphylococcus aureus from the sinuses of patients with chronic rhinosinusitis, both before and after surgery, but has not produced convincing evidence that Staphylococcus aureus has a significant role in the pathogenesis or clinical course of the disease which was not the case in our study where we were able to demonstrate a direct relationship with incidence and severity of sinusitis with Staphylococcus aureus

Itzhak Brook etal (12) did a study on Bacteriology of chronic maxillary sinusitis associated with nasal polyposis and found that majority of the isolates were aerobic or facultative organisms (0.85 per specimen). The predominant aerobic or facultative organisms was S. aureus. Although he isolated S. aureus from 7 of 46 (15 %) of his patients, it was not the most predominant isolate and was mixed with other flora in five instances. This percentage was less than what we isolated (25%) in our study. Bachert et al., 2001 stated that colonization with enterotoxin-forming staphylococci, whose products act as super antigens and cause local polyclonal IgE formation, has recently been described as a possible pathological mechanism in bilateral eosinophilic nasal polyposis with associated asthma and aspirin sensitivity. This directly meant that S. aureus was associated with severity of sinusitis as well as in its complications including lower respiratory tract infections as was found in our study.

Karina Mantovani etal (13) obtained 12 cultures with Gram-positive bacteria growth, in which the most frequently found organisms were: *Staphylococcus aureus* and *Staphylococcus epidermidis* (13.9% each) which was less than what we found in our study (25%). He also quoted Nigro etal.17 who found a predominance of coagulase negative *Staphylococcus* (12.1%) and *Staphylococcus aureus* in 9.7%, while in our series 92% (N=46/50) was coagulase positive and 8% (N=4/50) was coagulase negative. He concluded by saying that *Staphylococcus aureus was the second commonest* bacteria (after *Pseudomonas aeruginosa*) and represents the main microbiota present in the paranasal sinuses of patients with CRS in his region.

Erica Ortiz etal (14) did a study on Microbiology of rhinosinusitis in immunosupressed patients from the University Hospital and found Staphylococcus aureus to be the causative agent in sinusitis in 2/42 (4.76%) in immuosupressed patients and 3/42 (7.41%) in immunocometent patient. The incidences are far below the incidence in our study which was 25%. This also thus stated that despite being a commensal in the nose its incidence does not remarkably increase in immunocompromised states.

Anthony W. Chow etal (15) released IDSA Clinical Practice Guideline for Acute

Bacterial Rhino sinusitis in Children and Adults and suggested that Although S. aureus (including methicillin-resistant S. aureus [MRSA]) is a potential pathogen in ABRS, on the basis of current data, routine antimicrobial coverage for S. aureus or MRSA during initial empiric therapy of ABRS was not recommended (strong, moderate) which we suggest may not be true as we found a very high (25%) incidence of the organism in sinusitis and we think that antibiotic converge for S. aureus must be included in initial empirical therapy of ABRS

**CONCLUSION**

Sinusitis is a very common disease and an estimated 134 million Indians suffer from chronic sinusitis (16). We did a study to determine the association of S. aureus in rhino sinusitis patients and also to determine the relationship of S. aureus and severity of rhino sinusitis, we concluded that

1. S. aureus was found in the culture of the patients with sinusitis in 25% of cases
2. Most number of cases are in the age group of 20-40 years of age.
3. In younger age group (0-20 years) disease was found to be more severe
4. Disease was more severe in the males as compared to females in all the three grades of severity
5. Most number of Staphylococcus aureus culture positive patients were in the severe sinusitis category
6. We found a direct correlation between severity of the disease and Staphylococcus aureus culture positivity.
7. Since most severe cases were of Pansinusitis hence we also concluded that S. aureus is also associated with extent of rhino sinusitis along with spread of disease beyond sinuses like pharynx, ear, chest.
8. Most (92%) patients in our series who gave a positive culture response to S. aureus were Coagulase positive.
9. Based on the above observations we recommend that the antibiotic therapy for sinusitis of various grades especially severe grade must include drugs which cover S. aureus.

**SUMMARY**

In conclusion, the data suggests that staphylococcal aureus should be included as an important causative agent in rhino sinusitis as out of 200 patients that met our inclusion criteria 25% of the cases were culture positive for S. aureus. Hence an appropriate antibiotic coverage must be included in the patients so as to treat the disease and prevent its complications although a study with bigger patient numbers is needed to validate our research.

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**Ethical Considerations of the Study:**

1. Ethics Committee Approval: Ethics committee approval was received for this study from the Institutional Ethics Committee of Mayo Institute of Medical Sciences, Gadia, Barabanki
2. Written Informed Consent was obtained from concerned subjects and authority of institutions.
3. Privacy, confidentiality and anonymity were granted.
4. Scientific objectivity was maintained with honesty and impartiality.

**Authors Contributions**: Concept – SS,MA; Design – SS,MA; Supervision – SS,MA; Resource - SS,MA; Materials - SS,MA; Data Collection and/or Processing – SS,MA; Analysis and/or Interpretation – SS,MA.; Literature Search – SS,MA; Writing – SS,MA; Critical Reviews - SS,MA.

**Conflict of Interest**: The authors declare that this study has had no conflicts of interest.

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**Declaration:** This is an ICMR – STS project allotted to Ms. Mugdha Awasthi under supervision of faculty Dr. Sumit Sharma; Associate Professor, Department of E.N.T., Mayo Institute of Medical Sciences, Gadia, Barabanki. ICME-STS REFERENCE ID: 2018-03811.

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