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Effect of Seasonal Allergic Rhinitis on Nasal Microbiota and Its Effect on Etiopathogenesis of Sinusitis in Allergic Rhinitis

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ABSTRACT

Introduction: Rhinosinusitis refers to an inflammatory condition involving the nasal sinuses. Sinusitis is a common condition, with between 24 and 31 million cases occurring in the United States annually. Microbes and allergens can stimulate the nasal mucosa, potentially leading to the development of acute bacterial rhinosinusitis (ABRS). This study is to be designed to determine if allergen exposure alters the sinonasal microbiome. Allergic rhinitis is considered a major risk factor for acute bacterial rhinosinusitis (ABRS).

Aim and objective: To determine the change in normal nasal flora due to seasonal allergic rhinitis and its association with sinusitis

Methodology: We have confirmed allergic rhinitis by doing AEC/Serum IgE levels from blood of allergic rhinitis patients. Nasal swab of 50 patients of seasonal rhinitis were obtained as per protocol. Nasal swab were also obtained from middle meatus of sinusitis patients not having allergic rhinitis, as controls.

Result: The maximum patients of allergic rhinitis were found in the age group 16-25 years (36%), with female preponderance 3:2 and mostly the patients were married (58%). Mostly sterile swab (no growth) was obtained in 80% of both male and female population. Incidence of sinusitis in allergic rhinitis patients was (n=21 patients) 52% in female population.

Discussion: The nose represents an important bacterial reservoir for endogenous infections, Nasal carriage is a major risk factor for Staphylococcus aureus infection, especially for methicillin-resistant strains (MRSA). Alterations in the sinonasal microbiome might be one mechanism that predisposes allergic subjects to acute bacterial rhinosinusitis (ABRS).

Keywords: Acute bacterial rhinosinusitis, serum AEC, serum IgE, sinonasal microbiome

INTRODUCTION

Rhinosinusitis refers to an inflammatory condition involving the nasal sinuses.[1] Sinusitis is a common condition, with between 24 and 31 million cases occurring in the United States annually [2,3]Microbes and allergens can stimulate the nasal mucosa, potentially leading to the development of acute bacterial rhinosinusitis (ABRS). This study was designed to determine if allergen exposure alters the sinonasal microbiome Allergic rhinitis is considered a major risk factor for acute bacterial rhinosinusitis (ABRS).

Although there are several theories to explain the mechanism of this relationship, one unifying idea is that allergic inflammation creates an environment suitable for bacterial infection, e.g., through skewing of mucosal inflammation toward as Th2-type response, disruption of immune defence, alteration in epithelial barriers, or mechanical ostial obstruction. Interestingly, adults with upper respiratory tract infections and allergic rhinitis have increased sinus inflammation by computed tomography than do patients with upper respiratory tract infections who

are not allergic.

Similar studies in children have found a higher prevalence of ARS in children with allergic rhinitis compared with those who are not allergic. However, the specific underlying cause of increased risk of either ARS or ABRS in patients with allergic rhinitis remains unclear.

Another major paradox in the field is that 60% of cases of ABRS resolve with no treatment. In many cases, no pathogen is identified in culture, leading to empiric therapy, inappropriate antibiotic use for viral causes, and resultant antibiotic resistance ARS, therefore, is a major driver of important public health burdens, in terms of human suffering, societal cost, and infection risk via the development of resistant organisms. Thus, documenting the association between bacterial flora and allergic inflammation would potentially lead to progress toward understanding this mechanism. Previous studies have implicated Streptococcus pneumoniae and Haemophilus influenzae as the main pathogens associated with ABRS, with confirmatory studies in animal models.

Many cases of ARS do not grow any bacteria when measured with culture-based assays, suggesting the possibility that bacteria that we were unable to cultivate by using conventional microbiological methods may be involved in this disease (although a viral etiology is not precluded in some cases). Disruption of the normal sinus microbial ecosystem by environmental perturbation may therefore result in the emergence of increased numbers of pathogenic flora, leading to disease.

Specifically, allergic rhinitis could predispose to ABRS by altering the balance of microbial flora in the sinonasal tract. Non-cultivation-based methods of assessing bacteria are now available to address this question. Importantly, environmental effects on human microbiota (the collection of microbes that live on and inside humans, including the nose and upper airway) remain an underexplored arena with important implications for human health and disease.

The fact that microbial cells outnumber human cells by 10 to 1 and that, in the gut at least, they provide symbiotic metabolic functions that have been shown to affect physiology and disease, provides proof of principle of this concept. Nevertheless, environmental effects on the microbiome outside of diet have been poorly characterized. In the airway, e.g., little is known about the effects of important environmental influences such as pollution, smoking, temperature, medication use, or allergen exposure.[3]Chronic sinusitis affects approximately 12.5% of people. [4.] Indirect societal costs such absenteeism and presenteeism, with related reduced productivity, are likely to be even higher, on the order of $25 billion annually5.

In this work, we hypothesized that allergens can stimulate the nasal mucosa of allergic subjects to affect the composition of the microbes at the mucosal surface, potentially affecting the development of ABRS

MATERIALS AND METHODS

Source Of Data: The study was conducted in the department of ENT, Mayo Institute Of Medical Science, Barabanki, UP, for a period of 2 years from December 2020 to March 2022.

Inclusion Criteria: History of allergic rhinitis suggested by watery nasal discharge, nasal obstruction, nasal itching, loss of smell and watering from the eyes

- Age 5-60 yrs of age
- Informed consent from patients.
- Basal AEC more than 350.
- Basal IgE levels more than 100 IU.

Exclusion Criteria

- Patients less than 5 yrs of age (difficult to take sample)
- Patients on intranasal steroid.
- Non seasonal allergic rhinitis.
- Language barrier and non complaint patients.

OBSERVATION AND RESULTS

The study group consist of 50 patients with seasonal allergic rhinitis whose nasal swab was sent for culture and sensitivity along with serum AEC and serum IgE. The reports were obtained and their values compared along with controls. The incidence of sinusitis in allergic rhinitis is also noted along with establishing a correlation between sinusitis and bacteriological flora of middle meatus in patients of allergic rhinitis.

RESULTS

Table 1 - Age Wise Distribution of Study Subjects of Allergic Rhinitis

In this study, we found that most of the patients 36% (n=18) reside in the age group of 16-25 years, which correspond with the study K. Priya *et al*. and Pakkasela *et.al*.

It was also observed that the earliest age of diagnosis resides maximum in the age group of 16-25 years

Table 2-Marital Status of Allergic Rhinitis Patients

In our study, we found that 58%(n=29) of patients were married vs. 42%(n=21) patients who were unmarried, whereas in the study by Dissanayake et all, both married and unmarried acquired same percentage.

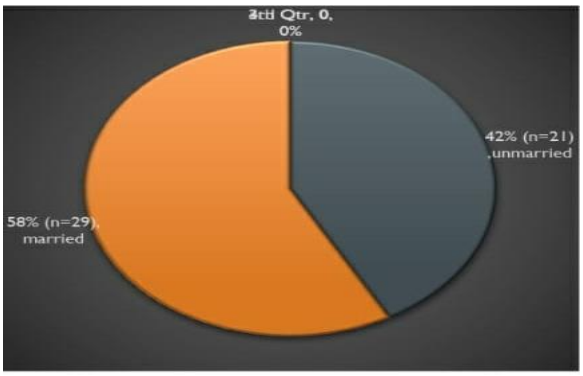
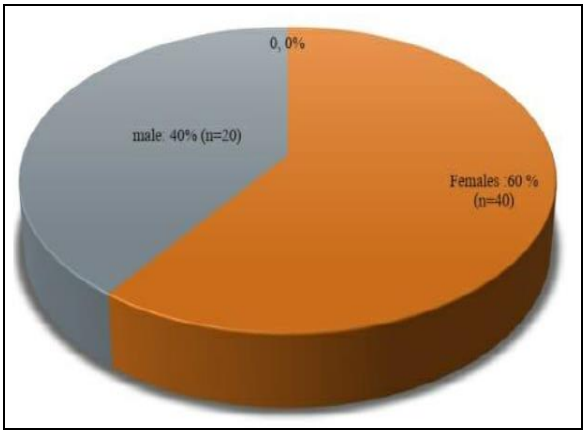
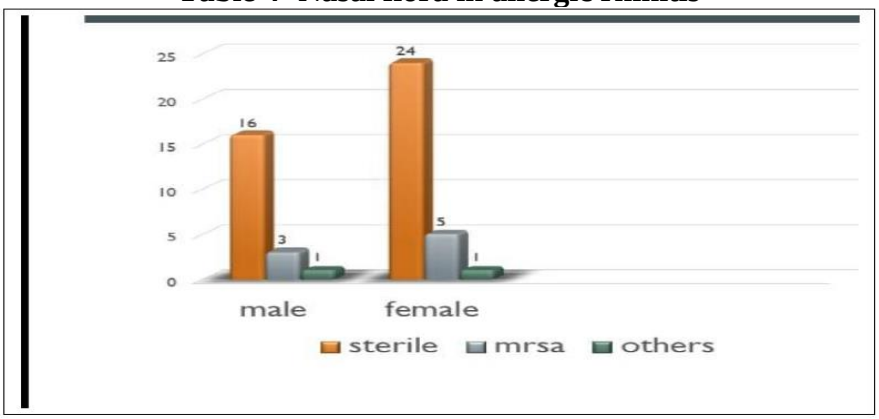


Table 3- Distribution Based on Sex



We also found that 60% (n=30) patients were females, and this female predominance corresponded with a similar study of Pal *et al*. and Rajsekaran *et.al.*, thereby suggesting female population to be a risk factor.

Table 4- Nasal flora in allergic rhinitis



The study also concluded that the nasal swab obtained from allergic rhinitis patients were sterile swabs (80% both male and female), which did not correspond with the study done by Taylor *et al.* and Rajsekaran *et al*. where they stated that they predominantly obtained Staphylococcus epidermidis.

Table 5- AEC and S. IgE in patients of allergic rhinitis

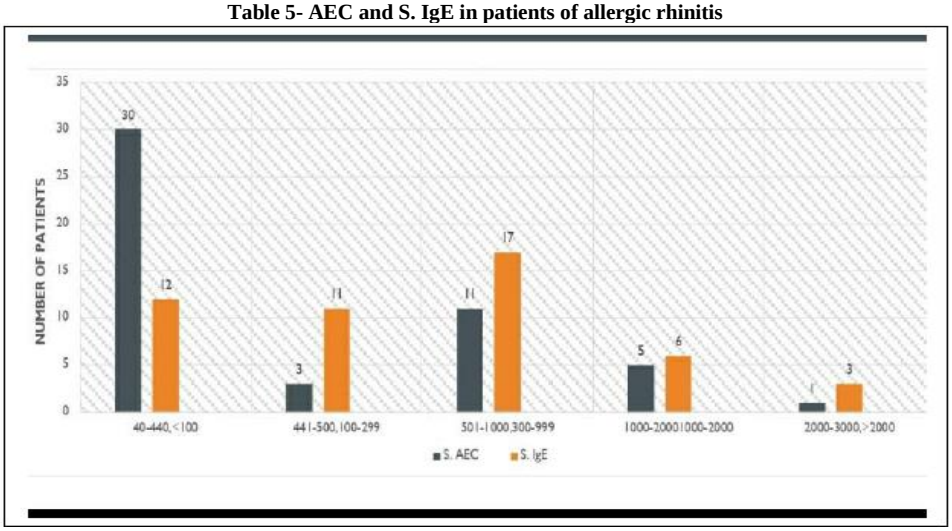
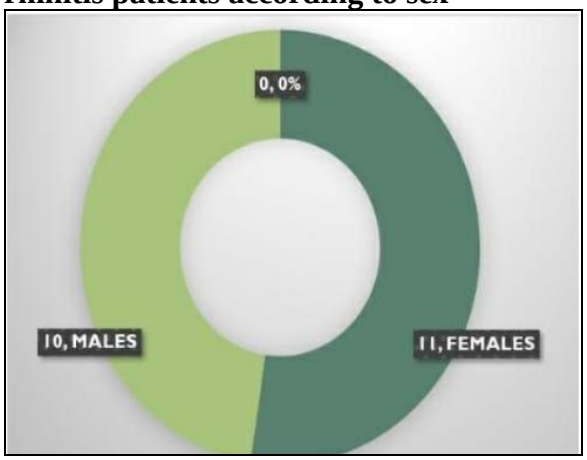


Table 6: Incidence of sinusitis in allergic rhinitis patients according to sex



In our study we found that 52% (n=11) of allergic rhinitis patients having symptoms of sinusitis were females which corresponded with the study of Devyani Lal et al.

Table 7-Incidence of sinusitis in allergic rhinitis according to age

We also found that most of my patients having allergic rhinitis with sinusitis reside in the age group of 16-25 years (52%), whereas the study done by Devyani Lal *et al.* stated that their mean age was 54 years and in Sharma G K *et al.* mean age was 43.5 years.

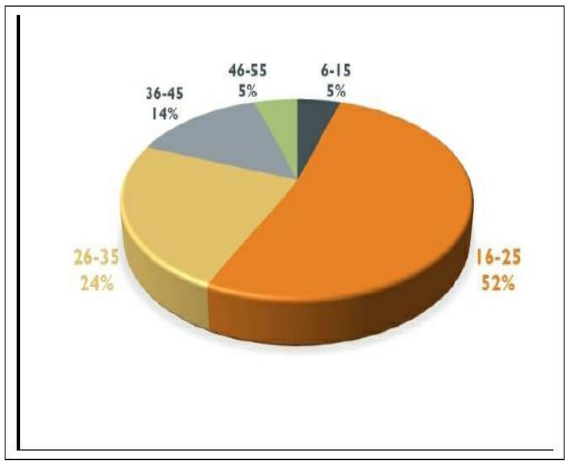
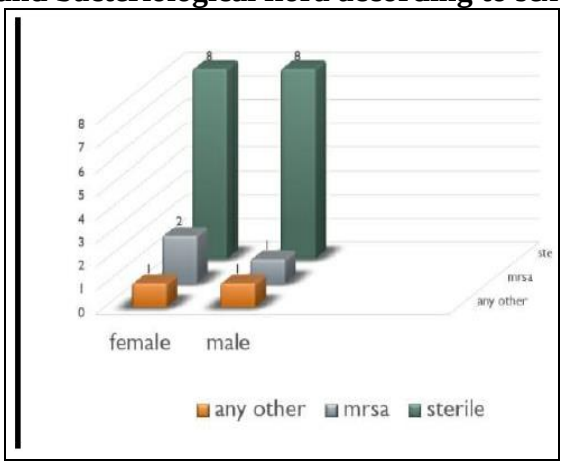
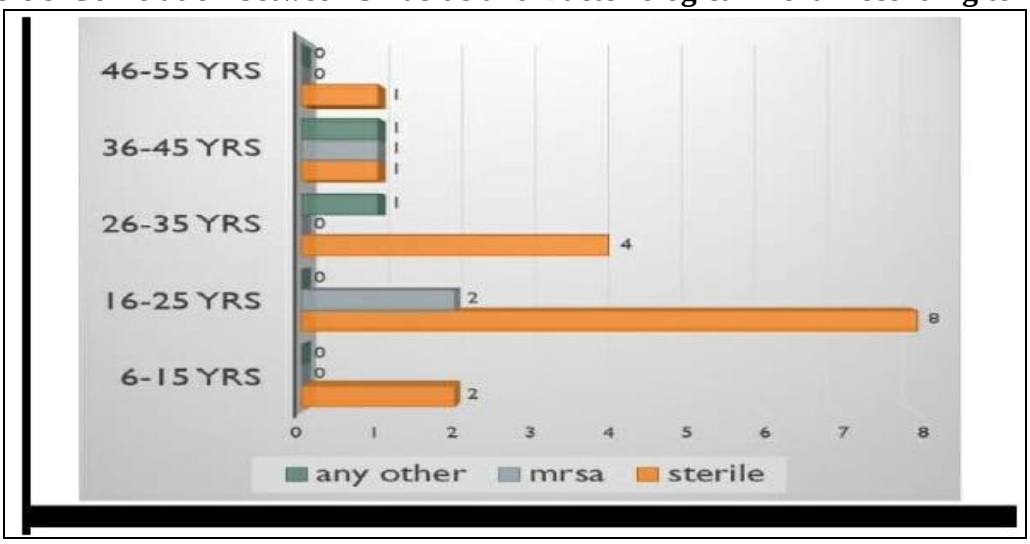


Table 8- Correlation between sinusitis and bacteriological flora according to sex



Male (80%) and female patients (72%) have sterile nose swab, which corresponded with the study of Sharma GK et al. The result was significant with $p<0.05$.

Table 9-Correlation between Sinusitis and Bacteriological Flora According to Age



In our study the bacteriological flora remained mostly sterile in all age groups except MRSA and Klebsiella sp. in few, which did not correspond to the study by Joanna Leszcyzynska *et al.* where the nasal flora in such patients changed with age, i.e. Proteus spp. and pseudomonas aeruginosa in older patients as compared to staph epidermidis and aureus in younger patients.

DISCUSSION

The nose represents an important bacterial reservoir for endogenous infections, Nasal carriage is a major risk factor for Staphylococcus aureus infection, especially for methicillin-resistant strains (MRSA). Despite the different studies approaching the subject of Allergic rhinitis, we still do not have a clear understanding of the true pathogenic mechanisms and agents involved in this disease. Pinto et al. suggest that alterations in the sinonasal microbiome might be one mechanism that predisposes allergic subjects to acute bacterial rhinosinusitis (ABRS). Rajasekaran et al. noted that of the 50 patients with allergic rhinitis, the predominant isolate was Staphylococcus epidermidis, 80% (n=40). Other organisms were diphtheroids 70% (n=35), S. aureus 40% (n=20), Klebsiella pneumoniae 30% (n=15), Pneumococcus 20% (n=10), Hemophilus influenzae 10% (n=5), Escherichia coli 2% (n=1) and Micrococci 2% (n=1). There are several implications of these data that could translate to clinical medicine and provide information on airway physiology. Alterations in commensal bacteria in allergic subjects could cause effects on sinonasal epithelia, enhancing or blocking immune responses to allergen or other stimuli, with effects on lower airway disease. Controlling inflammation may prevent change of sinonasal microbiota and decrease number of acute bacterial sinus infections. For example, steroids can effectively reduce bacteria-induced mucin expression in the airways[6] and can mitigate the proinflammatory responses to pathogens.[7] Recent advances in culture-independent sequencing technologies have enabled the determination of microbiomes of various sites of the human body, including nose.[8-10]Using various methods, many previous works have examined the association between atopy and sinusitis. Several of these reported that patients with sinusitis have a higher incidence of positive allergy skin tests than the normal population[12,13]. Other studies examined the incidence of sinusitis in allergic patients and concluded that chronic sinusitis could represent a complication of perennial allergic rhinitis[11,14,15]. It is important to determine whether the patients examined had perennial or seasonal allergic rhinitis,

since it has been demonstrated that the latter does not predispose to sinusitis.[16]. In conclusion, our results suggest an association of perennial allergic rhinitis with chronic sinusitis; allergic patients exhibit more extensive sinusitis than the general population. Presence of microbes in pollen was demonstrated in study by Heydenreich et al[17].These microbes in pollen can act as adjuvant and initiate an allergic immune response. The microbes in pollen could possibly explain the change in flora and recurrent infection in allergic rhinitis patients. Evans et al. reported a very high rate of false negative nasal cultures, but the material was small (only 24 patients)[18]. Also Gwaltney et al.[19], who studied sinusitis in such patients, and Kessler [20], who studied chronic sinusitis, considered the correlation of nasal and sinus cultures to be poor, whereas Bjorkwall[21] found a high overall sensitivity (95%) of a positive nasal culture in 95 patients with sinusitis and allergic rhinitis. In case of suspicion of inhalant allergy, skin prick tests or RASTs should be performed to confirm the presence of an underlying sensitization and the patients treated accordingly. In case of sensitization to inhaled allergens, therapy should be conducted following recently developed evidence-based guidelines for treatment.[22] Many therapy techniques have been used to treat allergic rhinitis. Intranasal steroids and antihistamines are the gold standard of medical therapy. Even without contraindications, many patients do not want to take any medication for the relief of allergic rhinitis.[23] Koreck et al.[24] proposed that phototherapy, using a combination of UV-A (25%), UV-B (5%) and visible light (70%), may represent a therapeutic alternative for patients with allergic rhinitis. They also noted the efficacy of phototherapy in treating allergic rhinitis and stated that it suppressed significantly the clinical symptoms of allergic rhinitis and locally reduced the number of inflamed cells.[24]

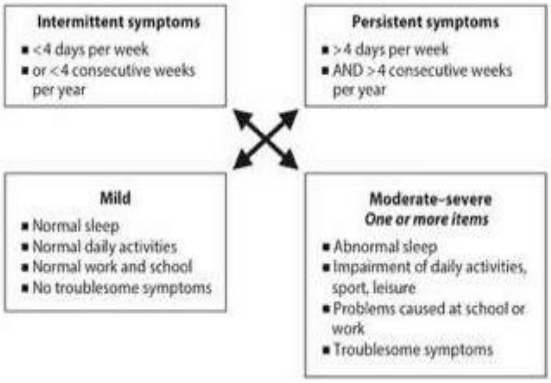
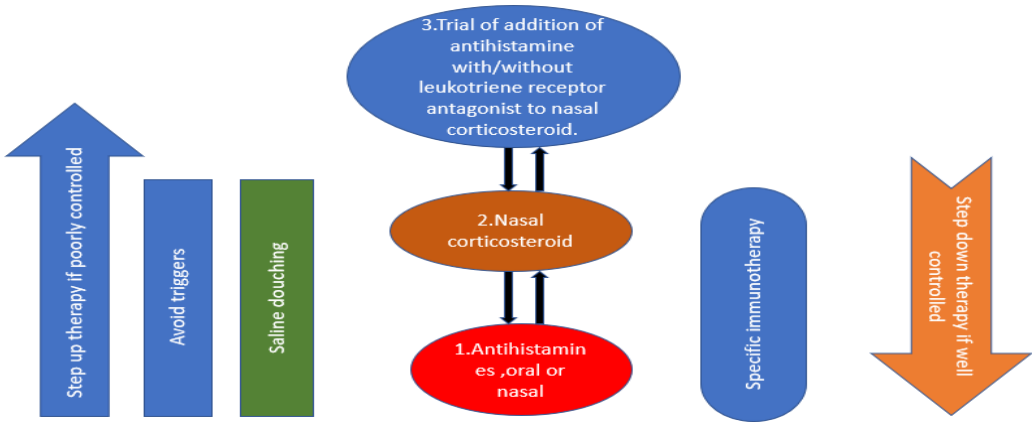


Fig. 1 shows ARIA classification for allergic rhinitis.

On the basis of the ARIA guidelines (allergic rhinitis and its impact on asthma), the patients whose duration of allergic symptoms was less than 4 days per week or 4 weeks per year were classified into the intermittent groups and the rest of them were classified as the persistent groups. According to severity, the patients were divided into the mild groups and the moderate-severe groups.[25] Patients failing to respond to standard treatment should be considered for referral, in order to determine whether the correct diagnosis has been made and if so to seek treatment management optimization. Patients with a firm diagnosis, who do not respond to standard therapy in whom symptoms are persistent and/or disabling, merit referral for consideration of Immunotherapy. Treatment aims at safe and effective symptom relief plus prevention of complications and disease progression. There is evidence that outcomes are improved when evidence based guidelines are applied.[26] Entry to therapy can occur at 1, 2 or 3 year, depending on severity of presenting symptoms. Poor control should lead to a step up, good control to a step down, so that the minimum therapy necessary is used. For seasonal disease, regular therapy should be commenced 2 weeks before the anticipated start of symptoms. *Oral antihistamines may be better tolerated, while intranasal antihistamines have a more rapid onset of action. **Reconsider diagnosis if not controlled within 1-2 weeks. If <2 years of age and unresponsive to antihistamine within a week, reconsider diagnosis before

stepping up therapy. If poorly controlled, consider a short rescue course of a decongestant or low-dose oral prednisolone to gain symptom control; topical ipratropium may be useful for rhinorrhoea (adapted from Roberts *et al* [27] (with permission)). Allergen avoidance, where possible, is recommended across the spectrum of disease severity. Those suffering from hay fever are asymptomatic outside the pollen season and symptoms in nose and eyes are reduced by nasal air filters,[28] and pet avoidance shows clear benefits; for house dust mite (HDM) reduction, individual measures gave equivocal results or lack of benefit.[29]



CONCLUSION

- The maximum patients of allergic rhinitis were found in the age group 16-25 years (36%), with female preponderance 3:2 and $p<0.00001$ which is significant and mostly the patients were married (58%) which is significant as $p<0.05$.
- Mostly sterile swab (no growth) was obtained in 80% of both male and female population.
- Incidence of sinusitis in allergic rhinitis patients was (n=21 patients) 52% in female population which was significant as $p<0.00001$.
- Most common category of Sr. AEC of patient reside in the group 40-440 (n=30) and Sr. IgE in the group 300-999 (n=17).
- Incidence of sinusitis in allergic rhinitis patients was 52% residing in the age group 16-52 years.
- In my study it was found that 72% of females and 80% of males had sterile swab culture, mostly belonging to the age group 16-25 years who had sinusitis associated with allergic rhinitis.
- Mean age of allergic rhinitis is 29.24 years.

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Conflict of Interest: None
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Ethical Approval: Approved

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