Original Article

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Aetiological Subclassification of Chronic Rhinosinusitis: A Retrospective Study

Ear, Nose and Throat Section

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ABSTRACT

Introduction: Chronic Rhinosinusitis (CRS) is a major health problem with very high prevalence worldwide. The information available about the pathophysiology of the disease is not enough to allow development of curative therapies. Classification of CRS is based on the presence of asthma and allergy that can be useful to understand the disease aetiology and allow better patient's care through individualised treatment plans.

Aim: To classify CRS cases into subgroups depending mainly on the presence of asthma and allergy in addition to comparing the characteristics of these subgroups.

Materials and Methods: A retrospective descriptive study was carried out, and the data of CRS' patients were collected from medical records of consecutive patients attending the ENT clinic in, King Abdulaziz Medical City, Saudi Arabia. Based on collected data, CRS cases were classified into six subclasses, and patients' characteristics such as gender and Immunoglobulin E (IgE) values in these subclasses were compared. Data entry and statistical analysis was carried out in Statistical Package for the Social Sciences (SPSS). Mean, Standard Deviation (±SD) for numerical parametric variables and Inter-Quartile Range (IQR) for numerical non-parametric variables was calculated. Appropriate statistical tests like Analysis of Variance (ANOVA) for parametric data and Kruskal Wallis test for non-parametric were applied.

Results: The most prevalent subclass was Non-Asthmatic Sinusitis without Allergy (NASsA) 30 (48.4%) followed by, Asthmatic Sinusitis Without Allergy (ASsA) 13 (21.0%), Asthmatic Sinusitis With Allergy (AScA) 6 (9.7%), Non-Asthmatic Sinusitis With Allergy (NAScA) 5 (8.1%) and Allergic Fungal Sinusitis (AFS) 5 (8.1%). The highest levels of total IgE were found in patients with NAScA. It was found that nasal polyps' presence was significantly linked to higher Computed Tomography (CT) Lund-Macky scores and MASNOT (Modified Arabic Sino-Nasal Outcome Test) scores.

Conclusion: Classification of CRS based on the presence of asthma and allergy can be an informative tool for providing better care to CRS patients.

Keywords: Allergy, Allergic fungal sinusitis, Asthma, Immunoglobulin E, Nasal polyps

INTRODUCTION

Chronic Rhinosinusitis (CRS) remains one of the most common chronic diseases worldwide. A study conducted in 2016 to assess the prevalence of the disease in Saudi Arabia revealed that almost half of individuals in the studied sample were suffering from rhinosinusitis [1]. It is a chronic disease that is characterised by inflammation of sinonasal mucosal tissues, and it significantly affects the quality of life due to the recurrent rhinorrhea, nasal obstruction and facial pain [2]. In spite of the continuous trials to reveal the exact pathophysiology of CRS, it is still not fully understood, and accordingly, no specific treatment can be used to eradicate the disease. Instead, most of the available therapies aim at controlling symptoms [3]. In the past, it was thought that Endoscopic Sinus Surgery (ESS) could be an effective treatment for many patients with CRS. However, the symptoms persisted in many cases after undergoing ESS [4] The same is for antifungal treatment that was hoped to cure all rhinosinusitis cases but this was proven later on to be ineffective [5]. Like many other conditions, following the same therapeutic approach for all CRS patients will not be efficient; while considering an individualised long-term management plan for each patient, based on rhinosinusitis phenotype, will improve treatment outcomes and quality of life [2,6]. Using Endoscopy, the disease can be clinically classified into two categories; CRS with and CRS without nasal polyps. However, it is unclear whether this classification represents different disease subtypes or just different stages of the same disease [7]. Moreover, to make a more meaningful classification, CRS can be classified into different subgroups based on the presence of allergy and asthma that are known to significantly affect the development of the disease [6].

The current study aimed at classifying all CRS cases into subgroups depending mainly on the presence of asthma and allergy in addition to comparing the characteristics of these subgroups. This is to allow a better understanding of the disease and eventually enhance patient's care through individualised surgical and medical treatment plans.

MATERIALS AND METHODS

This descriptive retrospective record based study was conducted in which the consecutive patients attending the ENT clinic in, King Abdulaziz Medical City, Saudi Arabia an academic institution during the period from January 2019 to April 2020 were analysed. A total of 62 patients diagnosed with CRS and subsequently confirmed in laboratory and radiological tests, during the study period were included in the study after obtaining consent. All other patients who came to ENT clinic who were not confirmed of CRS were excluded. Institutional review board approval was obtained before conducting any study-related procedures. (H-01R-012). Demographic data, Nasal Endoscopy (NE) and CT scores using Lund-Mackay scoring system were collected [8]. MASNOT score, Total IgE, and histopathology of nasal polyps was also recorded. Based on collected data, CRS cases were classified into six phenotypic subclasses [6]; Aspirin-Exacerbated Respiratory Disease (AERD), AScA, ASsA, NAScA, NASsA and AFS of CRS subclasses is described in [Table/Fig-1].

Subclass	History	Atopy	Asthma
AERD	Positive Aspirin sensitivity	±	±
AScA	Positive pulmonary function test and allergy test (in vivo or in vitro)	+	+
ASsA	Positive pulmonary function test and negative history or allergy test	-	+
NAScA	No history of asthma and positive allergy	+	-
NASsA	No history of asthma or allergy	-	-
AFS	Positive fungal stain on eosinophilic mucin	+	±

[Table/Fig-1]: Definition of CRS subclasses.
*AERD: Aspirin-exacerbated respiratory disease; AScA: Asthmatic sinusitis with allergy; ASsA: Asthmatic sinusitis without allergy; NAScA: Non-asthmatic sinusitis with allergy; NASsA: Non-asthmatic sinusitis without allergy; AFS: Allergic fungal sinusitis. The subclassification of CRS has cystic fibrosis as a subtype. Cystic fibrosis is a rare genetic disease and no case has been diagnosed during the study period. So we have included other six subtypes of CRS in present study

STATISTICAL ANALYSIS

Data were statistically described regarding mean±SD for numerical parametric variables, median and IQR for numerical non-parametric variables, or frequencies (number of cases) and percentages for categorical variables. Comparison of numerical variables between the subgroups was done using one-way ANOVA for parametric data and Kruskal Wallis test for non-parametric data. The p-values <0.05 were considered statistically significant. All statistical calculations were done using computer program IBM SPSS (IBM Corp, Armonk, NY, USA) release 21 for Microsoft Windows.

RESULTS

A total of 62 CRS patients were included in the study. Patients' age ranged from 18 to 80 years with a mean (±SD) value of 41.0±15.1 years and a median (IQR) of 37.0 (24) years. Males constituted 25 (40.3%) of the patients while 37 (59.7%) were females.

It was found that the mean (±SD) value of neutrophils was 48.7±23.0% with a median (IQR) value of 50.7% (17.15%). CT scores showed a mean (±SD) value of 14.5±6.8 and a median (IQR) value of 14.5 (11) [Table/Fig-2].

Investigation	Mean±SD	Median (IQR)
Neutrophils (%)	48.7±23.0	50.7 (17.15)
Eosinopils (%)	11.9±29.2	5.2 (5)
Total IgE (in IU/mL)	478.5±768.3 IU/mL	174 (492)
Computed Tomography (CT) scores	14.5±6.8	14.5 (11)
MASNOT (modified Arabic Sino-Nasal outcome test) score	26.8±13.2	24.5 (18.25)

[Table/Fig-2]: Histopathologic inflammatory markers and CT scores in subjects with CRS.

A total of 22 patients (35.5%) were asthmatic while 40 patients (64.5%) were non-asthmatic. Based on medical history, the presence of asthma and allergy, CRS cases were classified into six subclasses. The most prevalent subclass was NASsA constituting almost half of the cases (30 patients, 48.4%) [Table/Fig-3].

S. No.	Chronic Rhinosinusitis subclass	Number (%)
1	Non-Asthmatic Sinusitis without Allergy (NASsA)	30 (48.4%)
2	Asthmatic Sinusitis without Allergy (ASsA)	13 (21.0%)
3	Asthmatic Sinusitis with Allergy (AScA)	6 (9.7%)
4	Non-Asthmatic Sinusitis with Allergy (NAScA)	5 (8.1%)
5	Allergic Fungal Sinusitis (AFS)	5 (8.1%)
6	Aspirin-Exacerbated Respiratory Disease (AERD)	3 (4.5%)

[Table/Fig-3]: Chronic Rhinosinusitis (CRS) subclasses.

There was no significant difference between the subclasses regarding gender distribution (p=0.335) [Table/Fig-4].

The total IgE differed significantly between the subclasses (p=0.006) as the highest values were reported in patients with NAScA. Total IgE among patients with allergy (even if they were asthmatic or not) was significantly higher than those without allergy [Table/Fig-5].

	Males		Females		Total		
Subclass	Count	Percent	Count	Percent	Count	Percent	p-value
AERD	2	3.2	1	1.6	3	4.5	p-value=0.335
AScA	3	4.8	3	4.8	6	9.7	
ASsA	5	8.1	8	12.9	13	21.0	
NAScA	2	3.2	3	4.8	5	8.1	
NASsA	9	14.5	21	33.9	30	48.4	
AFS	4	6.5	1	1.6	5	8.1	
Total	25	40.3	37	59.7	62	100.0	

[Table/Fig-4]: Gender distribution among the CRS subclasses.
ANOVA test was applied and was p value>0.05

Subclasses	Statistic		Std. error	p-value
AERD	Mean	499.3	239.6	0.006
	Median	684.0		
	Inter quartile range	383		
	Std. deviation	415.0		
AScA	Mean	435.2	143.0	
	Median	309.5		
	Inter quartile range	486		
	Std. deviation	350.2		
ASsA	Mean	149.6	48.7	
	Median	89.0		
	Inter quartile range	138		
	Std. deviation	175.5		
NAScA	Mean	1215.2	625.8	
	Median	344.0		
	Inter quartile range	2220		
	Std. deviation	1399.4		
NASsA	Mean	321.6	112.7	
	Median	140.0		
	Inter quartile range	242		
	Std. deviation	617.0		
AFS	Mean	1578.6	494.0	
	Median	1746.0		
	Inter quartile range	1463		
	Std. deviation	1104.7		

[Table/Fig-5]: Total IgE values in the different CRS subclasses.
ANOVA test was applied.

Out of the 62 CRS patients, 14 patients (22.6%) had nasal polyps. Characteristics of patients with and without nasal polyps were compared. Significantly higher CT scores (p=0.02) and MASNOT score (p=0.006) were observed among patients with nasal polyps [Table/Fig-6,7].

	Statistic		Std. error	p-value
Without nasal polyps	Mean	12.9	0.9	0.02
	Median	12.0		
	Inter quartile range	8		
	Std. deviation	5.7		
With nasal polyps	Mean	17.8	1.7	
	Median	20.5		
	Inter quartile range	22.3		
	Std. deviation	6.4		

[Table/Fig-6]: Computed Tomography (CT) scores among patients with and without nasal polyps.
Kruskal Wallis test to compare between patients with and without nasal polyps

	Statistic		Std. error	p-value
Without nasal polyps	Mean	23.8	1.7	(p=0.006)
	Median	21.0		
	Inter quartile range	15		
	Std. deviation	11.2		
With nasal polyps	Mean	35.9	4.0	
	Median	35.0		
	Inter quartile range	23.5		
	Std. deviation	15.0		

[Table/Fig-7]: MASNOT scores among patients with and without nasal polyps. Kruskal Wallis test to compare between patients with and without nasal polyps

Using Kruskal Wallis test other tested parameters; age (p=0.730), gender (p=0.531) neutrophils (p=0.136), eosinophils (p=0.219) and total IgE (p=0.482) showed no significant differences between patients with and without nasal polyps.

DISCUSSION

Due to its extremely high prevalence and significant effect on quality of life, CRS is considered as a major health problem worldwide. According to Lü W et al., blocked nose, runny nose, dizziness and impaired sense of smell or taste are the symptoms with the highest effect on patient's quality of life [9,10]. Unfortunately, only symptomatic treatment options are available rather than curative for this chronic disease. This is because only a little information is known about the aetiology of CRS and this makes it hard to develop efficient, targeted and curative therapies [11]. To overcome this problem, it is important to get more information about CRS subclasses and the pathophysiological characteristics of each subclass. After the classifications depending on the presence or absence of nasal polyps were proven to be non-efficient, CRS has been classified based on co-morbidities including allergy and asthma [6]. In the current retrospective study, CRS was classified into six phenotypic subclasses depending mainly on medical history and presence of asthma and allergy.

AFS is usually misdiagnosed because of its unique pathophysiology compared to other subtypes of rhinosinusitis, and this is why it requires special care from Health Care Providers (HCPs) to be properly diagnosed and managed. Based on the results of present study, total IgE can be a useful diagnostic tool for this immune-modulated disease and this is consistent with the study reported by Glass D and Amedee R [12]. In the current study, total IgE in patients with the allergy was significantly higher than those without allergy; this is corroborated by the study done by Manning SC and Holman M et al., in which AFS patients were found to have high levels of IgE [13]. Further, largest AFS case series reported by Schubert MS and Goetz DW over a period of eight years in southwestern United States reported all patients with AFS had inhalant allergy and elevated IgE levels [14]. Upon comparing the characteristics of patients with nasal polyps to those without nasal polyps, no significant differences were found regarding age, gender or laboratory results while CT score (using the Lund-Mackay scoring system) [15], in patients with nasal polyps was significantly higher (p=0.02) compared patients without nasal polyps. Moreover, this supports the validity of Lund-Mackay scoring system where the score increase with the more severe sinus mucosal inflammation and fluid [8]. A similar retrospective study by Benjamin MR et al., in 507 patients with chronic sinusitis without nasalpolyp and 874 patients of chronic sinusitis with nasal polyp, found prevalence of atopy to be 52% and 76% in patients with chronic sinusitis without nasal polyp and patients of chronic sinusitis with nasal polyp respectively and more severe CT changes in CRS patients with nasal polyps [16].

Study done by Al-Safran F et al., also reported significantly higher MASNOT score [17], same as reported in present study (p=0.006) were observed in patients with nasal polyps. This means that presence of nasal polyps is associated with significantly worse CRS symptoms including sneezing, runny nose, blocked nose, need to blow nose, loss of sense of taste or smell, cough and itchy nose.

Limitation(s)

As this was record based retrospective study and data was obtained by computer algorithm and confirmed manually, some cases might have missed because of improper documentation and some cases which were included in the study based on records available couldn't be contacted to validate the information mentioned in medical records.

CONCLUSION(S)

Classification of CRS is based on medical history and the presence of asthma and allergy which can be a base for exploring curative and targeted treatment options. Total serum IgE is an important factor in diagnosis, sub-classification and choosing an appropriate treatment plan for CRS patients. We recommend further research in this area considering larger sample size and multi-centre study design to yield more informative results about the characteristics and appropriate treatment plans for each CRS subclass.

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