

## Mood Disorders among Chronic Rhino-Sinusitis Patients

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### Abstract

**Background:** Chronic rhinosinusitis (CRS) is one of the prevalent inflammatory diseases all over the world. Recent studies have shown some kind of relation between CRS and mood disorders such as depression and anxiety this study aims to assess this relationship in an outpatient setting.

**Methods:** In this case control study 162 CRS patients and 151 healthy subjects as control group were selected. Hospital anxiety and depression scale (HADS) questionnaire was presented to all of them. Depression and anxiety subscales of the questionnaire were compared in two groups.

**Results:** According to depression 21.6% of case group and 21.2% of control group were scaled as depressed and 34% of cases and 32.7% of control subjects were in need of medical care for anxiety. None of these differences were statistically significant.

**Conclusion:** Although depression and anxiety are prevalent in CRS patients but it is not more prevalent than normal population.

**Keywords:** Chronic rhino-sinusitis; Mood disorders; Depression; Anxiety

### Introduction

Chronic rhinosinusitis (CRS) is one of the most prevalent inflammatory diseases defined as inflammation of nasal cavity and paranasal sinuses lasting at least 12 consecutive weeks, presenting with symptoms such as itching, sneezing, rhinorrhea, and nasal congestion [1]. Its prevalence among US adult population was estimated about 16% according to 2010 national health interview survey [2]. In studies conducted in Iran the estimated prevalence of CRS is about 14.5% to 22.5% in adult population [3,4]. Regarding high prevalence of CRS it's rational to expect a high socioeconomic burden for this disorder as it was shown in Bhattacharyya study, who reported the economic burdens of CRS patients to be \$8.6 billion annually [5]. Looking at CRS as a chronic disease, lots of studies sought its effect on quality of life. Most of these studies reported a significantly impaired health related quality of life in these patients [6]. Searching for the reasons of diminished quality of life in these patients and the fact that psychological disorders usually have comorbidity with chronic diseases, has navigated researches attention toward the association of CRS and psychological problems especially depression and anxiety. Some of these studies reported a very high prevalence of depression and anxiety in CRS patients. Brandsted et al. reported the prevalence of depression to be 26% among patients with sinonasal symptoms [7]. In another study using hospital anxiety and depression scale (HADS), 25.9% and 14.7% of CRS patients had high levels of anxiety and depression, respectively [8]. In a cohort study in 2011 the incidence of depression in patients with CRS was 77% more than control group with a hazard ratio of 1.56 [8] while these studies report depression as a highly prevalent disorder in CRS patients there are some other studies which report the prevalence of highly probable depression as low as 3 to 4% [9,10]. In 2016 Schloser et al. reviewed 13 studies and reported the prevalence of probable depression to be from 11 to 40% [11]. Considering this wide range of results and the fact that causality in this association is not yet understood, it seems necessary to conduct more studies in this field. The aim of this study was to determine the average score and the prevalence of depression and anxiety within CRS patients using HADS questionnaire.

### Methods

In present study we used a case-control design to determine the state of anxiety and depression in CRS patients in comparison with non CRS subjects, using a HADS questionnaire. The study was held in the otolaryngology outpatient clinic of Alzahra hospital (which is a tertiary care center affiliated to Medical university of Isfahan, Iran), from November 2015 to July 2016. CRS patients were diagnosed by an expert otolaryngologist based on European adult Sinusitis guideline [12], but due to economic limitations radiographic assessment and endoscopic evaluation was not administered. As both genetic and environmental features play a significant role in psychological disorders the control group was selected among patient's attendants in order to minimize sociocultural and genetic differences. Subjects in the control group were examined by the otolaryngologist to rule out any chance of rhinosinusitis disorders. Subjects less than 18 years old and those with a history of psychiatric disorders other than depression and anxiety, surgical operation or hospitalization in previous month, and the ones who were candidate for surgical operation in following month were not included. The questionnaire was provided to the patients and control subjects in the same time and same room. Considering different levels of patient's socioeconomic status, one of the research team members was present as the patient filled the questionnaire in order to explain the study to him/her and answer their questions in case of need.

### Questionnaire

The questionnaire we used consists of three main parts. In the first part demographic variables including date of birth, gender (male/

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female), educational level (illiterate or primary education/high school education/academic education), marital status (single/divorced/married/widowed), occupational status (employed/unemployed/student/retired) were asked. Second part consisted of 4 questions, 2 of them about patient's history of his/ her past medical and drug history, one question about severity of CRS in relation to different seasons and a question about CRS duration. The third section was HADS questionnaire which is designed by Zigmond and Snaith in 1982 [13]. This questionnaire has been developed to assess depression and anxiety scales in the setting of a medical hospital outpatient clinic. It consists of 14 multiple choices questions that the patient should answer to base on his/her last week experiences. Seven questions indicate depression and anxieties. Each question can be rated from 0 to 3 based on the patient's choice so the each subscale can be rated from 0 to 21. The score from 0 to 7 indicates no anxiety or depression, 8-11 indicates probable or mild anxiety or depression and the score more than 11 is translated as highly probable depression or anxiety which need medical care. In this study we used Persian format of the questionnaire which was developed by Montazeri et al. with a Cronbach's alpha coefficient of 0.78 for anxiety and 0.86 for depression subscale [14].

Statistical analysis Sample size was calculated using compare of means formula, with an 80% power and 5% significance, resulted in 150 case-control sets (one control for each case) were needed.

Data were analyzed, using SPSS version 19.0 (Statistical Package for the Social Sciences). Student T-test and chi square were used to assess the differences of quantitative and categorical variables between two groups. Logistic regression model was used to assess the odds of CRS occurrence in relation to age, gender, education, marital status, disease history, drug history, depression, and anxiety. Values are presented in mean and standard deviation (SD), percentage, odds ratio (OR) and confidence interval (CI). Differences with a p value of less than 0.05 were considered as statistically significant. Missing values of each group

were replaced by mode and mean of the same group for categorical and quantitative variables, respectively.

## Results

One hundred and sixty two CRS patients (45.7% male) with the mean age of  $35.3 \pm 11.4$  and 151 control subjects (45.0% male) with the mean age of  $33.5 \pm 8.5$  were included in this study. Demographic factors distribution differences between case and control subjects were not statistically significant (Table 1). We could not gather control match for 11 cases because 8 patients had visited the physician by themselves, 2 of the patient's attendants were diagnosed as having kind of rhinosinus disorder and 1 of them was less than 18 years old. Forty two (25.9%) patients had a history of some kind of diseases other than CRS and 31 (19.1%) of them used medication, whereas in control group 26 (17.9%) had a positive medical history and 18 (11.9%) reported medication use but this difference was not meaningful ( $P > 0.05$ ) (Table 1).

Mean depression score was  $7.2 \pm 4.2$  among CRS patients and  $7.2 \pm 4.3$  in control group and the difference was not statistically significant (P value=0.893). Using HADS scoring system 86(53.1%) CRS patients were categorized as normal, 41(25.3%) was scored as having mild depression, and 35(21.6%) of them were depressed and in need of medical care, the distribution in control group was 71(47.0%), 48(31.8%) and 32(21.2%) respectively and the difference between two groups was not significant (P value=0.420).

Mean anxiety score in case and control groups was  $9.15 \pm 4.38$  and  $9.07 \pm 4.39$  respectively and did not differ statistically (p-value=0.870). Thirty four percent of CRS patients and 32.7% of control subjects were diagnosed as in need of medical care for anxiety and the difference between two groups was not statistically significant (P value = 0.971). Data on depression and anxiety scores and scale in each group is presented in Table 1.

Characteristics		CRS patients	Control	P-value*
Age: Year	Mean $\pm$ SD	$35.3 \pm 11.4$	$33.5 \pm 8.5$	0.106
Sex: N (%)	Male	74 (45.7%)	68 (45.0%)	0.909
	Female	88 (54.3%)	83 (55.0%)	
Education: N (%)	Illiterate/primary	35 (21.6%)	26 (17.2%)	0.327
	High school	70 (43.2%)	60 (39.7%)	
	Academic	57 (35.2%)	65 (43.0%)	
Occupation: N (%)	Employed	76 (46.9%)	73 (48.3%)	0.816
	Student	25 (15.4%)	23 (15.2%)	
	Retired	9 (5.6%)	5 (3.3%)	
	Unemployed	52 (32.1%)	50 (33.1%)	
Marital status: N (%)	Single/divorced	48 (29.6%)	46 (30.5%)	0.872
	Married/widowed	114 (70.4%)	105 (69.5%)	
Positive medical history: N (%)	Yes	42 (25.9%)	26 (17.2%)	0.062
	No	120 (74.1%)	125 (82.8%)	
Medication history: N (%)	Yes	31 (19.1%)	18 (11.9%)	0.079
	No	131 (80.9%)	133 (88.1%)	
Depression score	Mean $\pm$ SD	$7.16 \pm 4.16$	$7.23 \pm 4.35$	0.893
Depression scale: N (%)	Normal	86 (53.1%)	71 (47.0%)	0.420
	Mild	41 (25.3%)	48 (31.8%)	
	Indicating medical care	35 (21.6%)	32 (21.2%)	
Anxiety score	Mean $\pm$ SD	$9.15 \pm 4.38$	$9.07 \pm 4.39$	0.870
Anxiety scale: N(%)	Normal	59 (36.4%)	56 (37.3%)	0.971
	Mild	48 (29.6%)	45 (30.0%)	
	Indicating medical care	55 (34.0%)	49 (32.7%)	

\*P-values of less than 0.05 is statistically significant

Table 1: Comparison of demographic and clinic characteristics based on the allergic group and controls.

A logistic regression was performed to ascertain the effects of age, gender, education, marital status, disease history, drug history, depression, and anxiety on CRS occurrence. None of the variables had a statistically significant odds ratio (Table 2).

## Discussion and Conclusion

It was hypothesized that depression and anxiety are highly prevalent in CRS patients in comparison to healthy population. In this study it was proved that these psychological disorders are prevalent among CRS patients but when it comes to comparison with normal healthy population the hypothesis failed and there was no significant difference.

We estimated the prevalence of depression to be about 21% in CRS patients which is in line with other studies that used HADS questionnaire and reported the prevalence of 11-23.8% [11]. The main reason of this wide range in these studies can be related to different HADS cut-off points used by them. Where the studies which used score 6 as their cut-off point for depression diagnosis reported the highest prevalence and the study which used 11 as cut-off reported the lowest [8,15]. In our study we used 11 as depression cut-off score but the prevalence of depression was like the ones who used lower scores to define depression and it shows a higher prevalence of depression in our study. In other studies which used different methods to evaluate depression, the results are somehow different. Jung et al. reported the prevalence of mild and moderate depression to be about 40% using Beck depression inventory (BDI) scale [9,16]. Schlosser et al. used BDI too and reported the prevalence of 31% in CRS patients [17]. One important clue which can explain the differences in depression prevalence report of our study in contrast to studies which used BDI is that HADS cannot assess somatic symptoms of depression as exhaustion or sleep disturbances whereas BDI assess both somatic and mood symptoms. So, considering CRS as a chronic disease which impairs sleep and can cause day time exhaustion; the difference seems logical.

Thirty four percent of CRS patients were in need of medical care according to their anxiety score. This is in line with a study conducted in 2013 by Nanayakkara et al. that reported the prevalence of 32% in 57 CRS patients in London [15]. Other studies using HADS questionnaire reported lower prevalence in a range of 12% to 26% [8,10,18]. Herein

different studies used different scoring systems, too. And this can be the reason of different prevalence. Also, it should be considered that in some studies subjects were selected through patients undergoing a sinonasal surgery and it can make them stressful.

Comparing psychological disorders between CRS patients and control group no significant difference was seen and this is in contrast with most studies in this field. Katotomichelakis et al. in a study evaluated psychological status among CRS patients, observed that olfactory impairment can play a role in promoting psychological disorders. But when it comes to patients with normal olfactory function psychological assessments reveal no impairment [19]. In another study Tomum et al. showed that HADS score and rhinosinusitis disability index are highly correlated but there were no correlation with Lud-Kennedy endoscopic score [18]. Considering these two studies it is possible that dysfunctions caused by CRS are in relation with more psychological problems. Unfortunately we didn't assess CRS-caused dysfunctions in our study to have a better estimate of differences between the two groups.

Schlosser et al. in a study in 2016 used BDI as depression scale in a case control study. It was shown that CRS patients had depression twice more than control subjects but depression prevalence diagnosed by a clinician did not differ between two groups [17]. As mentioned before BDI assess both somatic and cognitive symptoms as HADS assess just cognitive ones and it is interesting that in Schlosser study BDI somatic subscale scores were significantly different but cognitive differences were not statistically significant. And this finding is in line with our study and it can be hypothesized that CRS effects on mood is through somatic impairments and not cognitive ones.

In some studies using functional magnetic resonance imaging (fMRI) some neural pathways in insula and anterior singulate cortex has been found that process both pain and mood [20]. And also in depressed and anxious subjects a hypothalamic-pituitary-adrenal axis is activated that causes cytokine response resulting in a chronic preinflammatory state [21,22]. Therefore it is possible that CRS causes mood disturbances through somatic symptoms at first and then this mood disorder causes more severe CRS symptoms and this continues in a cyclic manner. Considering this hypothesis it seems rational that depression spectrum disorders incidence rise in CRS subjects during

Variables		OR(95%CI)	P-value*
Age	Year	0.98 (0.95-1.01)	0.179
Sex	Male	1.03 (0.61-1.73)	0.916
	Female	Ref.	
Education	Illiterate/primary	0.64 (0.32-1.29)	0.212
	High school	0.67 (0.40-1.13)	0.135
	Academic	Ref.	
Marital status	Single/divorced	0.81 (0.43-1.53)	0.507
	Married/widowed	Ref.	
Occupation	Occupied	0.89 (0.49-1.62)	0.700
	Student	0.73 (0.31- 1.72)	0.470
	Retired	0.87 (0.22-3.40)	0.838
	Non occupied	Ref.	
Disease history	No	1.27 (0.54-2.90)	0.593
	Yes	Ref.	
Drug history	No	1.44 (0.58-3.58)	0.430
	Yes	Ref.	
Depression	Score	1.026 (0.96-1.10)	0.484
Anxiety	Score	0.99 (0.92-1.06)	0.743

\*P-values of less than 0.05 is statistically significant

**Table 2:** Association of demographic and clinic characteristics on allergic groups using logistic regression model.

a period of time as it was shown in a cohort study in Taiwan on 15,371 CRS cases and 61,484 non-CRS controls, where depression incidence in cases was approximately two times more than control group [23].

In this study CRS diagnosis was based on history and physical examination alone, and due to economical limitations we didn't use radiologic and endoscopic assessments so we couldn't categorized CRS patients based on the severity, we didn't consider functional impairment in our study, either. These are the most important limitations of our study. Another limitation of this study is that our control group was not a good representative of normal healthy population. We tried to control genetic and socioeconomic factors by selecting patients attendants (most of them their siblings), but patient's disease can cause adverse effects on their attendant's mood, too.

As genetic plays an important role in mood disorders it is suggested that future studies consider this factor as one of the confounder variables. Also studies has defined the role of some specific neurotransmitters such as serotonin and dopamine in both mood disorders and inflammatory processes [24]; focusing on these subjects in future studies can illuminate the way through association of these disorders.

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