



Original Article

## Relationship of vitamin D3 deficiency and chronic rhinosinusitis with nasal and sinus polyposis in patients referring to the Department of Ear, Nose, and Throat Diseases Department of Vali-asr Hospital in Brigand, Iran

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### Abstract

**Introduction:** Chronic rhinosinusitis may require referral to an ear, nose, and throat specialist for possible endoscopic sinus surgery if medical management fails. Vitamin D is one of the essential vitamins for the body that is effective in inflammatory processes. Therefore, it seems necessary to confirm the association between the deficiency of this vitamin and the occurrence of chronic rhinosinusitis with nasal polyposis. This study aimed to determine the relationship of vitamin D3 deficiency and chronic rhinosinusitis with nasal and sinus polyposis in patients referring to the Otorhinolaryngology Department of Valiasr Hospital, Birjand, Iran, in 2017.

**Methods:** A case-control study was performed on individuals, including a group of patients with rhinosinusitis and a control group (n=20 each), referring to the Department of Ear, Nose, and Throat Diseases Department of Vali-asr Hospital. Among patients diagnosed with chronic rhinosinusitis, the cases that had polyps on endoscopic examination were included in the study. After completing the consent form, venous blood samples (10cc) were collected from the patients in fasting conditions. The electrochemical luminescence method was used for measuring the level of serum vitamin D. A questionnaire containing demographic information and clinical findings was completed by reviewing the patients' records. Data analysis was performed in SPSS software (Version. 22) using Chi-square and Mann-Whitney U-tests.

**Results:** The mean and median scores of vitamin D level were obtained at  $14.13 \pm 12.99$  and 10.25 in the case group, and  $18.72 \pm 9.29$  and 18.77 in the control group, respectively. The level of vitamin D was significantly higher in the control group than in the chronic group ( $P=0.04$ ). In the case group, 16 (80%) patients lacked vitamin D and 3 patients had an insufficient level of vitamin D. In the control group, 13 (65%) patients lacked vitamin D and 4 cases had an insufficient level of vitamin D. There was no significant difference in vitamin D levels between the two groups ( $P=0.61$ ). No significant difference was observed between the two clinical symptoms.

**Conclusion:** It was revealed that the lack of vitamin D was likely to be an effective factor in the rhinosinusitis disease; therefore, proceedings need to be taken to cure the deficiency of this vitamin.

**Keywords:** Vitamin D, Sinusitis, Polyps

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## Introduction

Any inflammation of the mucous membranes of the sinuses lasting for more than 12 weeks is designated as chronic rhinosinusitis. Acute and chronic rhinosinusitis is one of the most common diseases worldwide, as estimations indicate that 30% of Americans experience some symptoms of rhinosinusitis, and medical expenses for rhinosinusitis amount to 2million dollars (1-3). Chronic rhinosinusitis is a widespread disease of the nose and paranasal sinuses, in which an extensive range of inflammatory symptoms and changes manifest as an increase in the thickness of the mucosal polypoids to visible nasal polyps (4-5). Nasal and sinus polyps can seldom lead to compression necrosis and corrosion of the sinus wall bone and cause changes in the shape of the facial skeleton in addition to inducing symptoms that include nasal congestion, respiratory issues, headache, anosmia (i.e. loss of smell), rhinorrhea (i.e. runny nose), and postnasal drip(6).

Chronic rhinosinusitis is characterized by long-term inflammation of the nasal mucosa and sinuses. Polyps in the paranasal sinuses are caused by an increase in the number of cells and protrusion of the lamina propria of the mucosa of the secondary sinuses, which leads to chronic inflammation. In most cases, allergic sinusitis is involved in the formation of polyps; nevertheless, chronic sinus infections cause polyps in various cases as well. Allergic sinusitis occurs in 10% of the population and usually affects all sinuses symmetrically (7). The treatment of chronic sinusitis is a long-term one that in some cases leads to surgery. However, even after surgery, such medications as rinsing and topical steroids should be continued and periodic postoperative examinations are necessary (2-5).

Vitamin D acts as a steroid hormone and induces immunological impacts, such as a decrease of Th1-dependent immune response, regulation of macrophage response, stimulation of antimicrobial peptide gene expression in various immune cell lines, regulation of dendritic cell differentiation, reduction of active B cell proliferation, increased activity of regulatory T cells, and maintenance of

an innate immune response (8).

The role of vitamin D in inflammatory processes has been highlighted, and the link between vitamin D deficiency and chronic rhinosinusitis with nasal and sinus polyposis (discussed in a study conducted by Wang et al.) (9) have been discussed in studies. However, to the best of our knowledge, no study has been dedicated in Iran to investigate the mentioned issue. Therefore, this study aimed to examine the relationship of vitamin D deficiency and chronic rhinosinusitis with nasal polyposis in affected patients.

## Materials and Methods

This case-control study was conducted on patients of the Department of Ear, Nose, and Throat (ENT) Diseases Surgery Department at Valiasr Hospital, an affiliation of Birjand University of Medical Sciences, Birjand, Iran, in 2017. The sample size was determined at 20 cases in each group using the formula comparing the two ratios, with 95% certainty and 80% power and including the exposure ratio in the chronic rhinosinusitis with polyposis group (P1) by 45.5%, while the exposure ratio was 6.3% in the control group (P2) based on the results of the study performed by Wang et al. (9).

The sampling of chronic rhinosinusitis with polyposis group was conducted by non-probability convenience method from patients referring to the ENT department of Valiasr Hospital, who were eligible to be included in the study. The inclusion criteria were based on examinable criteria and patient complaints, consisting of two major criteria or one major criterion and two minor criteria that were persistent for a minimum of 12 weeks. The major criteria included facial pain, nasal congestion, rhinorrhea, nasal pus discharge, or a sense of facial swelling, while minor criteria included headache, fever, bad breath, fatigue, toothache, and earache. Patients who reported two major criteria or one major criterion and two minor criteria for at least 4 weeks were diagnosed with rhinosinusitis. Patients in the control group were also selected by the non-probability convenience method from

the patients referring to the ENT Department with a diagnosis other than rhinosinusitis and nasal polyposis, however, nasal congestion at times, which included septal fracture, septal deviation, and enlarged and inverted conchae, and among those who did not report conditions associated with chronic inflammation.

This study obtained the license of the Ethics Committee of Birjand University of Medical Sciences (IR.bums.REC.1396.137). Once written and informed personal consents were collected from eligible individuals, 10 cc of fasting state intravenous blood was drawn and transferred into clot tubes to separate serum. The blood samples were immediately centrifuged, kept at minus 80°C after serum separation, and used for the following experiments. All samples were evaluated by the same method and conditions. Serum vitamin D levels were measured by luminescence electrochemistry.

Objective-based information form was completed through interviews, which included patients' demographic information, such as age, gender, race, and body mass index (BMI). Patients' weights

were measured by a digital scale with an accuracy of 0.1 kg and their heights were assessed by a meter with an accuracy of 1 cm. Similarly, the history of asthma or allergies and clinical findings at the time of referral (i.e., facial pain, sense of facial swelling, nasal congestion, rhinorrhea, headache, fever, bad breath, fatigue, toothache, and earache) were also noted within the form. Data analysis was performed in SPSS software (Version.22) using descriptive and inferential sections.

The Chi-square and Mann-Whitney U-tests were used to compare the basic characteristics of the two groups. Given the abnormality of the Vitamin D level variable, the Mann-Whitney U test was employed once more to compare the variable within two groups, namely chronic rhinosinusitis with polyposis and control.

## Results

In this study, 20 individuals in the subject group were compared with the same number of individuals in the control group. (Table 1) presents a comparison of subject and control groups in terms of demographic variables and clinical symptoms.

**Table 1.** Comparison of groups in terms of gender, age group, body mass index, and disease symptoms

| Variable         | Classification        | Chronic rhinosinusitis group | Control group       | Test statistics | Degree of freedom | P-value* |
|------------------|-----------------------|------------------------------|---------------------|-----------------|-------------------|----------|
|                  |                       | Number (percentage)          | Number (percentage) |                 |                   |          |
| Gender           | Male<br>Female        | 9 (45%)                      | 15 (75%)            | 75.3            | 1                 | 0.053    |
| Age group        | 15-40<br>41-55<br>55< | 11 (55%)                     | 5 (25%)             | 237.0           | 2                 | 0.888    |
| Body mass index  | 18.5>                 | 13 (65%)                     | 14 (70%)            | 958.0           | 2                 | 0.619    |
|                  | 18.5-25               | 3 (15%)                      | 2 (10%)             |                 |                   |          |
|                  | 25<                   | 4 (20%)                      | 4 (20%)             |                 |                   |          |
| Headache         | Yes                   | 1 (3.5%)                     | 1 (5%)              | 143.0           | 1                 | 0.753    |
|                  | None                  | 11 (9.57%)                   | 9 (45%)             |                 |                   |          |
| Nasal congestion | Yes                   | 7 (8.36%)                    | 10 (50%)            | 173.0           | 1                 | 0.677    |
|                  | None                  | 5 (25%)                      | 4 (20%)             |                 |                   |          |
| Earache          | Yes                   | 15 (75%)                     | 16 (80%)            | 0               | 1                 | 1.00     |
|                  | None                  | 17 (85%)                     | 16 (80%)            |                 |                   |          |

\*Chi-square test

The results of the Chi-square test indicated no difference between age groups, BMI, gender, and clinical symptoms within the two groups (Table 1).

In this study, 45% and 55% of the cases were males and females in the chronic rhinosinusitis with polyposis group, respectively. The control group consisted of 75% (15 subjects) males and 15% (5 cases) females. In the chronic rhinosinusitis group, 65% (13 subjects) 15% (3 individuals), and 20% (4 cases) were aged between 15 and 40, 41 and 55, and over 55 years old, respectively. In the control group, 70% (14 individuals), 10% (2 individuals), and 20% (4 individuals) were aged between 15 and 40, 41 and 55, and over 55 years old, respectively. The percentage and number of individuals in each group are presented for BMI, headache, nasal congestion, and earache.

The examination of the age and BMI distribution among patients revealed that these two variables lacked a normal distribution. Therefore, the Mann-Whitney U-test was employed to compare the mean age and BMI between the two groups, the results of which indicated that the mean rank in these two variables was not significantly different between the studied groups (Table 2).

In the chronic rhinosinusitis with polyposis group, the mean level of vitamin D was  $14.13 \pm 12.99$  with a median of 10.25 and a mid-quarter range of 5.28-18.80. In the control group, the mean level of vitamin D was obtained at  $18.72 \pm 9.26$  with a median of 18.70 and a mid-quarter range of 12.78-23.68. The results of the Mann-Whitney U-test designated that the vitamin D levels were significantly higher in the control group than in the chronic rhinosinusitis group (Table 2).

**Table 2.** Comparison of groups in terms of age, body mass index, and vitamin D levels

| Variable        | Group                  | Number | Mean rank | Test statistics | P-value* |
|-----------------|------------------------|--------|-----------|-----------------|----------|
| Age             | Chronic rhinosinusitis | 20     | 40.22     | 162             | 0.314    |
|                 | Control                | 20     | 60.18     |                 |          |
| Body mass index | Chronic rhinosinusitis | 20     | 55.19     | 181             | 0.620    |
|                 | Control                | 20     | 45.21     |                 |          |
| Vitamin D       | Chronic rhinosinusitis | 20     | 88.16     | 127.5           | 0.049    |
|                 | Control                | 20     | 13.24     |                 |          |

\*Mann-Whitney U-test

It was revealed that in the chronic rhinosinusitis group, 16 (80%) patients showed vitamin D deficiency, while 3 (15%) patients had inadequate vitamin D levels. In the control group, 13 (65%) and 4 (20%) patients were diagnosed with vitamin D deficiency and in adequate vitamin D levels, respectively. The results of the Chi-square test did not display a statistically significant difference between vitamin D levels in the two groups ( $P=0.61$ ).

In the chronic rhinosinusitis group, the mean vitamin D level was estimated at  $14.8 \pm 13.95$  and higher in individuals with nasal congestion than in those without nasal congestion. However, the results of the Mann-Whitney U test indicated that this difference was not statistically significant

( $P=0.77$ ,  $P=0.765$ , respectively). In the control group, the mean vitamin D level in patients with nasal congestion was calculated at  $18.36 \pm 12.76$ , which rendered no statistical significance with that of the chronic rhinosinusitis group according to the Mann-Whitney U test results ( $P=0.82$ ,  $P=0.820$ , respectively). Among all participants, the mean vitamin D level was  $16.53 \pm 11.60$  and higher in those with nasal congestion than in those without nasal congestion; this difference was not statistically significant according to the Mann-Whitney U test results ( $P=0.95$ ).

## Discussion

According to the findings and performed tests, the two groups were the same in terms of basic



characteristics, including age, BMI, gender, and clinical symptoms. As a result, the two groups can be regarded as comparable. In the study of vitamin D levels, the lowest and highest levels were obtained at 3 and 61.2, respectively. Moreover, the mean vitamin D level in all patients was determined to be 16.43, indicating that the mean level of this vitamin is lower than normal.

The comparison of the frequency of vitamin D levels was not statistically significant in the two groups of chronic rhinosinusitis with polyposis and control. The mean vitamin D level in the chronic rhinosinusitis with polyposis group was  $14.13 \pm 12.99$ , while the same value was  $18.72 \pm 9.26$  in the control group, which denoted that the vitamin D level was significantly higher in the control group than in the chronic rhinosinusitis with polyposis group. The results of the study conducted by Wang et al. also showed that vitamin D levels were significantly lower in patients having chronic rhinosinusitis with nasal polyps ( $5.7 \pm 21.4$ ) than in those in the control group. In their study, the prevalence rates of vitamin D deficiency ( $<20\text{ng/ml}$ ) in patients having chronic rhinosinusitis with nasal polyposis and in those in the control group were reported as 45.5% and 6.3%, respectively. Additionally, the prevalence rates of vitamin D inadequacy in patients' having chronic rhinosinusitis with nasal polyposis and in those in the control group were observed as 50% and 62.5%, respectively. These results indicated a significant inverse relationship between vitamin D levels and the degree of polyposis; in other words, the low levels of vitamin D were associated with high degrees of polyposis.

In the present study, the results showed that the mean vitamin D levels were significantly lower in the chronic rhinosinusitis group than in the control group (9). However, the findings of a study performed by Sansoni et al. revealed no significant difference between vitamin D3 levels in the two groups, namely patients having chronic rhinosinusitis with nasal polyps and without polyps, which was inconsistent with the results of the present study. This discrepancy in the results

can be attributed to study limitations, such as inadequate sample size (10). Al-Ebiary conducted a study to examine the role of vitamin D in chronic rhinosinusitis and concluded that vitamin D levels were significantly lower in patients with nasal polyps, which might have a causal relationship. Nevertheless, no relationship was marked between vitamin D levels and chronic rhinosinusitis without nasal polyps (11). Consequently, it can be concluded that vitamin D levels are associated with healthcare status and supplementation programs in different countries. As a result, vitamin D levels vary from patient to patient in different countries. The results of our study showed that the comparison of the frequency of vitamin D levels in relation to age and gender in the case and control groups was not significant. The findings of a study showed that age, gender, atopic status, and asthma were not associated with vitamin D3 levels, which were in line with those of the present study (12).

The examination of the frequency of vitamin D levels in both groups based on BMI showed that the mean BMI was not significant. Furthermore, no significant relationship was observed between case and control groups in the frequency of vitamin D levels in relation to nasal congestion, headache, and earache. The results of various studies have shown that vitamin D levels are not associated with the patient's clinical symptoms and BMI (10-12-13).

One of the limitations of the study was the lack of sufficient information regarding patients with rhinosinusitis due to the outpatient and clinical treatment of these patients and the small sample size. Given the low vitamin D levels in both groups, the administration of this vitamin in line with the national guidelines proposed for vitamin D supplementation is strongly recommended. It is also suggested to perform additional research concerning this issue, along with further serological studies for other inflammatory factors.

## Conclusion

According to the results of the study, vitamin D deficiency was considered to be an influential factor in chronic rhinosinusitis with polyposis.

Accordingly, necessary measures should be adopted to cure vitamin D deficiency in line with the scientific sources.

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## Conflicts of interest

There is no conflict of interest.

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