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# Serum Levels of Vitamin D Among Patients with Nasal Polyps in Bolu, Turkey

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## Abstract

**Background:** Nasal polyps are common chronic non-neoplastic growths of the nasal or paranasal sinus mucosa. Vitamin D deficiency, in particular, has been linked to a high rate of both infectious and inflammatory diseases, including those of the upper and lower airways.

**Aim:** In this study, we analyzed the association between plasma 25-hydroxy vitamin D (25[OH]D) levels in patients with nasal polyps.

**Material and method:** Sixty patients (31 male and 29 female), whose ages ranged from 18 to 55 years, were enrolled in this prospective, clinical study.

**Results:** Serum levels of 25 (OH) vitamin D were measured by using a 25 (OH) vitamin D enzyme immune assay kit. There were no statistically significant differences between the control and study groups in plasma 25(OH) D levels, gender, or age ($p<0.05$).

**Conclusions:** This pilot study did not show an association between serum plasma levels of 25-hydroxy vitamin D and bone defect with nasal polyposis among patients living in Bolu, Turkey.

**Keywords:** Nasal polyps; Vitamin D; Chronic sinusitis; Allergy; Rhinitis

## Introduction

Chronic rhinosinusitis (CRS) can be subdivided into two categories: CRS with nasal polyps (CRSwNP) and CRS without nasal polyps (CRSsNP) [1]. Nasal polyps (NP) are common chronic non-neoplastic polyps of the nasal or paranasal sinus mucosa. The pathogenesis of NP is still unclear, but the disease is believed to be a manifestation of complex inflammatory reactions [2,3]. These inflammations histopathologically consist of basement membrane thickening, atypical gland formation, goblet cell hyperplasia, inflammatory cell infiltration, and subepithelial edema [4].

Vitamins are essential components of the diet and have been known to influence the immune system [5]. Vitamin D deficiency, in particular, has been linked to a high rate of both infectious and inflammatory diseases, including those of the upper and lower airways, such as rhinosinusitis, pneumonia, influenza A, and otitis media [6]. Recently, studies have identified additional important effects of vitamin D on the growth and differentiation of many cell types and regulative influence on immunological processes or their anti-proliferative and anti-inflammatory properties [7,8]. Positive effects in the treatment of many autoimmunological disorders have also been reported [9]. Therefore, we hypothesized that CRSwNP, defined as a chronic inflammatory process of the upper respiratory system, could be influenced by Vitamin D deficiency. In this study, we analyzed the association between plasma 25-hydroxy vitamin D (25[OH]D) levels in patients diagnosed with CRSwNP.

## Materials and Methods

This prospective study was conducted on patients 18-55 years of age who came to our Ear, Nose, and Throat Clinic at the Abant Izzet Baysal University, Bolu, Turkey, due to nasal polyps. The study was conducted with the approval of the Ethics Committee of the Medical Faculty of Abant Izzet Baysal University. Patients diagnosed with CRSwNP were included in the study. Exclusion criteria included pregnancy, patients taking multivitamins containing vitamin D for at least six months, patients on systemic steroids or non-steroidal anti-inflammatory agents for at least three months, and subjects who did not live in Turkey. None had a history of rickets. Each diagnosis was established on the basis on the patient's history, endoscopic examination, and CT imaging. All the subjects had bilateral polyps on the first examination and CT imaging and met diagnostic criteria for CRSwNP. Twelve patients had asthma and aspirin triad disease. The control group consisted of 20 healthy subjects with normal nasal mucosa without CRSwNP and not undergoing surgical procedures. After ten hours of fasting, at 9:00 a.m., while in a sitting position, the patients had blood samples drawn into a Vacutainer tube containing K3EDTA (Vacuette, Greiner Bio-One GmbH, Kremsmünster, Austria). All specimens were stored until assayed for levels of 25[OH]D by the central laboratory.

### Bone erosion scoring

We analyzed the degree of bone erosion in all paranasal sinuses by computed tomography. The degree of bone erosion was analyzed by the radiology department, using a previously published staging system. A computed tomography (CT) bone remodeling score was assigned by

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both graders and then averaged to yield a mean CT bone erosion score for each patient. The graders were blinded to age, race, gender, and 25-hydroxy vitamin D status of the patients [10,11].

### Biochemical survey

All measurements were conducted in the same laboratory, by the same researcher, with the same kit. The blood samples were centrifuged for 15 min at 1250 x g at +4°C. Subsequently, sera were aliquoted and frozen at −70°C until the day of the experiment. The blood samples were gradually thawed the day of the experiment. Serum levels of 25 (OH) vitamin D were measured by using a 25 (OH) vitamin D enzyme immune assay kit (Catalog No: K 2110, Immunodiagnostic AG, Bensheim, Germany). The test results are reported in ng/ml. The intra-experimental (interassay) coefficient of variation (CV) was 10.7% for 1.8 ng/ml, and the interday (interassay) CV was determined to be 13.7% for 39.8 ng/ml. Thermo Scientific Wellwash 4 Mk 2was used as the microplate washer in the ELISA assessment of serum levels of 25 (OH) vitamin D. Bio-Rad Benchmark Plus was used as the ELISA reader.

## Statistical Analysis

All of the statistical analyses were performed with the SPSS 11.0 statistical package (SPSSFW, SPSS Inc., Chicago, IL, USA). Descriptive statistics were given as the arithmetic mean ± standard deviation (SD). For comparing the values of the two different groups, we used an independent sample t-test. A value of $p<0.05$ was considered statistically significant.

## Results

Our series consisted of 60 subjects between 18 and 55 years of age. The study group consisted of 40 patients with nasal polyps (22 women and 18 men), and 20 subjects without nasal polyps made up the control group (7 women and 13 men). Table 1 presents the demographic data of the two groups. When we compared the two groups, the vitamin D levels were 24.62 ± 7.4 ng/ml in the patients with nasal polyps and 24.95 ± 9.6 ng/ml in the control group. There were no statistically significant differences in plasma 25(OH)D levels, gender, or age ($p<0.05$). The mean of serum 25(OH)D in females (n=22, mean age=35.8) was not significantly different from that of the males (n=18, mean age=35.1) in the study group (26.4 ± 7.8 ng/ml vs. 23.56 ± 7.1 ng/ml, p= 0.24).

## Discussion

The pathogenesis of CRSwNP remains unclear; the disease is believed to be the manifestation of complex inflammatory reactions [2,12]. Some theories consider polyps to be a consequence of conditions that cause chronic inflammation in the nose and nasal sinuses characterized by stromal edema and variable cellular infiltrate [13,14]. Many studies have focused on eosinophilic mediators in NP tissue. Allergies have been found to predispose individuals to CRSwNP, as the symptoms of watery rhinorrhea and mucosal swelling were present in the diseases, along with an abundance of eosinophils in the nasal secretions. Some studies have shown that eosinophils are possibly the most important inflammatory cells in the pathogenesis of chronic rhinosinusitis with nasal polyposis [2,15]. Staphylococcus aureus is a common bacterial pathogen that may play an important role in the pathogenesis of CRSwNP via tissue remodeling and eosinophilic inflammation. The role of a number of cytokines in the development of CRSwNP is being intensively investigated. Interleukine-5 (IL-5) has been found to be significantly higher in subjects with NP compared to healthy controls [16,17]. According to some papers, elevated levels of IL-6 (Interleukin-6) and IL-8 (Interleukin-8) may participate in the pathology of primary changes and recurrences of chronic sinusitis and NP [18,19]. Stimulation with tacalcitol and calcitriol decreased levels of pro-inflammatory cytokines (IL-6 and IL-8) in fibroblasts derived from NP, which demonstrates that calcitriol and tacalcitol are capable of affecting pro-inflammatory cytokine (IL-6 and IL-8) levels in NP cultures [2]. The antiproliferative activity of tacalcitol and calcitriol in NP cultures has been confirmed. Due to its lower toxicity and higher activity, tacalcitol seems to be the more promising agent in CRSwNP therapy [20].

| | Patient diagnosed with CRSwNP (n=40) | Control group (n=20) | p |
|---|---|---|---|
| Gender (Male/Female) | 18 / 22 | 13 / 7 | 0.853 |
| Age (Years, mean ± SEM) | 35.4 ± 7.2 | 32.2 ± 8 | 0.126 |
| 25[OH]D (ng/ml, mean ± SEM) | 24.62 ± 7.4 | 24.95 ± 9.6 | 0.886 |

**Table 1:** Gender, age and serum levels of 25 (OH) vitamin-D of the patient with CRSwNP group and control group.

Our understanding of vitamin D metabolism has grown in recent years, and it has become clear that vitamin D has extensive immunomodulatory effects. The cellular effects of vitamin D within the lungs are important for host responses against infection and the development and treatment of allergic lung diseases, such as asthma. Epidemiological studies suggest that vitamin D deficiency predisposes individuals to viral respiratory tract infections and mycobacterial infections [21]. Vitamin D is a steroid hormone that appears to play an important role in the regulation of innate immunity in the upper respiratory tract [22].

Lastly, it has been concluded that vitamin D deficiency is associated with more severe bone erosion. This is associated with increased bone erosion in CRSwNP and acute fungal rhinosinusitis [10,11]. Taken together, these findings support a role for vitamin D as a key player in the immunopathology of CRSwNP [11,22]. We hypothesized that CRSwNP, defined as a chronic inflammatory process of the upper respiratory system, could be influenced by Vitamin D deficiency. However, our study showed no association between serum vitamin D level and CRSwNP. In addition, there were no differences in serum level of 25(OH)D between males and females.

Clinical examinations revealed single or multiple grey polypoid masses in the nasal cavity. In patients with more severe bone erosion into the orbit and/or skull base, computerized tomography allows evaluation of the extent of the disease and is essential if surgical treatment is to be considered [11]. We analyzed the degree of bone erosion in all paranasal sinuses by computed tomography; in all of the subjects with NP, the level of 25(OH)D was normal, and we did not see any bone defect.

The active form of vitamin D, 1,25-dihydroxyvitamin D, is known to regulate calcium and phosphorus metabolism, and is thus a key player in bone formation [22]. Vitamin D is also a steroid hormone that may play a role in respiratory health. It has a potent immunomodulatory role, acting on cells of the immune system to inhibit pro-inflammatory cytokine production and induce antimicrobial peptide synthesis [23].

A study by Yaman at al. [24] concluded that in cases of unilateral polyps, histopathological examination of the entire material is mandatory. However, they stated that routine histological examination of bilateral nasal polyposis might possibly not be necessary in cases where the clinical assessment very clearly has not disclosed any unusual or suspicious signs. This is the first study to compare nasal polyps and

serum level of 25[OH]D. The limitations of our study were the small sample size and the fact that nasal polyp tissues were not evaluated. Further study must be performed to look at the tissue of nasal polyps for evaluation of the association between 25[OH]D and diagnosed CRSwNP.

## Conclusion

Vitamin D deficiency has been linked to a high rate of both infectious and inflammatory diseases, including those of the upper and lower airways. Our study showed no association between plasma 25-hydroxy vitamin D level and bone defect in patients with nasal polyposis living in Bolu, Turkey.

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