Assessment of the level of serum Vitamin D in Chronic Rhinosinusitis.

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Abstract

Background: The paranasal sinuses inflammation that lasts for twelve weeks is known as chronic rhinosinusitis (CRS). There is little mortality from CRS, but the disease has a heavy financial toll and negative effects on people's quality of life. Proposed explanations for this sinonasal mucosa chronic inflammation include ostiomeatal complex blockage, poor mucociliary clearance, nasal microbiota distortion, biofilm development, and atopy, however the precise causes remain unknown. Potent steroid hormone vitamin D regulates calcium homeostasis and bone mineralization. Furthermore, vitamin D has several anti-infectious and anti-inflammatory characteristics and may enhance immune responses. **Aim:** This work was conducted to assess the levels of serum Vitamin D in patients with CRS and to determine the significance and relationship of these levels with CRS severity and disease outcomes. **Methods:** This case control study included 100 participants; they were classified into two groups: Group (A) contain 50 patients (26 males and 24 females) with CRS. The range of their ages from 18 to 50 years, with a mean of 35±10.6

years, Group (B) comprised 50 healthy volunteers (25 males and 25 females) as controls. The range of their ages from 23 to 50 years, with a mean of 34.8± 9.6 years. **Results:** According to this study, controls had significantly greater vitamin D levels than CRS sufferers (P-value<0.001). Additionally, the study demonstrated a substantial correlation (P-value<0.05) between the presence of nasal polyposis and vitamin D levels. **Conclusion:** According to this research, Serum vitamin D levels are significantly associated with chronic rhinosinusitis (CRS). The results raise the possibility that vitamin D insufficiency contributes to CRS pathophysiology.

1. Introduction:

The nasal and paranasal sinuses are often affected by chronic rhinosinusitis (CRS), an inflammatory disorder that lasts for more than 12 weeks and causes symptoms such nasal blockage, face discomfort, nasal discharge, and hyposmia or anosmia [1]. Both the quality of life and the strain on healthcare systems throughout the globe are diminished by this illness [2].

Genetic predisposition, environmental exposures, and immunological responses all participate in the multifactorial causes of CRS [3]. Fat-soluble Vitamin D is widely recognized for its roles in preserving strong bones and blood calcium level. However, new evidence suggests that it may also have important impacts on immunomodulation and inflammation. [4]. Vitamin D may have a role in controlling immunological responses due to the expression of vitamin D receptors (VDR) on several immune cells [5].

Many studies have demonstrated that those with low vitamin D levels may be more likely to suffer from chronic inflammatory disorders, such as respiratory illnesses [6]. Serum vitamin D levels, however, have not been thoroughly investigated for their potential involvement in CRS development and progression. Although there isn't yet definitive proof, certain studies have shown that CRS symptoms are worse in low vitamin D levels patients.

The aim of this work is to assess the levels of serum Vitamin D in patients with CRS and to determine the significance and relationship of these levels with CRS severity and disease outcomes.

2. Patients and methods:

Study Design:

This research was planned as a case-control study carried out in the Otorhinolaryngology department at Beni-Suef University Hospital from June 2021 to June 2022. The ethical committee gave its approval to this project (FMBSUREC/06122020/Ahmed).

Study Population:

The study included two groups:

Patient Group (n=50): diagnosed with Chronic Rhinosinusitis (CRS).

Inclusion Criteria: Patients with CRS without nasal polyps (CRSsNP) and with nasal polyps (CRSwNP) who met the EPOS 2020 diagnostic criteria, aged 18-50 years.

Exclusion Criteria: Patients with immunologic disorders, chronic renal disease, severe liver disease, granulomatous disease, skeletal disorders, other systemic disorders affecting vitamin D absorption/metabolism, pregnancy, lactation, those taking multivitamins containing vitamin D, and those on systemic steroids or NSAIDs.

Control Group (n=50): Comprised of 50 healthy volunteers matched by age and sex to the patient group.

Data Collection:

All participants underwent:

1. History Taking: Emphasis on symptoms like nasal obstruction, discharge, reduced smell, or facial pain.

2. ENT Examination: Comprehensive ENT examination and endoscopic evaluation of the nose, sinuses, oral cavity, and pharynx.

3. Laboratory Investigations:

Serum levels of Vitamin D were detected using the Competitive Immunoluminometric Assay technique (MAGLUMI 25-OH Vitamin D (CLIA) kit, Shenzhen New Industries Biomedical Engineering Co., Ltd., China).

Procedure: 3 ml of venous blood was collected, centrifuged, and serum 25(OH) D levels were measured. The assay involves the use of a purified 25-OH Vitamin D antigen marked with N-(4-aminobutyl)-N-ethylisoluminol (ABEI) and a monoclonal antibody labeled with fluorescein isothiocyanate (FITC). The concentration of 25-OH Vitamin D was calculated using a calibration curve.

Other Tests: Renal and liver function tests were conducted on all participants to ensure

overall health and rule out conditions affecting vitamin D metabolism.

Statistical Analysis

Data analysis was conducted using version 25 of (SPSS). The scale was summarized using the Mean, standard deviation, median, and range, whereas percentages and frequencies were used to portray categorical information. For scale variables, we used an independent T-test, and for categorical variables, we used a Chi-squared test to compare the two groups. To detect the Vitamin D threshold for CRS prediction, the Receiver Operating Characteristic (ROC) curve was used. After taking vitamin D levels and other risk variables into account, the incidence of CRS was predicted using binary logistic regression analysis. For statistical purposes, a p-value below 0.05 was deemed significant, but a p-value of 0.05 or above was deemed non-significant.

Ethical considerations:

The Ethical Committee of Beni-Suef University examined and accepted the research protocol (approval number FMBSUREC/06122020/Ahmed). Every single person who took part in the research gave their informed permission.

3. Results:

The baseline features of the groups in this study did not differ as significantly as shown in **Table 1.**

Table (1) Baseline features of the groups studied:

Items	Cases (no=50) Group A	Controls (n=50) Group B	P-value
Age (mean±SD)	35±10.6	34.8±9.6	0.906
Sex Male Female	26(52.0%) 24(48.0%)	25(50.0%) 25(50.0%)	0.841
Occupation housewife accountant doctor engineer lawyer nurse student teacher unemployed worker	20(40%) 1(2.0%) 0(0.0%) 0(0.0%) 0(0.0%) 2(4.0%) 5(10.0%) 1(2.0%) 1(2.0%) 20(40.0%)	13(26%) 1(2.0%) 2(4.0%) 4(8.0%) 1(2.0%) 3(6.0%) 6(12.0%) 6(12.0%) 0(0.0%) 14(28.0%)	0.068
Smoking	15(30.0%)	11(22.0%)	0.362

Regarding the clinical presentation of the disease, in cases the results were as follows: 48 patients (96.0%) complained of nasal obstruction, 44 patients (88.0 %) complained of nasal discharge, 38 patient (76.0%) complained of facial pain and only 10 patients (20%) complained of reduction of smell. Regarding endoscopic examination findings, the results were as follows: twenty-six patients (52%) have nasal polyps, twenty-one patients (42%) have mucopurulent discharge, twenty-seven patients (54%) have edema of middle meatus, and forty patients (80%) have thickening of sinus mucosa. Most cases (90%) tried medical treatment for CRS and only 10% of cases underwent FESS operation. Regarding laboratory parameters, all cases had kidney and liver function tests within normal range.

Vitamin D level ranged from 7.2 to 36.3 ng/ml with a 20.6±9.5 ng/ml as a mean level in cases and ranged from 16.2 to 37.3 ng/ml with mean 29.7±5.1 in control group with a significant difference between both groups as shown in **table 2.**

Table (2) Comparison between the groups studied regarding the vitamin D level:

Vitamin D level ng/ml	Cases (no=50) Group A	Controls (n=50) Group B	P-value
Median (IQR) **mean±SD**	21.1(10.09-30.2) 20.6±9.5	30.1(25.9-33.8) 29.7±5.1	<0.001* (MW)
Deficiency [<10 ng/ml] **Insufficiency [10-29.9 ng/ml)]** **Sufficiency [30-100 ng/ml)]**	11(22%) 26(52%) 13(26%)	0(0%) 24(48%) 26(52%)	0.0004*

IQR: Interquartile Range *P-value is significant Mann-Whitney U test.

There was a significant relation between Vitamin D level and presence of nasal polyps (P-value<0.05) as shown in **Table 3.**

Table (3) Relation between CRS clinical presentation and Vitamin D level:

Items	Clinical presentation		P-value (MW)
	Absent **(mean±SD of Vit D)**	**Present** **(mean±SD of Vit D)**	
Nasal obstruction	20.3±2	21.1±9.3	0.645
Nasal discharge	25.2±9.9	20±9.3	0.214
Fascial pain	16.6±8.9	21.9±9.3	0.093
Reduction of smell	19.8±9.7	24.1±7.4	0.191
Nasal polyp	24.5±8.8	17±8.7	0.010*
Mucopurulent discharge	22.6±9.6	17.8±8.6	0.077
Edema of middle meatus	21.2±9.8	20.1±9.2	0.695

*P-value is significant

Vitamin D level had a significant role in prediction of CRS at a cut off <28.8 ng/ml with sensitivity 70%, specificity 66%, PPV 67.3%, NPV 68.7%, and Area under curve equals 0.765 as shown in **Figure 1.**
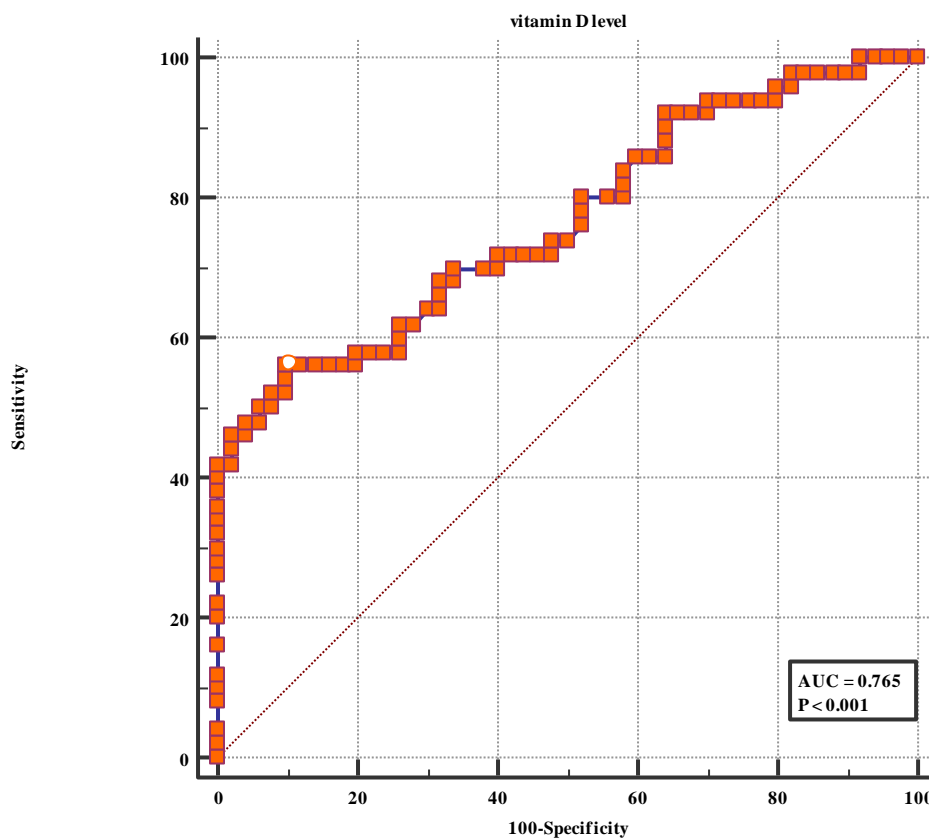

Figure (1) ROC curve for detection of the cut off for Vitamin D in prediction of CRS.

This study revealed that age, being male, and smoking were not statistically significant predictors of CRS in the presence of vitamin D levels. However, vitamin D levels were a significant predictor, and an increase in vitamin D level was associated with a lower probability of having CRS when other variables were held constant as shown in Table 4.

Table (4) Binary logistic regression analysis for prediction of CRS from different baseline characteristics in presence of Vitamin D:

Independent variables	P-value	Odds ratio (OR)	95% confidence interval (CI) for OR	
			Lower	Upper
Age	0.211	0.968	.921	1.018
Being male	0.449	0.647	.210	1.998
Smoking	0.338	1.933	.502	7.440
vitamin D level (ng/dl)	<0.001*	0.851	0.794	0.913

*P-value is significant   OR: odds ratio   CI: confidence interval

4. Discussion:

This study looked at how serum levels of vitamin D relate to chronic rhinosinusitis (CRS), and we found that low levels are significantly associated with CRS. This study adds to the increasing amount of data linking vitamin D insufficiency to CRS development and severity.

Consistent with other studies, this study finds that chronic inflammatory disorders may be linked to vitamin D insufficiency. Bavi et al. showed that patients with CRS had significantly decreased levels of blood Vitamin D compared to healthy controls [8]. Similarly, in our study, the mean Vitamin D concentration was 20.6±9.5 ng/ml in CRS patients, significantly decrease than the 29.7±5.1 ng/ml observed in the control group ($p < 0.05$). This significant difference supports the hypothesis that Vitamin D deficiency may be shared in the development and persistence of CRS.

Moreover, Cannell et al. found that Vitamin D plays a critical role in immune modulation and the preservation of mucosal barrier integrity, which are important in preventing chronic sinus inflammation [9]. Vitamin D receptors (VDR) are expressed on different immune cells, suggesting that Vitamin D influences immune function. It has been shown to regulate the expression of

antimicrobial peptides, reduce the production of pro-inflammatory cytokines, and enhance the integrity of epithelial barriers [4][5]. These mechanisms could potentially reduce the susceptibility to infections and inflammation within the sinonasal mucosa, thereby mitigating CRS symptoms.

According to our research, Vitamin D levels had a significant role in predicting CRS. At a cut-off level of <28.8 ng/ml, Vitamin D had a sensitivity of 70%, specificity of 66%, positive predictive value (PPV) of 67.3%, negative predictive value (NPV) of 68.7%, and an area under the curve (AUC) of 0.765. According to These results Vitamin D levels could be a helpful biomarker for determining individuals at risk of developing CRS. This is like the results of Jolliffe et al., who highlighted the potential of Vitamin D as a predictive marker for various chronic conditions [8].

Our analysis of the connection between Vitamin D levels and various clinical presentations of CRS revealed several noteworthy findings. Patients with nasal polyps had significantly decreased Vitamin D levels (17±8.7 ng/ml) compared to those without nasal polyps (24.5±8.8 ng/ml, p = 0.010). This result met in line with the study by Li et al., which reported that lower Vitamin D levels were associated with more

severe CRS presentations, particularly in patients with nasal polyps [10].

Patients with mucopurulent discharge, facial pain, and nasal obstruction also had reduced Vitamin D level however these differences not statistically significant. For instance, the mean Vitamin D level was lower in patients with nasal obstruction (21.1±9.3 ng/ml) compared to those without (20.3±2 ng/ml), though this difference was not statistically significant (p = 0.645). These results suggest a fact where Vitamin D deficiency might be associated with severe manifestations of CRS, warranting further investigation.

Vitamin D's immunomodulatory effects may explain its involvement in CRS. The presence of Vitamin D receptors (VDR) on different immune cells suggests that Vitamin D influences immune function. It has been shown to regulate the manufacturing of antimicrobial peptides, decrease the expression of pro-inflammatory cytokines, and enhance the integrity of epithelial barriers [4][5]. These mechanisms could potentially reduce the susceptibility to infections and inflammation within the sinonasal mucosa. Additionally, evidence from studies by Liu et al. suggests that Vitamin D enhances the innate immune response by regulating the expression of

antimicrobial peptides, which are crucial in combating respiratory pathogens [6].

The significant association between low Vitamin D levels and CRS underscores the importance of considering Vitamin D status in the management of CRS. Routine screening for Vitamin D deficiency in patients with CRS could be beneficial. Furthermore, Vitamin D supplementation may serve as an adjunctive treatment to improve clinical outcomes in these patients. Vitamin D supplementation may be beneficial for individuals with CRS and other respiratory infections, according to a meta-analysis by Martineau et al. [11]. Nevertheless, vitamin D supplementation for CRS treatment requires randomized controlled studies to prove its safety and effectiveness. Research conducted by Esposito et al. shed light on the intricate relationship between hereditary variables and vitamin D in respiratory disorders. This suggests that tailoring supplementing strategies to individual needs might be advantageous. [12].

5. Conclusion:

Vitamin D insufficiency may have a role in Chronic Rhinosinusitis since our research shows a strong correlation between low blood levels of the vitamin and the condition. Patient outcomes and disease burden might be improved if vitamin D insufficiency could be addressed in CRS patients by screening and treatment. To further understand vitamin D's function in CRS and to provide treatment recommendations based on scientific data, more studies are necessary.

Strengths and Limitations

Our study's strength lies in the fact that we used clear inclusion and exclusion criteria to keep the sample population consistent and reduce the likelihood of bias. Our results are more likely to be accurate since we used a control group that was age- and gender-matched.

Some limitations exist in our investigation, nevertheless. Limitations to the findings' applicability include a limited sample size and the study's focus on a single centre. To detect how vitamin D impacts the development and severity of CRS over time, longitudinal studies are required.

Recommendations

Further research with larger, multicenter studies is required to validate our results and determine the mechanisms linking Vitamin D deficiency and CRS. Investigating the results of different dosages and forms of Vitamin D supply on CRS symptoms and disease progression would also be valuable. Additionally, exploring the potential interactions between Vitamin D and other

factors involved in CRS, such as microbial infections and genetic predispositions, might offer a more thorough comprehension of the disease.

6. References:

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