

Clinical Correlation Of Vitamin D In Patients Of Chronic Rhinosinusitis With And Without Nasal Polyposis: A Cross Sectional Study In A Tertiary Care Hospital In Mandya

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Abstract

Background: Chronic rhinosinusitis (CRS) is a chronic inflammatory disease of the paranasal sinuses. Many factors including ciliary impairment, allergy, asthma, aspirin sensitivity and genetic factors are involved in the development of CRS. Clinical symptoms consist of nasal obstruction, congestion, facial pain and pressure, anosmia, headaches, excessive mucus production. CRS may be divided into two subtypes, with (CRSwNP) and without (CRSSNP) nasal polyposis. Vitamin D₃ acts as a steroid hormone that has anti-inflammatory effects and plays an important role in regulating dendritic cells (DC). Studies have shown that vitamin D₃ is able to stop the production of cytokines and inhibit differentiation of immune cells. This study helps us to understand the relationship between Vitamin D and Chronic Rhinosinusitis. This also helps us assess the requirement of Vitamin D supplementation in the management of patients with Chronic Rhinosinusitis and such as study has not been conducted previously in the locality of Mandya.

Materials and Methods: A Cross-Sectional study conducted in outpatient department, Department of Otorhinolaryngology. 78 diagnosed patients with Chronic Rhinosinusitis were included in the study. The diagnosis were made on the basis of routine investigations, Diagnostic nasal endoscopy and CT Nose and Paranasal sinuses. The blood samples were drawn from Chronic Rhinosinusitis patients for the measurement of Absolute eosinophil count and vitamin D levels which is routinely done for the above patients and correlation was made using Lund Mackay staging obtained from CT Nose and Paranasal sinuses.

Results: The study consisted of 78 patients of which 44 were males and 34 females with nasal obstruction as common symptom followed by headache. Vitamin D level of 30-100ng/ml is evaluated as sufficient, 10 to 30 ng/ml as insufficient, and below 10 ng/ml as a deficiency. Out of 78 patients, 10 patients had deficiency, 33 patients had insufficient levels. The mean serum vitamin D level was 17.36 ± 2.53 ng/ml. Serum vitamin D levels inversely correlate with Lund-Mackay scores. Lower vitamin D levels correlated with higher radiologic disease severity as measured by Lund-Mackay scale.

Conclusion: The results of the present study revealed was a significant relationship between the serum level of vitamin D and severity of the disease in patients with Chronic Rhinosinusitis ($p < 0.05$). Serum vitamin D levels inversely correlate with Lund-Mackay scores. Lower vitamin D levels correlated with higher radiologic disease severity as measured by Lund-Mackay scale. Regarding this, serum vitamin D levels could be added to the routine workup of patients suffering from Chronic Rhinosinusitis. Henceforth its necessary that Chronic Rhinosinusitis patients be supplemented with Vitamin D alongwith the regular steroid nasal spray and antihistamines.

Key Word: Chronic Rhinosinusitis, Vitamin D, Association, Lund-Mackay staging

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I. Introduction:

Chronic Rhinosinusitis (CRS) is a chronic inflammatory disease of the paranasal sinuses. It seems that many factors including ciliary impairment, allergy, asthma, aspirin sensitivity and genetic factors are involved in the development of CRS⁽¹⁾. Clinical symptoms consist of congestion, facial pain and pressure, anosmia, headaches, excessive mucus production and increased susceptibility to acute bacterial infection of the sinuses,

which may impair the quality of life. To confirm a diagnosis of CRS, symptoms must persist continuously for over 12 weeks and also include an objective sign of mucosal inflammation in computed tomography (CT) to provide a comprehensive view of the opacification within the paranasal sinuses and the nasal cavity or via the nasal endoscopy (NE) to directly visualise the nasal cavities and paranasal sinus ostia^(1,2). According to European Position Paper on Nasal Polyps and Chronic Rhinosinusitis (EPOS) guidelines⁽¹⁾, CRS may be divided into two subtypes, with (CRSwNP) and without (CRSSNP) nasal polyposis. Previous studies have tried to distinguish nasal polyp (NP) patients based on predominant inflammatory cell type/cytokine expression; the most common classification differentiates them into eosinophilic and non-eosinophilic CRSwNP. Increased activity of T-helper type 2 (Th2) cells leads to eosinophils recruitment and is mostly associated with CRSwNP, whereas Th1 increased activity leads to neutrophil recruitment and is more frequently associated with CRSSNP⁽³⁻⁶⁾.

Vitamin D has long been known to be an essential nutrient for the human body, particularly with regard to the absorption of dietary calcium and phosphate. Vitamin D has 2 major forms, cholecalciferol (vitamin D3) and ergocalciferol (vitamin D2). Both forms of vitamin D (D2 and D3) can be found in foods or supplements; however, only vitamin D3 is produced in skin and it is the only naturally occurring form of vitamin D in humans and other animals. Human vitamin D endocrine system includes 3 forms of vitamin D, namely vitamin D3, calcidiol (25(OH)D3), and calcitriol (1,25(OH)2D3). Vitamin D3 is the naturally occurring form of vitamin D, derived from either dietary sources or formed from 7-dehydrocholesterol (7-DHC or provitamin D3) by the skin. 25(OH)D3 is a prohormone in the blood that is made directly from vitamin D3, and it is also what is directly tested to measure vitamin D3 in the blood (To clarify, 25(OH)D levels usually contain both the vitamin D2 and D3 forms). 25(OH)D3 is an active form of vitamin D3. 1,25(OH)2D3, which is made from 25(OH)D3, is the hormone form of vitamin D3 and the most biologically active metabolite of vitamin D3. Upon exposure to ultraviolet B radiation (wavelengths of 290–315 nm), 7-DHC transforms into vitamin D3, which enters the circulation and binds vitamin D-binding protein. In the classic vitamin D3 pathway, vitamin D3 then undergoes hydroxylation in the 25-position by vitamin D-25-hydroxylase (25-OHase) in the liver to form 25(OH)D3 and in the 1-position by 25-hydroxyvitamin D-1-alpha-hydroxylase (1 α -OHase) in the kidney (functioning as an endocrine gland) to form 1,25(OH)2D3, which is the form that promotes intestinal absorption of calcium and phosphate⁽⁷⁾.

Several studies suggest that vitamin D3 acts as a steroid hormone that has anti-inflammatory effects and plays an important role in regulating dendritic cells (DC). The mechanism of immune system modification by vitamin D3 is similar to other corticosteroids. Various studies have shown that vitamin D3 is able to stop the production of cytokines and inhibit differentiation of immune cells. It prevents maturation and differentiation of monocytes to DCs, increases interleukin-10 production by DCs and thereby decreases DC stimulation of Th1/Th2 differentiation, resulting in higher tolerance. Active (1,25)OH-vitamin-D3 also recruits interleukin-10, producing T-regulatory cells which could help reduce inflammation. In previous studies, an inverse relationship was found between serum vitamin D levels and the level of dendritic cells in CRSwNP patients⁽⁸⁾.

This study helps us to understand the relationship between Vitamin D and Chronic Rhinosinusitis. This also helps us assess the requirement of Vitamin D supplementation in the management of patients with Chronic Rhinosinusitis and such as study has not been conducted previously in the locality of Mandya.

II. Materials And Methods

This was a cross-sectional type of study conducted at tertiary care centre for a period of 6 months from December 2023 to May 2024. Data collection was started after approval from the Institutional Ethics Committee of Mandya Institute of Medical Sciences. Informed written consent was taken from the study subjects after explaining to them the plan and intention of the study in the language best known to them.

Study Design: Cross-sectional study

Study Location: Department of Otorhinolaryngology at Mandya Institute of Medical Sciences, Mandya, Karnataka, India.

Study Duration: December 2023 to May 2024

Sample size: 78

Sample size calculation: Here, $N = Z^2 \times P(1-P)$

d2

Here,

Z= standard normal variate(1.96)

P= 55%(Insufficient Vitamin D levels in Chronic Rhinosinusitis patients)(9)

d= relative error(20% of P)= 20/100 of 55 = 11

N= 1.96x1.96x55x45/11x11 = 78

Subjects & selection method: Patients with symptoms and signs of Chronic Rhinosinusitis presenting to Out-patient department, ENT, MIMS, Mandya.

Inclusion Criteria:

1. Patients with symptoms and signs of Chronic Rhinosinusitis
2. Patients willing to give informed consent to participate in the study.

Exclusion Criteria:

1. Patients with history of vitamin D supplementation, anticonvulsant use, 1 or more cycle of low or high oestrogen OCP usage in last 3 months or corticosteroid use in the last 3 months.
2. Patients with history of any chronic disease associated with low vitamin D3 serum levels such as chronic renal, cardiac, and liver diseases and malnutrition.
3. Patients who did not give informed consent.

Procedure Methodology:

Patients with history of nasal obstruction, anosmia, headache, nasal discharge for a period of over 3 months who presented to the OPD was examined. Detailed history regarding onset, duration, progression of nasal discharge, nasal obstruction, headache and anosmia was noted in the case proforma. Anterior and posterior rhinoscopic examination was done and findings were noted in case proforma. Patient was subjected Diagnostic Nasal Endoscopy and Computed Tomography of Nose and Paranasal sinuses. Based on the Clinical assessment and Investigations a diagnosis of Chronic Rhinosinusitis with or without Sinonasal Polyposis was made and disease severity assessed using the Lund Mackay staging system. Absolute Eosinophile Count was also done to clarify allergic status of patients. Serum level of 25-hydroxy Vitamin D was measured which is routinely done for patients with Chronic Rhinosinusitis and results were observed in comparison with the normal serum 25- hydroxy Vitamin D levels. These results were then subjected to statistical analysis.

Lund Mackay Staging system

Sinus System	Left	Right
Maxillary	0-2	0-2
Anterior Ethmoidal	0-2	0-2
Posterior Ethmoidal	0-2	0-2
Sphenoidal	0-2	0-2
Frontal	0-2	0-2
Osteomeatal complex	0 or 2	0 or 2
Total points for each side	0-24	0-24

Scoring for all sinus systems: 0- no abnormalities, 1- partial opacification, 2- total opacification for Osteomeatal complex: 0- not occluded, 2- occluded

Figure 1. Stages of sinusitis.

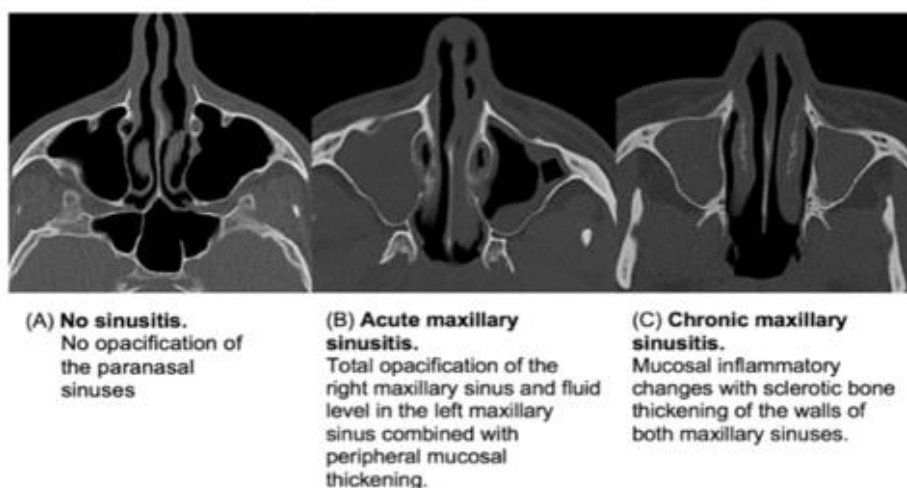


Figure 2. Grading of disease severity in patients with sinusitis.



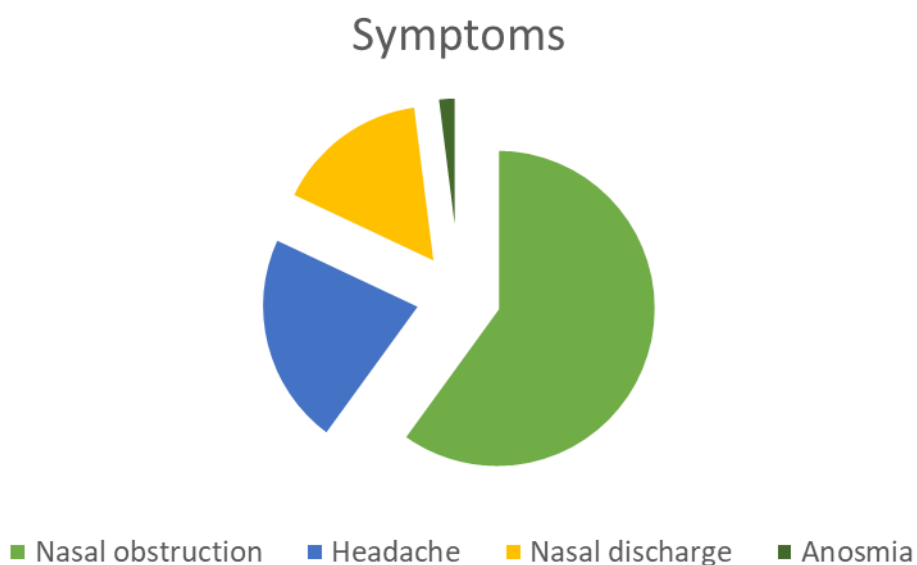
Statistical Analysis:

All collected data were entered in excel sheet and the data was statistically analysed by using SPSS software. Descriptive statistical tests like frequency and proportion for categorical data. Mean, standard deviation for quantitative data and inferential statistical tests like Chi square test and Paired t-test were used to find significance of correlation between Serum level of 25-hydroxy Vitamin D and disease severity in patients of Chronic Rhinosinusitis. Significance level was considered at $p < 0.05$.

III. Result

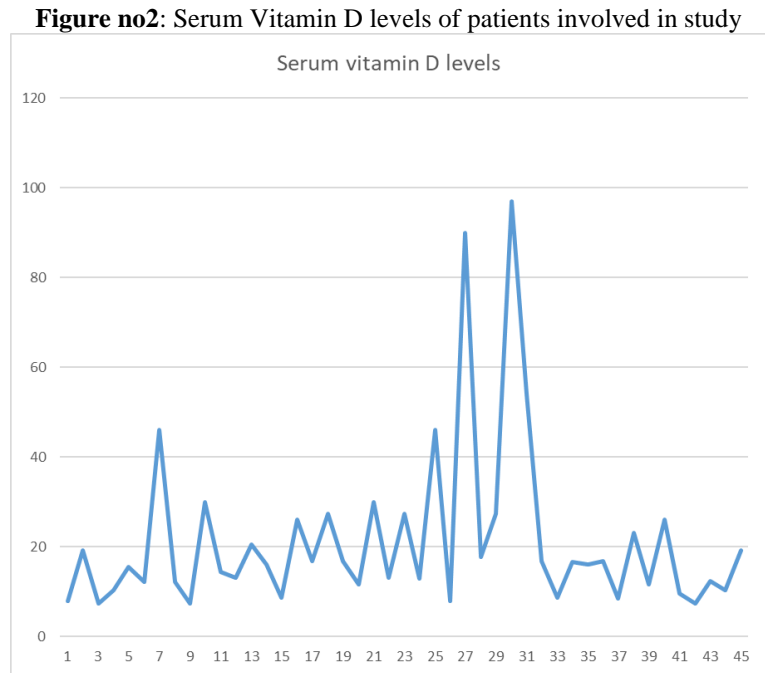
The study consisted of 78 patients of which 44 were males and 34 females with nasal obstruction as common symptom followed by headache.

Figure no1: Symptoms seen in patients involved in study



Vitamin D level of 30-100ng/ml is evaluated as sufficient, 10 to 30 ng/ml as insufficient, and below 10 ng/ml as a deficiency.

Out of 78 patients , 10 patients had deficiency , 33 patients had insufficient levels.
The mean serum vitamin D level was 17.36 ± 2.53 ng/ml.



MILD(1-6)	MODERATE (7-12)	SEVERE(13-24)
25 patients	35 patients	18 patients
32%	45%	23%

Table no1: Lund-Mackay staging of patients involved in study

Lund Mackay staging	Serum Vit D levels in Males	Serum Vit D levels in Females
Mild(1-6)	19.61 ± 5.47	23.49 ± 5.47
Moderate(7-12)	17.61 ± 5.47	12.2
Severe(13-24)	12.02 ± 5.47	20.5

Table no2: Correlation Of Lund Mackay staging with serum vitamin D levels

Serum vitamin D levels inversely correlate with Lund-Mackay scores. Lower vitamin D levels correlated with higher radiologic disease severity as measured by Lund-Mackay scale.

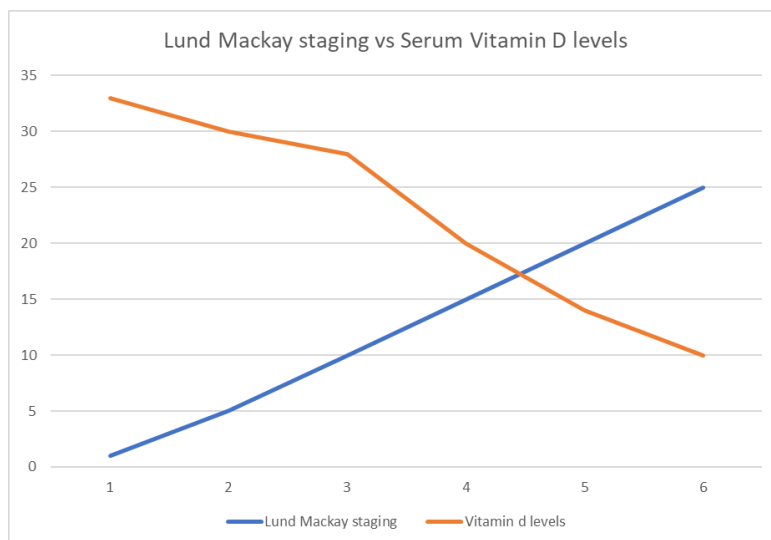


Figure no3: Association between Lund-Mackay staging and serum Vitamin D

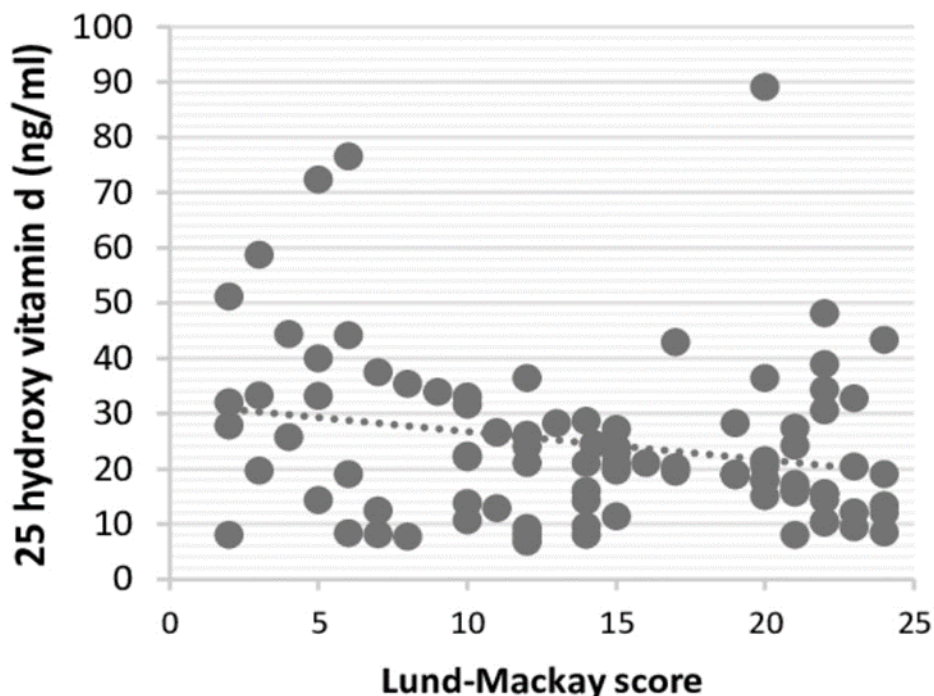
IV. Discussion

This study evaluated the serum vitamin D levels in patients with Chronic Rhinosinusitis and its correlation with disease severity in Chronic Rhinosinusitis patients.

Chronic rhinosinusitis (CRS) is a chronic inflammatory disease of the paranasal sinuses. It seems that many factors including ciliary impairment, allergy, asthma, aspirin sensitivity and genetic factors are involved in the development of CRS.

Vitamin D is a fat-soluble vitamin and functions primarily in the regulation of the calcium and phosphorus balance. Growing body of evidence suggests that VD and vitamin D receptor (VDR) are directly involved in T-cell antigen receptor signaling, indicating their role in the anti-inflammation processes.

In case of chronic inflammation like that seen in patients with Chronic Rhinosinusitis decrease in vitamin D levels have been noted.



Various studies done in the past like Schlosser R J et al in USA in 2014 to determine the association between Vitamin D3 levels and Chronic Rhinosinusitis showed insufficient Vitamin D3 levels in 55% of patients who underwent the study. Also Computed Tomography (CT) scan of nose and paranasal sinuses showed more severe mucosal disease in patients having Lower Vitamin D3 levels(9). Other studies like the cross sectional study conducted by Habibi A F et al in Iran in 2019 involving 80 patients with nasal polyposis and 80 healthy subjects showed a correlation of increasing trend of disease severity with decreasing levels of serum Vitamin D levels and increasing CRP levels(10). Another study conducted by Chandrakar A K et al in Puducherry, Tamil Nadu in 2020 involving 117 Adults showed significantly lower serum 25-hydroxy Vitamin D3 levels in CRS patients as compared to non CRS patients(11). Another study like the one conducted by Shrestha P et al in New Delhi in 2022 in order to assess the association between severity of disease in CRSwNP patients and serum Vitamin D levels showed decreased Vitamin D levels and High Absolute Eosinophile Count (AEC) in the diseased group(12).

V. Conclusion

The results of the present study revealed was a significant relationship between the serum level of vitamin D and severity of the disease in patients with Chronic Rhinosinusitis($p < 0.05$). Serum vitamin D levels inversely correlate with Lund-Mackay scores. Lower vitamin D levels correlated with higher radiologic disease severity as measured by Lund-Mackay scale. Regarding this, serum vitamin D levels could be added to the routine workup of patients suffering from Chronic Rhinosinusitis. Henceforth its necessary that Chronic Rhinosinusitis patients be supplemented with Vitamin D alongwith the regular steroid nasal spray and antihistamines.

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