

## Serum Vitamin D<sub>3</sub> Level in Migraine Patients- A Hospital based Case Control Study.

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### ABSTRACT

#### Introduction:

The most prevalent type of headache is migraine and it typically presents with a unilateral, pulsatile severe headache lasting from 4 to 72 hours accompanied by nausea, photophobia, and transient neurological symptoms. Also, in recent years Vit D3 deficiency has emerged as a global public health problem amounting to about 30-80% of children and adults having Vit. D3 deficiency. The study was to be taken for the role of vitamin D3 in the severity of migraine patients.

#### Materials and Methods:

This case-control study was conducted in the Department of ENT and Biochemistry, VIMSAR Burla from Jan 2023 to Jun 2023. Age groups of 10 - 60 years of either sex (sample size 65 each) were examined clinically and the severity of migraine was evaluated by MIDAS Score and Biochemical estimation of serum vitamin D3 level was done by CLIA analyzer (Electra FA). Statistical analysis was performed with SPSS software version 21.0 (SPSS IBM corporation, Armonk. New York). The p-value < 0.05 was taken as statistically significant.

#### Results:

A total of 65 subjects each from case (clinically diagnosed cases of migraine patients) and control group were evaluated. In the present study, 21 males and 44 females were from the case and 22 males and 43 females were included in control groups. The mean age of males and females were (43.23± 2.3) and (32.58 ± 2.4) in case (42.23± 2.5) and (36.58 ± 2.6) were in control groups. Serum vitamin D3 level was lower in case groups (18.01 ng/mL) and in control, it was (34.09 ng/mL). The association of serum vitamin D3 concentration with case and control was highly significant (p<0.05).

#### Conclusion:

There was a significant deficiency of Vitamin D3 in migraine patients as compared to control where serum vitamin D3 levels were normal.

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**Keyword:** Migraine, Serum vitamin D<sub>3</sub>

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### Introduction

Deficiency of vitamin D3 is a worldwide problem. When compared according to the demographics females in their 20's and 30's are affected the most [1, 2]. Although in the eastern

countries there is excellent sun exposure this deficiency exists there too in the majority population [3]. Vitamin D3 is not only required for bone maintenance but it is also required for immunity [4, 5]. Vitamin D3 is a stimulator of the vasodilator chemical and it also induces phagocytic cells in the body [6]

Migraine is prevalent amongst one-tenth of the population worldwide. It is basically a disorder of neurons of the brain [7]. The characteristic symptom of migraine is extreme pain in the head that worsens with an increase in physical movements. It is associated with the inability to tolerate high-intensity light and sound; other symptoms include vomiting [8]. It is reported in various studies that migraine can be associated with other co-morbid diseases which include cardiovascular disease, epilepsy, asthma, stroke, and depression [9]. Frequently, insomnia is also associated with migraine. A syndrome known as restless leg syndrome is found in migraine patients [10]. This syndrome has a characteristic symptom where the patient cannot keep the leg in the same position for longer duration, this occurs generally when the patient is at rest and mostly at night [11]. A study has reported that the restless leg syndrome is associated with migraine in the patients and this is found in 11-50% of the population [12]. This study aims to evaluate the role of Vitamin D3 deficiency in patients with migraine.

**Materials and Methods**

This case-control study was conducted at the Department of ENT and Biochemistry VIMSAR Burla from Jan 2023 to Jun

2023 for the duration of 6 months. The study protocol was approved by the Institutional Ethical Committee having approval number 179-2022/I-F-O/65/ Dt.05.08.2022 and informed consent was obtained from the patients.

The sampling technique was systematic random sampling. Age groups of 10 - 60 years of either sex were evaluated clinically at the outpatient Department of ENT. Biochemical analysis was done in the Department of Biochemistry VIMSAR Burla. The aim as well as the steps of the study was clearly explained to each patient. The migraine was assessed as per MIDAS scores.

***Inclusion Criteria-***

- All clinically diagnosed cases of migraine between the age group of 10-60 years attending OPD of the department of ENT, VIMSAR, Burla

***Exclusion criteria-***

- Patients on Vitamin- D3 supplementation for other causes.
- Patients with other systemic diseases - IDDM, Thyroid disorders, Hypertension, Refractive error, or any intracranial disorder, etc.

***Biochemical Analysis-***

*Serum vitamin D3 analysis-* After taking all aseptic precautions 2mL of venous blood of the patients was collected from antecubital veins. After centrifugation serum was separated out and estimation of vitamin D3 was done within 24 hours in a fully automated CLIA analyzer (Electra FA) as per the manufacturer's instructions [13]. The reference range of serum vitamin D3 level (ng/mL) is shown in [Table 1]

**Table 1: Reference range of serum vitamin D3 level (ng/mL) as per manufacturer's instructions**

Serum Vitamin D <sub>3</sub> level	Reference range (ng/mL)
Deficient	0-10
Insufficient	10-30
Sufficient	30-100
Toxicity	>100

*Anthropological parameters* - For Body Mass Index (BMI), weight and height of the subjects were calculated using Quetelet index as, Body weight in (kg) divided by Height (m<sup>2</sup>). Body mass index was used for defining overweight and obesity [14].

### Statistical Analysis

Recorded data were entered, checked and analyzed using SPSS version 21.0 (SPSS IBM corporation, Armonk, New York). Student t test was done to analyze between two variables. The p-value <0.05 was considered to be significant. Quantitative data were expressed as a mean ± standard deviation (SD). Data such as age, gender, sun exposure and residential area were expressed as frequency and percentage.

### Results

The demographic characteristics of migraine patients were shown in [Table-2]. This study included 65 patients in each group. 21 (30.20%) males and 44(67.69%) females were from case and 22 (33.84%) males and 43(66.15%) female were included in control groups. The mean age of males and females were (43.23± 2.3) and (32.58 ± 2.4) in case (42.23± 2.5) and (36.58 ± 2.6) were in control groups. In this study maximum were of normal weight (Kg) i.e., 46(70.76%). And 11(16.92%), 06(9.23%) and 04(6.15%) were overweight, underweight and obese respectively in Case But in control it was 47(72.30%). And 10(15.38%), 09(13.84%) and 01(1.53%) were overweight, underweight and obese respectively. Among the subjects 15.38% were come from urban area and 84.61% from rural in case groups where as in control groups 13.84% from urban and 86.15% were come from rural areas. The patients were mostly of low economic status that was 53.54% to 55.38% as depicted in table-2.

**Table 2: Social demographic characteristics of case and control groups**

Age in years		
Male (Mean ± SD)	43.23± 2.3	42.23± 2.5
Female (Mean ± SD)	32.58± 2.4	36.58± 2.6
Gender		
Male N (%)	21(30.20%)	22(33.84%)
Female N (%)	44 (67.69%)	43(66.15%)
BMI (Kg/m <sup>2</sup> ) (WHO Indian standard)		
Normal or less (18.5 ≤ 24.9)	46(70.76%)	47(72.30%)
Overweight (≥25-29.9)	11 (16.92%)	10 (15.38%)
Obese (≥ 30)	06(9.23%)	09(13.84%)
Under weight (≤ 18.5)	04 (6.15%)	01 (1.53%)
Sun Exposure		
> 2 hours per day N (%)	46 (70.76%)	42 (64.61%)
< 2 hours per day N (%)	19 (29.23%)	23 (35.38%)
Place of residence		
Urban	10(15.38%)	09(13.84%)
Rural	55(84.61%)	56(86.15%)

Percentage of different features of migraine in case group patients depicted in [Table-3]. These symptoms like headache, nausea, family history, menstrual effect, duration of headache and level of disability were not statistically significant ( $p < 0.05$ ) but intensity of pain was statistically significant ( $p < 0.05$ ).

**Table 3: Percentage of different features of migraine in case group patients**

Subject (Case)	N (%)	P- value
<b>Headache</b>	65(100%)	
<b>Nausea</b>		
Yes	41(63.07%)	0.221
No	24(36.92%)	
<b>Family history</b>		
Positive	21(32.30%)	0.312
Negative	44(67.69%)	
<b>Menstrual effect</b>		
Yes	09(13.84%)	0.063
No	35(53.84%)	
<b>Intensity of pain (MIDAS Score)</b>		
No/ Little	00(0%)	0.021*
Mild	05(7.69%)	
Moderate	35(53.84%)	
Severe	25(38.46%)	
<b>Duration of headache</b>		
Up to 6 hrs	32(49.23%)	0.210
6hrs-24hrs	21(32.30%)	
24hrs-72hrs	12(18.46%)	
<b>Level of disability</b>		
None	06(9.23%)	0.105
Mild	37(56.92%)	
Marked	18(27.69%)	
Confined to bed	04(6.15%)	

The association of serum vitamin D<sub>3</sub> concentration with case and control shown in [Table-4] and was significant statistically ( $p$ - value 0.05).

**Table 4- Association of Serum vitamin D<sub>3</sub> level and migraine in cases and control groups**

Parameter	Case (N=65)	Control (N=65)	p- value
Serum vitamin D <sub>3</sub> level (ng/mL) (mean ±SD)	18.1± 1.992	34.09 ± .598	<b>0.0001*</b>

## Discussion

This study has successfully established a notable positive correlation between serum concentrations of vitamin D and the occurrence of migraines. Nevertheless, a notable correlation was observed between serum vitamin D levels and the intensity of migraines. A study was undertaken wherein two patients had migraine attacks either during their menstrual period or before that. The patients in this study exhibited inadequate levels of vitamin D. Following a two-month therapy regimen involving intake of calcium and vitamin D tablets at a dose of 1600 to 1200 IU per day, a noteworthy decrease in both migraines and symptoms associated with premenstrual syndrome was found. A further study conducted on elderly women who had migraine and vitamin D deficiency demonstrated that the administration of calcium and vitamin D supplements resulted in a reduction in the number and length of migraine attacks. In a study conducted, the researchers found that the average incidence of low levels of vitamin D was 26% in a total of 267 patients who were evaluated for severe and long-term pain, which included 25 individuals specifically experiencing headaches [13]. In a separate investigation, there was a notable correlation between severe pain and vitamin D levels was reported. However, this correlation was not evident in the male population. An inverse relationship was found between migraine occurrence and vitamin D levels, patients with high levels of vitamin D did not have severe migraine attacks [14]. This relationship was found to be true irrespective of gender, environmental condition and geographical location, the p-value was less than 0.05. The study found that patients with headaches exhibited decreased serum levels of vitamin D compared to patients without headaches.

The study demonstrated a correlation between individuals diagnosed with migraine and diminished levels of vitamin D [15] According to a study, a total of 14 percent of individuals diagnosed with chronic migraine exhibited plasma vitamin D levels that were equal or lower than 20 ng/ml. Additionally, twenty-five per cent of patients displayed serum vitamin D levels ranging between 20 and 30 ng/ml [6,7]. The primary factors contributing to the occurrence of headaches involve the possible sensitivity of both second and third-order neurons as a result of persistent stimulation of sensory receptors located in the periosteal covering. Insufficient levels of magnesium may be another potential explanation for headaches in persons with vitamin D deficiency. Additional methods involve the absence of vitamin D receptors, 1 hydroxylase (the enzyme accountable for the synthesis of the biologically active form of vitamin D), and vitamin D binding protein within the cerebral region, specifically the hypothalamus [13].

In our study we also found mean serum vitamin D<sub>3</sub> level to be 18.01 in migraine patients which is compared to very low to the serum vitamin D<sub>3</sub> level of control group which was 34.09. So, our study finding is similar to the above-mentioned studies.

## Conclusion

This study found an inverse relation between disease severity and vitamin D<sub>3</sub> level, which indicates the involvement of vitamin D<sub>3</sub> in migraine pathogenesis.

## Recommendation

So further study is needed to evaluate the definite role of vitamin D<sub>3</sub> in migraine so that serum vitamin D<sub>3</sub> estimation can be used as an early marker in migraine patients and can be considered as an additional therapy in migraine patients

## Limitation:

The main limitation in the present study was that the duration of study period was six months and patients who came for two days in a week for six months were selected. Further large-scale studies with longer duration should be undertaken to confirm the findings of our study.

## List of abbreviation:

MIDAS- Medical Information Data Analysis System

IDDM- Insulin dependent diabetes mellitus

IU- International Units

BMI- Body mass index

SPSS- Statistical program for social sciences

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## Conflicts of interest

There are no conflicts of interest.

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