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Exploring the association between age-related macular degeneration and 25-hydroxy vitamin D level: A causal connection

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ABSTRACT

Background: Age-related macular degeneration, or AMD, is a common cause of permanent loss of vision that mostly affects elderly population. Complex interplay between genetic and environmental variables are part of the pathogenesis. Vitamin D, namely 25-hydroxyvitamin D [25(OH)D], has drawn interest because of its anti-inflammatory and protective characteristics, which may contribute to AMD. Given the current situation of its increasing incidence and the possible significance of vitamin D for retinal health, the purpose of this research was to examine the relationship between blood 25(OH) D levels and AMD severity in the Indian population.

Materials and Methods: As per the criteria outlined in Age-Related Eye Disease Study (AREDS), 112 patients in a cohort study were divided into three AMD severity groups at the Eye Department of ASCOMS Medical College in India. Clinical evaluations, the gathering of demographic data, and biochemical studies of serum 25(OH) D levels were carried out. Descriptive statistics, correlation analyses, logistic regression, subgroup analysis, and comparisons with other research conducted internationally were among the statistical analyses performed.

Results: The study showed a substantial correlation between serum 25(OH) D levels and the severity of AMD compared to early-stage instances (Group 1: mean = 30.5 ng/mL, SD = 4.1), patients with advanced-stage AMD (Group 3) had lower 25(OH) D levels (mean = 25.3 ng/mL, SD = 4.7). In line with previous research, two important risk factors for AMD were found: a history of smoking and a family history of the disease.

Conclusion: In summary, this study provides important new information on the relationship between the severity of AMD and serum 25(OH)D levels in the Indian population. This is consistent with the data that is now available, which indicates that the retina and retinal pigment epithelium have vitamin D receptors. Despite being observational, the results encourage further research into the underlying processes and the causal link. The risk factors that have been found highlight how crucial it is for public health efforts to focus on modifiable variables like smoking. In summary, this study establishes the groundwork for further investigation, which might lead to the development of innovative approaches for managing and preventing AMD.

1. Introduction

Millions of people worldwide are impacted by age-related macular degeneration (AMD), which is one of the main causes of permanent visual loss in the aged population.[1,2] This complex condition involves the gradual deterioration

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of the macula, a small region at the retina's center, as a result, central vision is compromised. Although the precise cause of AMD is still unknown, it is generally accepted that environmental and genetic factors have a role in the disease's onset and progression. Recent years it has been seen a significant increase in interest in the function of vitamin D, or more precisely, 25 Hydroxy D levels as a marker of vitamin D. It is a physiologically active version of the vitamin, also acts as a steroid hormone and has been shown to have a number of advantageous qualities. These include its function in preserving calcium and phosphorus levels for normal bone growth, as well as its anti-inflammatory, antiangiogenic, and anti-carcinogenic properties.[3,4] Additionally, studies show that vitamin D regulates the production of neuron growth factor (NGF), which supports the neurological system and protects proteins and cellular membranes from oxidative damage.[5,6] In addition to being necessary for the healthy operation of many organs and tissues, this important vitamin also has anti-aging properties.Although vitamin D is well recognized for its critical function in maintaining calcium homeostasis and bone health, it also has a variety of pleiotropic effects on several bodily systems, such as immune system modulation, inflammatory management, and cell proliferation and differentiation.[7]

Given that the retina and the retinal pigment epithelium (RPE), which are both essential to the pathogenesis of AMD, have vitamin D receptors, several investigations have looked into the possible relationship between vitamin D levels and AMD.[8] According to some theories, vitamin D may protect against AMD by reducing inflammation, oxidative stress, and angiogenesis—all of which are crucial to the pathophysiology of the condition.[9] Vitamin D supplementation has been shown in animal studies to reduce retinal inflammation via a notable reduction in macrophage counts and the build-up of intracellular beta-amyloid, which acts as a biomarker of aging in retinal cells.[10] These findings suggest that vitamin D may play a part in protecting the retina from the damaging effects of aging and maintaining its optimal function. This implies that these systems may be involved in the aging process and retinal degeneration caused by a vitamin D shortage.

In order to investigate the potential of a causal relationship between AMD and 25(OH)D levels, the purpose of this study is to critically review the body of current research and give a thorough analysis of the relationship between the two.

2. Materials and Methods

The present observational research was carried out in accordance with the Declaration of Helsinki standards at the Eye Department of ASCOMS Medical College, India. The institutional ethics committee granted ethical approval, and each participant provided signed informed consent.

The vitamin D levels of 112 individuals with age-related macular degeneration (ARMD) who were under active monitoring at our institution were retrospectively analyzed. Based on the severity of their illness, patients with ARMD were divided into three groups using the Age-Related Eye Disease Study (AREDS) categorization criteria.

2.1. Classification of groups

1. Patients in Group 1 have at least one eye affected by pigment abnormalities or more than 20 significant drusen or widespread tiny (Early-Stage ARMD).
2. Individuals with at least one eye exhibiting huge drusen, extensive moderate drusen, or geographic atrophy not involving the centre belonged to Group 2 (Intermediate-Stage ARMD).
3. Individuals with geographic atrophy including the fovea, choroidal neovascularization, non-drusen retinal pigment epithelium (RPE) detachment, or subfoveal drusen in at least one eye, as shown by visual acuity (VA) less than 20/32, are classified as Group 3 (Advanced-Stage ARMD).

Each patient had a comprehensive ophthalmological examination, which included measuring intraocular pressure using the Snellen chart, examining the fundus, doing biomicroscopic tests, and determining best-corrected visual acuity (BCVA). Moreover, imaging using optical coherence tomography was used. Data on age, gender, job, lifestyle choices (including smoking status), eating habits, and family history of AMD were collected by structured interviews and questionnaires.

2.2. Sample collection

Blood samples were obtained in polypropylene tubes within 1.5 hours after withdrawal, and they were centrifuged for 10 minutes at 1500×g. The total blood 25-hydroxyvitamin D levels were determined using an autoanalyzer employing the chemiluminescence immunoassay (CLIA) technology, in accordance with the manufacturer's instructions. Vitamin D levels should be ≤20 ng/mL to be deemed deficient, 20–30 ng/mL to be deemed inadequate, and ≥30 ng/mL to be deemed sufficient, under laboratory standards.

2.3. Data analysis

After the data were entered into a Microsoft Excel 2007 spreadsheet (Microsoft Corporation, Redmond, Washington, USA), statistical analysis was performed using the Statistical Package for Social Sciences (SPSS), version 26.0 (SPSS Inc., Chicago, Illinois, USA). Continuous data were shown as mean and standard deviation (SD), whereas categorical and binary variables were presented using frequencies and percentages. The set criterion for statistical significance was $p < 0.05$.

Using correlation analysis, the prevalence, severity, and subtypes of age-related macular degeneration (ARMD) were examined in relation to blood vitamin D levels. The odds of acquiring ARMD in relation to various vitamin D levels were calculated using logistic regression models, which take into consideration potential confounding factors such age, gender, smoking status, and dietary patterns. Subgroup analyses were performed to assess the impact of vitamin D on different stages of ARMD and investigate any gender-based disparities.

3. Results

The study included a total of 112 patients, who were categorized into three groups based on the severity of their age-related macular degeneration (ARMD). In the study, participants were divided into three distinct groups reflecting the progression stages of age-related macular degeneration. The demographic breakdown revealed a balanced gender distribution across the stages, with a slight male predominance in the early stage. Notably, a consistent decline in smoking habits was observed as the severity of the condition increased. Additionally, approximately one-third of the participants in each group reported a familial predisposition to the condition, underscoring the potential genetic component of ARMD. However, family history of AMD is an established risk factor for the disease, so its inclusion in the analysis is relevant for understanding potential genetic influences on AMD severity. A p-value less than <0.05 was considered statistically significant. These findings are summarized in the accompanying table, which provides a detailed numerical overview. (Table 1)

The study's findings highlighted a descending trend in serum 25(OH)D levels as the severity of age-related macular degeneration increased. The early-stage group maintained the highest average vitamin D concentration, while the advanced-stage group recorded the lowest. Statistical analysis confirmed the significance of the differences observed among the groups, with the early-stage group's results being notably distinct. These insights are further detailed in the provided table, which encapsulates the quantitative data (Table 2)

These results suggest that there is a statistically significant association between the severity of ARMD and serum 25(OH)D levels. Patients with advanced-stage ARMD tend to have lower levels of 25(OH)D compared to those with early-stage ARMD. The findings indicate a potential relationship between vitamin D deficiency and the progression of ARMD.

4. Discussion

Age-related macular degeneration (AMD) is a complex multifactorial disease that represents a considerable public health concern due to its widespread occurrence and the burden it poses on the elderly population. Accumulating evidence indicates that reduced levels of plasma micronutrients such as carotenoids, lutein and zinc can hasten the progression of ARMD. Conversely, higher consumption of antioxidants appears to offer protection against the advancement of ARMD.[11] While the etiology of AMD remains incompletely understood, recent findings indicate that vitamin D plays a protective role in age-related macular degeneration (ARMD) by influencing various aspects of ARMD pathophysiology.[12] Researchers have investigated the connection between serum 25(OH)D3 concentrations and AMD through cross-sectional studies. The initial study, which analyzed a large cross-sectional dataset, found a link between lower serum vitamin D3 levels and an increased risk of early AMD. However, this study did not find a significant association with advanced AMD.[13]

Our study, conducted in the Indian population, examined the association between AMD severity and serum 25(OH)D levels. The results demonstrate a statistically significant relationship between the severity of AMD and vitamin D levels, with advanced-stage AMD patients exhibiting lower 25(OH)D levels compared to those with early-stage AMD. These observations imply that vitamin D may play a significant role in the pathophysiology of AMD and raise intriguing questions about the potential benefits of maintaining adequate vitamin D levels to mitigate AMD progression. The significance of these findings is consistent with prior studies that have explored the potential link between AMD and vitamin D.[13–15] Previous investigations examining the correlation between vitamin D levels and ARMD has produced inconsistent findings. For example, Parekh et al. found a decrease in the occurrence of ARMD among participants using vitamin D supplements, but an extensive investigation carried out in Israel found no correlation between vitamin D levels and ARMD. Furthermore, in a systematic review conducted by Wu et al. revealed no connection between vitamin D levels and ARMD types.[13,16,17] In a comprehensive meta-analysis, a significant link was observed between late-stage Age-Related Macular Degeneration (ARMD) and vitamin D levels below 25 ng/ml. Interestingly, individuals with vitamin D levels below 50 ng/ml faced an even higher risk of developing ARMD.

It has been postulated that vitamin D may exert its protective effects by reducing oxidative stress, inflammation, and angiogenesis, all of which are central to the pathogenesis of AMD.[9] Additionally, animal research has offered insights into the mechanisms through which vitamin D supplementation can mitigate retinal inflammation and reduce the accumulation of intracellular beta-amyloid, a marker of aging in retinal cells.[14] These findings collectively support the notion that vitamin D might preserve retinal function and protect against the effects of aging, implying that vitamin D deficiency could

Table 1: Demographic characteristics of study participants

Characteristic	Group 1 (Early-Stage ARMD)	Group 2 (Intermediate-Stage ARMD)	Group 3 (Advanced-Stage ARMD)	P-value
Number of Patients (n=112)	42	35	35	-
Age (years)	68.2 ± 6.5	72.1 ± 8.3	76.5 ± 7.2	<0.001
Gender (Male/Female)	18/24	15/20	14/21	0.672
Smoking Status (Yes/No)	12/30	8/27	6/29	0.421
Family History of AMD	14 (33.3%)	10 (28.6%)	12 (34.3%)	0.798

Table 2: Serum 25(OH)D levels in different ARMD groups

ARMD Group	Mean 25(OH)D Level (ng/mL)	Standard Deviation	p-value
Group 1 (Early-Stage ARMD)	30.5 ± 4.1	2.6	0.024
Group 2 (Intermediate-Stage ARMD)	27.8 ± 3.9	2.4	0.056
Group 3 (Advanced stage, ARMD)	25.3+4.7	3.1	<0.05

contribute to the aging and degeneration of the retina.

In addition, our study identified two significant risk factors associated with ARMD in our study participants: a history of smoking and a family predisposition to ARMD. These risk factors are consistent with a substantial body of existing literature, which has established that smoking is a significant modifiable risk factor for ARMD, and that individuals with a family history of ARMD are at higher risk of developing the condition. [18,19] Our findings reinforce the importance of public health campaigns emphasizing the dangers of smoking, especially in the context of ARMD prevention.

These results hold significant clinical implications. Understanding the role of vitamin D in AMD progression may pave the way for innovative strategies in the prevention and management of this prevalent eye condition. Given the global burden of AMD and the increasing aging population, identifying modifiable risk factors such as vitamin D levels is of paramount importance. Further investigation is warranted to elucidate the precise mechanisms through which vitamin D influences the course of AMD and to explore potential interventions to harness its protective effects.

It is important to acknowledge the limitations of this study. Our research, like others, is observational, and while it identifies a significant association, it does not establish causality. Moreover, this study was conducted in the Indian population, and the generalizability of the findings to other populations needs further examination. There may be additional confounding factors that were not considered in this study, and a more comprehensive evaluation is warranted.

5. Conclusion

Our study provides compelling evidence of an association between AMD severity and serum 25(OH)D levels in the Indian population. These findings align with the growing body of literature that suggests a potential link between vitamin D and AMD. This research opens new avenues for further exploration of the role of vitamin D in AMD pathophysiology, potentially leading to novel preventive and therapeutic approaches. While more research is needed, this study contributes to our understanding of the multifaceted nature of AMD and offers hope for improved strategies to combat this debilitating eye condition.

6. Source of Funding

None.

7. Conflict of Interest

None.

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