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The Association between Vitamin D Deficiency and Diabetic Retinopathy in Type 2 Diabetes

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Epidemiological data predicts a dramatic increase in the prevalence of diabetes and of diabetic retinopathy. The aim of the study it to assess the role of vitamin D in diabetic retinopathy. A descriptive cross-sectional study was carried out over the period of January 2021 to April 2021. Non-probability (Convenience) sampling was done by using a pre-prepared questionnaire. Two groups of patients were selected: 50 and 45 patients with and without retinopathy, respectively, as assessed by an experienced ophthalmologist. Subjects with advanced late diabetic complications were excluded to avoid confounding biases. Vitamin D concentrations and vitamin D deficiency was associated with the presence of diabetic retinopathy. Data was presented in the form of percentages, frequency and tables using the SPSS 26.0 for MacBook Pro. Patients with more advanced stages of retinopathy (grades 2–4) had lower concentrations of vitamin D and were more frequently vitamin D deficient as compared with patients not carrying this eye complication. To conclude, this study confirms that a positive correlation or association exists between vitamin D levels and the presence/severity of diabetic retinopathy in type 2 diabetes.

Keywords: Diabetic Retinopathy; Vitamin D Deficiency; Diabetes Mellitus Type 2

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INTRODUCTION

Diabetes mellitus (DM) is a large public health problem which affects more than 300 million individuals in the world, with significant morbidity and mortality worldwide [1]. Serum 25-hydroxy-vitamin D3 (25(OH)D) is a better indicator of vitamin D sufficiency than the active hormone, that is, 1,25-dihydroxy-vitamin D3 [2]. Therefore, the serum concentration of 25(OH)D is widely accepted as a good indicator of the status of vitamin D in a given subject. There is a vast array of pleiotropic actions of this vitamin that were already recognized more than two decades ago [2]. This area of investigation led to improved knowledge on the potential role of vitamin D on glucose homeostasis and in the pathogenesis of type 2 diabetes. Multiple studies have previously shown that vitamin D deficiency is highly prevalent in type 1 and type 2 diabetes [3]. Additionally, there is a growing interest on the potential role of vitamin in the development of diabetic micro- and macroangiopathic complications [4, 5].

Diabetic retinopathy (DR) is among the most common diabetic complications, and is the leading cause of blindness among working-aged individuals worldwide [6]. The prevalence of DR varies from 20% to 80% in different studies. Recent estimates suggest that the number of people with diabetic retinopathy will increase to 191 million by 2030 [7]. Diabetic retinopathy has a complex process. Many risk factors for DR have been established, such as poor glycemic control, long duration of diabetes, smoking, inflammation, obesity, and hypertension. Stratton et al. have given evidence that poor glycemic control and long duration of diabetes are independent risk factors of DR [8]. Praidou et al. found that increased physical activity is associated with less severe levels of DR, independent of the effects of HbA1c and body mass index (BMI) [9]. However, detailed pathophysiological mechanisms and other DR risk factors are not fully clarified.

In a cross-sectional study, Shimo et al. showed an association between vitamin D deficiency and the presence of diabetic retinopathy in a small sample of young adults with type 1 diabetes [10]. However, the only prospective study in this field was performed also in type 1 diabetes and did not confirm vitamin D deficiency as a risk factor for diabetic retinopathy or any other microvascular complications [11]. The primary objective of the current study was to assess whether there is an association of vitamin D status and diabetic retinopathy in type 2 diabetes. Additionally, as a secondary outcome, we aimed to assess the association of vitamin D concentrations and the frequency of its deficiency with the severity of retinopathy.

MATERIAL & METHODS

A descriptive cross-sectional study was carried out over the period of January 2021 to April 2021. Non-probability (Convenience) sampling was done by using a pre-prepared questionnaire. Two groups of patients were selected: 50 and 45 patients with and without retinopathy, respectively, as assessed by an experienced ophthalmologist. Subjects with advanced late diabetic complications were excluded to avoid confounding biases. Vitamin D concentrations were checked for both the

patient groups. Data was presented in the form of percentages and table using the SPSS 26.0 for MacBook Pro.

RESULTS

Out of the 50 patients in the No DR Group-30 were male and 20 were females. In the DR Group, out of the 45 patients, 22 were males and the rest 23 were females.

Vitamin D status	No DR (N=50)	DR (N=45)	*p* Value
25 (OH)D (ng/mL)	22 +/- 5.2	17 +/- 9.2	0.05
Vitamin D deficiency (<20 ng/dL)	10 (20%)	37 (82%)	0.03

Fig. 1 (Table): Results of the analysis of serum 25(OH)D concentrations and frequency of vitamin D deficiency according to the severity of diabetic retinopathy. Data are mean ± standard deviation or (%). DR: diabetic retinopathy; 25(OH)D: 25-hydroxy-vitamin D3.

DISCUSSION

Our study confirms the association of vitamin D deficiency with diabetic retinopathy in type 2 diabetes. As in previous reports, type 2 diabetic patients with retinopathy had lower serum 25(OH)D concentrations. Due to the cross-sectional nature of our study, the study shows a certain degree of limitation. This design allows only for the identification of an association between study variables. To our knowledge, there is no prospective follow-up study in type 2 diabetes and the only one available in type 1 diabetes did not identify vitamin D as a factor involved in the development of retinopathy [4]. Thus, the question on the potential role of vitamin D in the pathogenesis of diabetic retinopathy has not been answered yet.

Another limitation of our study is that we did not determine the time of sun exposure. This limitation is also shared with most previous studies, except for the one by Ahmadieh et al. who used a questionnaire to assess the time spent outdoors [12]. Physical activity may be used as a surrogate of sun exposure as most of this activity is performed outdoors. Therefore, future studies should include a measure of sun exposure as an essential contributor to 25(OH)D concentrations.

We should point out that 10 out of the 50 in the No DR Group showed low levels of Vitamin D in contrast to 37 out of the 45 in the DR Group. This makes about 82% of the cases in the DR Group having low vitamin d levels. We made sure that none of the subjects included in the current study had advanced renal disease and/or impairment. Renal disease in diabetes could contribute as an important confounder of vitamin D status [13]. Some of the previous studies either did not provide information on renal function or included patients with advanced renal disease. The careful revision of the previous publications on this matter confirmed that only the American population-based study by Patrick et al. included creatinine as a potential important confounder in the analysis of the association of 25(OH)D and retinopathy.

Besides, an association between vitamin D and cardiovascular disease has been previously described [14], also in type 2 diabetes [15]. Diabetic retinopathy may develop and progress to advanced stages without producing any immediate symptoms to the patient. Screening for DR is essential in order to establish early treatment of sight-threatening retinopathy and has been demonstrated to be successful at achieving vision loss.

Considering the heavy burden of DR and the association between serum 25(OH)D level and diabetic retinopathy, low 25(OH)D levels may help us to find more early-stage diabetic retinopathy patients [16]. Therefore, screening low 25(OH)D levels may be a potential simple way for screening diabetic retinopathy among type 2 diabetes in primary hospitals—especially where there is a shortage of ophthalmic equipment or ophthalmologists.

CONCLUSION

Our study confirms the association of a higher frequency of vitamin D deficiency and lower concentrations of 25(OH)D with diabetic retinopathy in patients with type 2 diabetes. Type 2 diabetes patients with vitamin D deficiency experienced an increased risk of diabetic retinopathy. However, further studies are required to better understand the relationship between vitamin D deficient type 2 diabetes patients and diabetic retinopathy, and well-designed randomized controlled trials are needed to determine the explicit effect of vitamin D supplementation on the prevention of diabetic retinopathy. Considering the high prevalence of vitamin D deficiency and the burden of the diabetic retinopathy, screening type2 diabetes patients who are at risk of vitamin D deficiency should be considered.

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