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Study of serum vitamin D and homocysteine levels in patients with diabetic retinopathy and retinal vein occlusion

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ABSTRACT

Background: Diabetic retinopathy and retinal vein occlusion are significant causes of vision loss in patients with diabetes. Emerging evidence suggests that vitamin D deficiency and elevated homocysteine levels may play a role in the pathogenesis of these conditions. This study investigates the serum levels of vitamin D and homocysteine in patients with diabetic retinopathy and retinal vein occlusion to elucidate potential associations.
Aim: Diabetic retinopathy (DR) is a sight threatening complications associated with diabetes mellitus. To find the correlation between vitamin D level and homocysteine plasma levels in patients of DR and Retinal Vein Occlusion patients.
Objective: Study the level of serum vitamin D and Homocysteine in patients with diabetic retinopathy as well as in retinal vein occlusions.
Materials and Methods: A case control type of study was conducted on 100 cases (70 diabetic retinopathy and 30 retinal vein occlusion) and age matched 100 control. Detailed relevant history and complete ocular examination was done . Serum vitamin D and homocysteine levels were noted.
Result: In our study, majority of the patients belonged to & > 60 years in the group of cases of diabetic retinopathy and most of the patients in the control group belonged to 50-60 years and & > 60 years of age group (40%). Mean age in the cases and controls was equal (58.4±8.4)
Majority of the patients in both cases (68.6%) and control (67.1%) group were males. Association was found to be statistically significant when chi square test (p = 0.03). The prevalence of hyper homocysteinenemia was also higher in DR group.
Conclusion: The prevalence of hyperhomocystinemia was more in cases of diabetic retinopathy compared to controls. The prevalence of vitamin D deficiency was more in cases of diabetic retinopathy compared to controls and the difference was significant.

1. Introduction

Diabetic retinopathy is one of the most serious eye problems associated with Type 2 Diabetes Mellitus. It is a microangiopathy which considerably leads to gradual loss of vision.[1] The duration and management of T2DM directly affect the prevalence of diabetic retinopathy. Around 95 million diabetes people worldwide or 35.4% of all diabetic patients have DR. The annual incidence and development of diabetic retinopathy are 2.2%–12.7% and 3.4%–12.3%, respectively.[2]

There are several known risk factors that contribute to the progression of retinopathy. Some factors like age, diabetes duration, and genetic predisposing factors, are non modifiable. Risk factors such as hyperglycemia,

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hypertension, anaemia, hyperlipidemia, obesity, and nephropathy, on the other hand are modifiable. Elevated levels of homocysteine in blood has been correlated with development and correlation of DR although evidence is anecdotic.[3,4]

As a result, there has been no conclusive evidence either to prove or disprove this association. Because of vitamin B12 and folate supplementation has been shown to reduce serum homocysteine levels to varying degrees in different studies, hyperhomocysteinemia may be a modifiable risk factor.[5,6]

Vitamin D regulates human calcium and phosphorus metabolism.

If a patient's inflammatory factor level is too high, VD can reduce the risk of diabetic microvascular lesions by inhibiting inflammatory factor secretion.

Among the numerous risk factors proposed for retinal vein occlusions, elevated homocysteine levels in blood have received recent attention and research. The effect modifier role of vitamin B12 and folate deficiencies in this association is also unknown. Among the numerous studies conducted on this subject, some have found a link between hyperhomocysteinemia and retinal vein occlusion, while others have not.

2. Materials and Methods

This investigational study will be conducted in the Department of Ophthalmology Dr. D Y Patil Medical college, Hospital and research Centre, Nerul, Navi Mumbai. A case control type of study was conducted from July 2021 to January 2023.

The study consists of 100 cases (70 diabetic retinopathy and 30 retinal vein occlusion) and 100 control (70 diabetic retinopathy and 30 retinal vein occlusion).

Dilated fundus of both eyes were evaluated. Retinal status was evaluated by direct ophthalmoscopy, slit lamp biomicroscopy by using 90D lens and indirect ophthalmoscopy after dilatation with Tropicamide/ Tropicamide plus eye drops. Serum Homocysteine was measured by Electro chemiluminescent immunoassay (ECLIA). Hyperhomocysteinemia is defined as > 15 micromol/L. Serum Vitamin D levels were assessed by Chemiluminescent microparticle immunoassay (CMIA) and levels would be assessed, less than 50 nmol/l.

The endocrine society recommends a preferred range of 40-60 ng/ml[16].

2.1. Statistical analysis

The results included mean value, standard deviations and P values were calculated. Chi square and unpaired T test was used where applicable.

3. Results

All the patients included in the study were diabetics and total of 70 diabetic retinopathy patients with 70 control with DM with no DM and 30 patients of retinal vein occlusion with 30 controls.

Slit lamp examination, Dilated fundus examination, vitamin D level and serum homocysteine level estimation was done for all.

3.1. Diabetic retinopathy

We conducted a case control study in the department of ophthalmology to study serum vitamin D and homocysteine levels in diabetic retinopathy patients. We included a total of 70 diabetic retinopathy patients with 70 controls.

In our study, the majority of patients with diabetic retinopathy were older than 60 years. In the control group, most patients were either between 50-60 years or older than 60 years, comprising 40% of the group. The mean age was similar in both groups, with a value of 58.4±8.4 years. Additionally, males predominated in both the case group (68.6%) and the control group (67.1%).

Our study showed that the majority of the patients had mild non proliferative diabetic retinopathy (NPDR) (50%) and 25% of the patients had moderate NPDR and 11.4% of the patients had severe NPDR. About 12.9% of the patients had proliferative diabetic retinopathy (PDR) which is similar to the study done by Khandekar R et al.[7] showed that 60% had NPDR and 18% PDR.

Majority of the patients in the cases group had serum homocysteine > 15 mcmol/L (60%) and most of the patients in the control had < 15 mcmol/L (60%) and majority of the patients with PDR and moderate and severe NPDR had serum homocysteine levels > 15 mcmol/L and 42.9% of the patients with mild NPDR had serum homocysteine levels > 15 mcmol/L. The association was statistically significant when chi-square test (p=0.03). The prevalence of hyperhomocysteinemia (Hcy levels greater than 15 micromol/L) was also significantly higher in the DR group than in the non-DR group.

Table 1: Age distribution among cases and controls

Age (in years)	Cases	Controls
30-40	1 (1.4%)	1 (1.4%)
41-50	13 (18.6%)	13 (18.6%)
51-60	26 (37.1%)	28 (40%)
>60	30 (42.9%)	28 (40%)
Total	70 (100%)	70 (100%)

Chi-square(X2)= 6.07, p value = 0.1

3.2. Retinal vein occlusion

Our study looked at the association of homocystein and vitamin D levels with RVO. Our study showed that the

Table 2: Severity of diabetic retinopathy among cases

Severity of diabetic retinopathy	Frequency	Percentage
Proliferative diabetic retinopathy (PDR)	9	12.9%
Mild non proliferative diabetic retinopathy (NPDR)	35	50%
Moderate NPDR	18	25.7%
Severe NPDR	8	11.4%
Total	**70**	**100%**

Table 3: Serum homocysteine among cases and controls

Serum homocysteine	Cases	Controls
<15 mcmol/L	28 (40%)	42 (60%)
>15mcmol/L	42 (60%)	28 (40%)
Total	70 (100%)	70 (100%)

Chi-square (X2)= 5.6, p value = 0.01

Table 4: Serum vitamin D among cases and control

Serum Vitamin D	Cases	Controls
Deficiency(<30 mmol/L)	45 (64.3%)	38 (54.3%)
Inadequate(30-50 mmol/L)	8 (11.4%)	4 (5.7%)
Adequate(50-75 mmol/L)	17 (24.3%)	28 (40%)
Total	70 (100%)	70 (100%)

Chi-square (X2)= 4.6, p value= 0.1
non-hypertensives

mean age in the cases (52.9±13.9) was more compared to control group (46.5±14.1). Majority of the patients in both cases (63.3%) and control group (66.7%) were males and the study was both age and gender matched. In our study where majority of the patients had Branch retinal vein occlusion (BRVO) (50%) and 46.7% had Central retinal vein occlusion (CRVO) and 3.3% had Tributary retinal vein occlusion (TRVO).

Toshniwal NN et al[8] found that levels of homocysteine are significantly higher in RVO group. Oli A et al[9] found that the mean levels of vitamin D was lower in cases (13.68±4.58).

Table 5: Age distribution among cases and controls

Age (in years)	Cases	Controls
30-40	9 (30%)	13 (43.3%)
41-50	3 (10%)	8 (26.7%)
51-60	7 (23.3%)	3 (10%)
>60	11 (36.7%)	6 (20%)
Total	30 (100%)	30 (100%)

Chi-square(X2)= 6.07, p value = 0.1

4. Discussion

The present study showed that the mean of serum vitamin D levels was more in mild NPDR (37.5±20.7) than moderate

Table 6: Comparison of homocysteine levels and vitamin D deficiency with other studies

Studies	Hyper Homocysteinemia	
	Cases	Controls
Our study	60%	40%
Bande SU et al[10]	38.8%	10.6%
Satyanarayana A et al[11]	65%	11%
Ali M et al[12]	75%	24.5%
Vitamin D deficiency		
Our study	64.3%	54.3%
Payne J F et al[13]	70%	55%
Reddy GB et al[14]	63%	45%

(29.5±17.5) and severe NPDR (24.0±23). Majority of the patients had mild non proliferative diabetic retinopathy (NPDR) (50%) and 25% of the patients had moderate NPDR and 11.4% of the patients had severe NPDR. About 12.9% of the patients had proliferative diabetic retinopathy (PDR). Majority of the patients with PDR (887.9%) and mild (45.7%), moderate (83.3%) and severe (75%) NPDR had deficiency of vitamin D and the association was statistically significant when applied chi-square test (p=0.05) where as the study done by Nadri G et al[15] showed that the mean serum vitamin D in the controls was 23.36±1 and 17.88±1.86 in NPDR and low vitamin D levels correlated with severity of retinopathy.

Table 7: Comparison of vitamin D deficiency with other studies

Studies	Vitamin D deficiency	
	Cases	Controls
Our study	64.3%	54.3%
Payne JF et al[13]	70%	55%
Reddy GB et al[14]	63%	45%

Table 8: Comparison of homocysteine levels and vitamin D deficiency with other studies

Studies	Mean Homocysteine	
	Cases	Controls
Our study	26.4±16.6	13.1±8.4
Toshniwal et al.[8]	23.8±13.2	12.4±10.5
Bhat VG et al.[16]	18.2±5.4	12.5±2.1
Mean Vitamin D		
Our study	29.5±23.5	50±25.6
Oli et al[9]	13.68±4.58	23.03±2.89
Muttar AZ et al[17]	14.21 ± 5.19	22.70 ± 4.43

Our study revealed a higher prevalence of hyperhomocysteinemia among patients with diabetic retinopathy compared to the control group. This finding suggests that elevated homocysteine levels may be associated with the development and progression of diabetic retinopathy. Previous studies have also indicated a potential link between hyperhomocysteinemia and various

vascular complications, including those affecting the retinal vasculature. Elevated homocysteine levels could contribute to endothelial dysfunction, oxidative stress, and inflammation, all of which are key mechanisms in the pathogenesis of diabetic retinopathy. Therefore, monitoring and managing homocysteine levels in patients with diabetes may be crucial for the prevention and control of diabetic retinopathy.

In addition to hyperhomocysteinemia, our study identified a significantly higher prevalence of vitamin D deficiency in patients with diabetic retinopathy compared to the control group. The difference was statistically significant, indicating a strong correlation between vitamin D deficiency and diabetic retinopathy. Vitamin D is known for its anti-inflammatory and immunomodulatory effects, and deficiency in this vitamin has been implicated in the pathogenesis of various chronic diseases, including diabetes and its complications. Vitamin D deficiency may exacerbate retinal inflammation and promote the progression of retinopathy by influencing pathways related to angiogenesis, oxidative stress, and cellular apoptosis.

The significant difference in vitamin D levels between the cases and controls underscores the potential importance of vitamin D in the prevention and management of diabetic retinopathy. Regular screening for vitamin D deficiency and appropriate supplementation could be considered as part of a comprehensive management strategy for patients with diabetes, particularly those at high risk for or already experiencing retinopathy.

Overall, our findings highlight the importance of addressing both hyperhomocysteinemia and vitamin D deficiency in the context of diabetic retinopathy. Future research should further investigate the underlying mechanisms linking these factors to diabetic retinopathy and explore potential therapeutic interventions targeting these modifiable risk factors. Such efforts could lead to improved strategies for the prevention and management of this sight-threatening complication of diabetes.

5. Conclusion

The prevalence of hyperhomocysteinemia was notably higher in patients with diabetic retinopathy compared to those in the control group, suggesting a potential association between elevated homocysteine levels and the presence of diabetic retinopathy. Furthermore, vitamin D deficiency was significantly more common among patients with diabetic retinopathy than among the controls. This significant difference highlights the potential role of vitamin D deficiency as a contributing factor or marker in the development of diabetic retinopathy. These findings underscore the importance of monitoring and managing homocysteine and vitamin D levels in patients at risk for or diagnosed with diabetic retinopathy. The prevalence of vitamin D deficiency was more in cases (75.9%) of retinal vein occlusion compared to controls (40.7%) and there was statistically significant difference . Majority of the patients with BRVO (33.3%) and CRVO (57.1%) hadhyperhomocystinemia compared to TRVO and the association was not significant.

6. Source of Funding

None.

7. Conflict of Interest

None.

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