

Diabetic Retinopathy: A Roadway to Other Systemic Conditions

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Diabetes mellitus and its micro vascular complications are major medical tribulations pervasiveness of which is increasing and affecting the masses. As such is the major liability of osteoporosis in the society and Both of them have the occurrence in same age group.

Are they related? Do they have any control upon each other? If so, then how are they linked? Is it possible to treat one and get some diagnosis on the other? And as it usually affects the same age group then is there any link between its causes and severity?

Various studies are there that link vitamin D levels with diabetic nephropathy and retinopathy.

AIMS AND OBJECTIVES:

-To study the association of vit D levels with diabetic retinopathy

-To study the association of vit D levels with grade and severity of diabetic retinopathy

-To study whether vit D adequate patients are having decreased pervasiveness of diabetic retinopathy.

MATERIALS AND METHODS:

CASE SELECTION

- Diabetic retinopathy Cases 18years and above

-Patients diagnosed as case of diabetes as per American Association of Diabetes

-Patients should not be previously diagnosed as vit D deficient. Patients should not be treated for any such conditions.

CONTROL SELECTION:

The control group comprise of age and sex matched with normal healthy volunteers.

EXCLUSION CRITERIA:

-Type 1 diabetes

-vit D intake greater than 1000IU/day

-disorders that change the metabolism of vit D

-Significant cardiac, hepatic, renal and cranial/

extracranial oncologic disease

-Use of medications known to affect serum phosphate levels

-TSH <0.1 or >7uU/ml

-Serum calcium <8 or >11mg/dl,

Serum creatinine >1.5mg/dl

-WBC<2000 or >15000/cmm

-Platelet count <100000 or >500000/cum

-Hormone replacement therapy, steroids or testosterone use.

Because of the long half - life of 25-OH vit D by ELISA method ,its level is used to assess vit D deficiency.

REVIEW OF LITERATURE

Vitamin D deficiency and its correlation with diabetic retinopathy-at a glance.

-1988, Pietschmann et al: Serum osteocalcin and 25 hydroxy vit D levels were significantly decreased in type 2 diabetic patients when compared with corresponding control subjects.

Diabetologia, volume 31, no. 12: 892-895

-1997, Koya et al: Hyperglycemia and diabetes may also affect other signal transduction pathways besides DAG-PKC.

Progress have been made to identify some of these potential secondary parameters of vascular pathologies, such as the levels of VEGF.

Diabetes, vol. 47. june 1998

-2000, Hu Lya Aksoy et al: Inverse relationship between the severity of retinopathy and serum 1,25[OH]2D3 concentrations, being the lowest in PDR and highest in patients without retinopathy.

Difference in serum 1,25[OH]2D3 concentrations between patients with retinopathy and control group suggest that neovascularisation in retina may involve a decrease in serum 1,25[OH]2D3 concentrations in patients with DR.

- Clinical Biochemistry*, vol 33, February 2000
- 2000, Mantell et al: Highlighted the potential use of 1,25[OH]2D3 in both prevention and regression of conditions characterized by pathological angiogenesis.
- Shown that 1,25[OH]2D3 has no effect on the expression of VEGF receptors genes by endothelial cells.
- Suggested that 1,25[OH]2D3 may be of use in the prevention of conditions involving pathological angiogenesis and may also be of use in the therapeutic regression of such conditions characterized by aberrant angiogenesis.
- American Heart Association*, 2000
- August 2001, Isaia et al: Found no difference in 25[OH]D levels between type 1 diabetic patients and control subjects, whereas 25[OH]D levels were significantly decreased in type 2 diabetic patients.
- Diabetes Care*, volume 24, number 8, august 2001
- 2001 and 2005, Taverna et al: The plasma concentration of 1,25[OH]2D3 has been inversely correlated with the severity of diabetic retinopathy, which raises the possibility that VD, through its anti-inflammatory, antioxidant, antiproliferative and antiangiogenic properties, may protect diabetic retina.
- Calcium homeostasis and calcium-dependent signaling pathways have an important role in the development of retinal hypoxia, a major process in severe DR.
- Diabetologia*(2002)45:436-442
- The Journal of Clinical Endocrinology & Metabolism 90(8):4803-4808
- 2004 Chiu et al: Showed in his study that a positive correlation of 25[OH]D concentration with insulin insensitivity and a negative effect of hypovitaminosis D on cell function.
- Am J Clin Nutr* 2004;79:820-5
- 2005 Ford et al: An inverse association between serum concentrations of vit D and the prevalence of the metabolic syndrome (including high blood pressure and hyperglycemia).
- Diabetes Care*, volume 28, number 5, may 2005
- 2006 Suzuki et al: Microvascular complications and insulin treatment in type 2 diabetes patients are associated with the co-existence of hypovitaminosis D.
- Subjects with proliferative diabetic retinopathy had lower serum 25[OH]D concentrations than those without retinopathy and those with simple diabetic retinopathy.
- Endocrine Journal* 2006,53(4),503-510
- 2007 Sugden et al: Single large dose of oral vit D2 improves endothelial function in patients with type 2 diabetes and vit D insufficiency.
- Low levels of 25[OH]D are associated with many markers of cardiovascular disease; for example, hypertension, increased vascular resistance and increased left ventricular mass index.
- Journal Compilation Diabetes UK. Diabetic medicine, 25, 2008:320-325
- 2010 March Millen et al: Relationship between serum 25[OH]D concentrations and the prevalence of early age-related macular degeneration [ARMD].
- Arch Ophthalmol*/vol 129(no.4), apr 2011
- 2010 October Nguyen et al: Demonstrated that among patients with diabetes, those with DR had a reduction in the skin microvascular responses to iontophoresis of both SNP {endothelium independent response} and Ach (endothelium-dependent response)
- Diabetes Care*:2011
- 2011 April Millen et al: Association between vit D status as reflected by low serum concentrations of 25[OH]D, and the prevalence of early ARMD was reported in a nationally representative, cross-sectional study.
- Ophthalmol*/vol 129(no.4), apr 2011
- 2011, Devaraj et al: Type 1 diabetes is associated with an increased risk of vascular complications and patients with T1DM with proteinuria and/or retinopathy have a significantly increased risk of fatal coronary artery disease.
- Am J Clin Pathol* 2011;135:429-433
- 2011 September Payne JF et al: An inverse relationship between the severity of the retinopathy, i.e., neovascularisation, and serum 1,25[OH]2D3, being the lowest in PDR and the highest in diabetic patients without retinopathy.
- Abstract PO223*, Presented October 17, 2010
- 2012 Jan Yan C. Li et al: Studies consistently demonstrated an association of low serum 25[OH]D

levels with high blood pressure, increased prevalence of cardiovascular disease and cardiovascular risk factors including hypertension, diabetes, obesity and hyperlipidemia.

Monotreatment with paricalcitril or doxercalciferol or combination therapy with these analogs and RAS inhibitors (losartan or enalapril) prevented cardiac hypertrophy.

Curr Opin Nephrol Hypertens 2012,21:72-79

-May 2015, Nuria Alcubierre et al: Study confirms the association of a higher frequency of vit D deficiency with diabetic retinopathy in patients with type 2 diabetes.

Reveal the potential role of vit D in the pathogenesis of diabetic retinopathy.

Journal of Diabetes Research, volume 2015, article ID 374178

-June 2015, Usluogullari et al: No significant difference is reported in serum 25[OH]D vit D concentrations was observed between the diabetic and control groups. No correlation was observed between HbA1C and serum 25[OH]D vit D levels. Vit D levels were lower in diabetic patients with nephropathy, and patients not using any medication.

When microvascular complications were evaluated, vit D levels were found to be lower in patients in whom these complications were more severe.

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Review of Literature Against the Hypothesis :

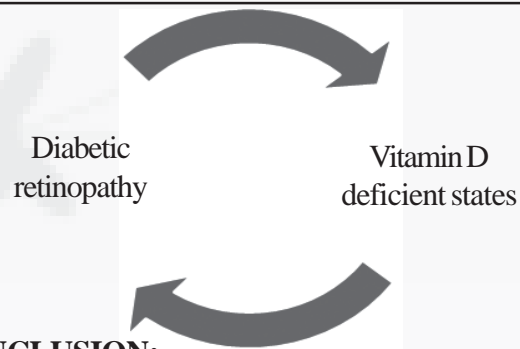
Uazman Alam et al: Vit D level is not associated with diabetic retinopathy and maculopathy.

Relationship between retinopathy and adequacy of vit d couldnot be explored adequately because of low power of the analysis.

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LIMITATIONS:

As all patient data could not be fully retrieved coz of small sample size and retrospective study, there is a need for well-designed prospective or controlled studies with larger sample sizes where vit D supplementation and complication regressions are followed and where the impact of the vit D levels on blood glucose regulation is observed



CONCLUSION:

Through various studies, reports and researches it has been revealed that a low concentration of serum vit D increases the risk of developing diabetes later in life and is also associated with an increased risk of diabetic micro vascular complications.

A patient with vit D deficiency condition also needs to be evaluated for blood sugar levels and diabetic retinopathy and vice versa.

Hence, the vit D status of patients with diabetes should be considered during their regular follow-up, and supplementation should be provided to those at risk of deficiency.

We as ophthalmologists rather than just being restricted to ocular complications of Diabetes can also help in providing a better approach to other systemic diseases like vit D deficiency conditions. So that both the diseases can be diagnosed at the earliest.

References :

1. Diabetologia, volume 31, no.12:892-895
2. Diabetes, vol.47, june 1998
3. Clinical Biochemistry, vol 33, February 2000
4. American Heart Association, 2000
5. Diabetes Care, volume 24, number 8, august 2001
6. Diabetologia(2002)45:436-442
7. The Journal of Clinical Endocrinology & Metabolism 90(8):4803-4808
8. Am J Clin Nutr 2004;79:820-5
9. Diabetes Care, volume 28, number 5, may 2005
10. Endocrine Journal 2006,53(4),503-510
11. Journal Compilation Diabetes UK. Diabetic medicine, 25, 2008:320-325
12. Arch Ophthalmol/vol 129(no.4), apr 2011
13. Diabetes Care:2011
14. Ophthalmol/vol 129(no.4), apr 2011
15. Am J Clin Pathol 2011;135:429-433
16. Abstract PO223, Presented October 17, 2010
17. Curr Opin Nephrol Hypertens 2012,21:72-79
18. Journal of Diabetes Research, volume 2015, article ID 374178
19. BMC Endocrine Disorders (2015)
20. Centre for Endocrinology and Diabetes, Institute of Human Development, University of Manchester, UK.