Study of Chronic Complications of Type 2 Diabetes Mellitus in Relation to Vitamin D- in Rural Area of Andhra Pradesh

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ABSTRACT

Introduction: Type 2 diabetes mellitus (T2DM) is one of the most common health problems facing mankind and is a major public health problem. Study aimed to evaluate the relation between 25(OH) vitamin-D levels and chronic vascular complications (micro and macrovascular) in T2DM.

Material and methods: A cross-sectional study carried in 2 years. 50 patients with T2DM fulfilling the inclusion and exclusion criteria were included in study.

Results: Common age in the study population is 50-60 years with mean age 58.2 ± 8.3 years. Sex ratio of males : females is 1.3:1. In our study prevalence of microvascular complications is 40%. Single microvascular complications (retinopathy or neuropathy or nephropathy) was present in 20% of cases while the combination of all three was present in 12% of cases. At least one Macrovascular complications in our study is 24% of patients. Prevalence's of individual vascular complications Nephropathy - 28%, Retinopathy - 24%, Neuropathy- 20%, CAD - 20%, CVD - 4%, PVD - 4%. In our study vitamin D deficiency is present in 60% of patients, vitamin D Insufficiency is present in 30% and only 10% of study group had normal vitamin D.

Conclusion: Vitamin D deficiency (<20 ng/ml) in type 2 diabetes is associated with any of the microvascular complications, and type 2 diabetics with decreasing vitamin D levels have significantly increasing prevalence of combination of microvascular complications. The vitamin D status of patients with diabetes should be considered during their regular follow-up.

Keywords: Chronic Complications, Type 2 Diabetes Mellitus, Vitamin D

INTRODUCTION

Fortunately many of diabetes complications can be prevented with early detection, aggressive glycaemic control and efforts to decrease risks of complications. Many risk factors are known in development of diabetes and its complications. It is important to define and control modifiable risk factors that contribute to diabetes and its complications. Vitamin D deficiency is one of the risk factors and its deficiency is more common in those diagnosed with diabetes. Our study focused on relation of complications in association with vitamin D deficiency.

The guidelines of Endocrine Society Task Force states that 25(OH) D levels of 30 ng/ml or higher have benefits when compared to levels of 20 ng/ml.[2] Study carried out in United Kingdom evaluated the prevalence of hypovitaminosis D in type 2 diabetic patients in an Asian community and its impact on the control of glycemia.[3] The results revealed that the prevalence of vitamin D deficiency (< 20 ng/mL) was > 80%, being more common in the diabetics than in the control group (83% vs. 70%; p = 0.07)[3].Vitamin D is involved not only in calcium and bone homeostasis but is also known to regulate genes involved with immunomodulation, proliferation, and regulation of cell growth and differentiation.[4]

Our Study was done to know chronic vascular complications (micro and macrovascular) in T2DM patients and to evaluate the relation between 25(OH) vitamin-D levels and chronic vascular complications (micro and macrovascular) in T2DM.

MATERIAL AND METHODS

It was a Cross sectional study conducted in patients with T2DM in Dr. PSIMS and RF during the period of November 2015 to September 2017. 50 patients with T2DM fulfilling the inclusion and exclusion criteria were included in study

Inclusion Criteria: Patients of type 2 diabetes mellitus.

Exclusion Criteria: Patients with chronic kidney disease stages 4 and 5 (egfr < 30 ml/min per 1.73 m^2, taking vitamin D supplementation.

Consent was taken from all patients and confidentiality was maintained. All 50 members that participated in the study were enquired for the presence of symptoms of diabetes related long term complications, with the help of predesigned proforma that contained symptom questionnaire validated in previous studies.

Resting pulse rate was recorded in all patients after 10 minute rest. Blood pressure was recorded using mercury sphygmomanometer in right arm supine position after rest and average of two recordings was taken. Blood pressure was recorded in standing position one minute after standing. Hypertension was defined as blood pressure ≥ 140/90 mmHg. Fall in blood pressure greater than 20/10 mm Hg was regarded as postural hypotension. 5 ml of blood was

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Age in years	Frequency	Percent
40-50	8	16
50-60	22	44
60-70	16	32
70-80	4	8
Total	50	100
Sex		
Female	21	42
Male	29	58
Total	50	100
Vit-D		
Deficiency	30	60
Insufficiency	15	30
Normal	5	10
Total	50	100

Table-1: Age and gender distribution of study group

collected in eight hour fasting state for fasting plasma glucose, serum cholesterol, triglycerides and HbA1c. 25 – hydroxyvitamin D3 levels were measured in patient blood sample by electrochemiluminescence immunoassay.

Retinopathy: Fundus examination was performed after dilating with tropicamide eye drops. Optic fundi were examined by consultant ophthalmologist, and graded according to International Classification of Diabetic Retinopathy.

Nephropathy: Albuminuria was assessed with MICRAL test (Immunological visual testing strips for semi quantitative determination of microalbuminuria).

MICRAL test: A ratio of albumin (mcg/L) to creatinine (mg/L) of less than 30 is normal; a ratio of 30-300 signifies

Prevalence of Nephropathy	HbA1C				Total		P-value
	6.5-7.5		>7.5				
	Count	%	Count	%	Count	%	
Absent	28	87.5%	8	44.4%	36	72.0%	0.002
Present	4	12.5%	10	55.6%	14	28.0%	
Total	32	100.0%	18	100.0%	50	100.0%	
Prevalence of diabetic retinopathy							
Absent	32	100.0%	6	33.3%	38	76.0%	<0.001
Present	0	0.0%	12	66.7%	12	24.0%	
Total	32	100.0%	18	100.0%	50	100.0%	
Prevalence of Neuropathy							
Absent	31	96.9%	9	50.0%	40	80.0%	<0.001
Present	1	3.1%	9	50.0%	10	20.0%	
Total	32	100.0%	18	100.0%	50	100.0%	

Table-2: Glycemic control and microvascular complications.

Variable	Nephropathy					
	Absent		Present		Total	
	Mean	SD	Mean	SD	Mean	SD
Age	55.42	6.792	65.36	7.581	58.20	8.278
FBS	151.69	11.566	174.86	18.547	158.18	17.239
HBA1C	7.217	.6153	9.007	1.7171	7.718	1.3085
S.CHOL	177.50	21.054	212.14	28.044	187.20	27.788
ST	204.86	31.760	263.36	65.256	221.24	50.539
VIT D	21.078	6.3519	19.021	6.8266	20.502	6.4848
Diabetic retinopathy						
Age	55.21	6.44	67.67	6.11	58.20	8.28
FBS	151.26	11.35	180.08	14.22	158.18	17.24
HBA1C	7.17	0.49	9.46	1.58	7.72	1.31
S.CHOL	175.95	18.60	222.83	21.28	187.20	27.79
ST	201.03	25.86	285.25	56.99	221.24	50.54
VIT D	21.55	6.34	17.18	6.03	20.50	6.48
Neuropathy						
Age	55.38	6.36	69.50	4.55	58.20	8.28
FBS	152.35	12.48	181.50	13.70	158.18	17.24
HBA1C	7.20	0.48	9.80	1.52	7.72	1.31
S.CHOL	177.38	18.81	226.50	22.92	187.20	27.79
ST	202.93	25.09	294.50	61.02	221.24	50.54
VIT D	21.31	6.25	17.26	6.72	20.50	6.48

Table-3: Comparison of the Study Group Characteristics for diabetic microvascular complications

Variable	VIT D	
	r-value	P-value
Age	-0.528	<0.001
FBS	-0.41	.003
HBA1C	-0.387	.006
Duration of DM	-0.39	.005
ST	-0.368	.008
S.CHOL	-0.412	.003

Table-4: Co relation of vitamin D with risk factors (quantitative variables)

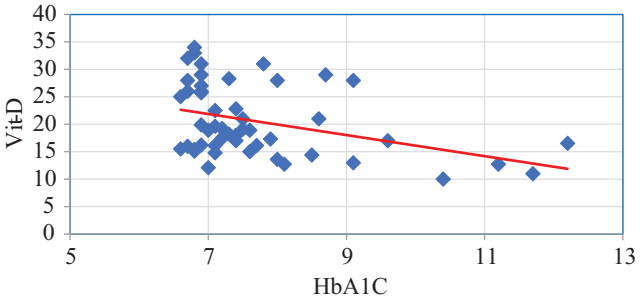

Figure-1: Co relation of vitamin D with duration of DM

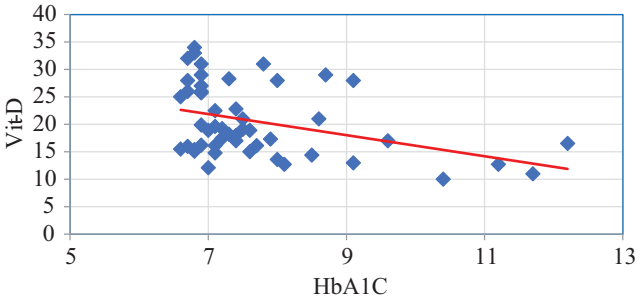

Figure-2: Co relation of vitamin D with HbA1C

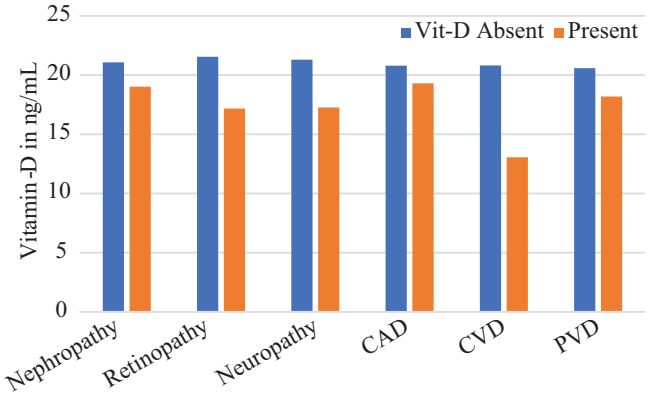

Figure-3: correlation of complications with vitamin D

microalbuminuria and values above 300 are considered as macroalbuminuria.

Neuropathy: Assessed with modified neuropathy disability score (NDS).

CAD: Coronary artery disease was diagnosed by history of myocardial infarction or angina, documented by previous treatment records or by ECG or by 2D Echo.

CVA: CVA was diagnosed by history, clinical examination and CT or MRI findings.

PVD: PVD was considered to be present if there is definitive history of intermittent claudication and one or more of peripheral pulses is absent in both feet or ankle brachial index < 0.8 by Doppler study.

STATISTICAL ANALYSIS

The statistical analysis was done using the SPSS version 22.descriptive statistics were applied. ANOVA, Independent t–test and karl pearson correlation were applied. p<0.05 was considered as statistically significant.

RESULTS

Total numbers of patients were 50 and 50-60 year age group was the largest in the study(33%).Out of 50 patients 29 are male and 21 are female (table-1).

Out of 14 patients with diabetic nephropathy 71 percent had HbA1C values greater than 7.5 and it is statistically significant (P <005) (table-2).

Vitamin d levels though low in patients with diabetic nephropathy, statistically it was insignificant (table-3,4). Figure 1,2 and 3 shows co relation of vitamin D with duration of DM, co relation of vitamin D with HbA1C and Correlation of complications with vitamin D respectively.

DISCUSSION

Diabetes mellitus is a chronic disease affecting many individuals in India, has increased over the past two decades and expected to continue in epidemic proportions. This increase has been attributed to the rapid economic, demographic and nutritional transition experienced in India. Diabetes is a significant public health issue with many types of adverse outcomes and disability. The overwhelming majority of diabetes morbidity and mortality is associated with chronic complications including retinopathy, neuropathy, nephropathy, peripheral vascular disease, cardiovascular disease and cerebrovascular disease. Low vitamin D levels have been demonstrated to predict the development of microvascular and macrovascular complications in diabetes.

Age distribution

The age of patients in our study varied from 42 – 76 years. The mean age of study group is 58.2 ± 8.3 years. The mean age in studies of bajaj et al[5], p jung chan – hee et al[6] and gaurav modi et al[7] is 52.85 ± 8.26, 58.8 ± 12.1 and 55.92 ± 12.6 years. The mean vitamin d is higher in the younger age group compared to the older age group which is 26.73 ± 5.78 in 40 -50 years age group compared to 12.55 ± 2.86 in70-80 years age group. Similar age group was also reported by other studies. According to the Centers for Disease Control and Prevention (CDC) in 2015 adults aged 45 to 64 were the most diagnosed age group for diabetes. In conclusion old age patients had more prevalence of vitamin D deficiency.

Total number of patients in our study is 50 out of which 42% were female patients and 58% are male patients. The mean vitamin D was found to be 18.50 ± 5.68 in females and 21.96 ±6.73 in males in diabetics, and the difference between two genders was found to be insignificant (P = 0.6). Scragg et al[8]. and Suzuki et al[9] in their observational study in type 2

diabetes mellitus (T2DM) subjects concluded that mean vitamin D level concentration in men were significantly higher than women. In our study no significant difference was observed with p value of 0.6. Vitamin D deficiency was present in 55.1% of males and 66.6% of females.

Duration of Diabetes and Vitamin D

Diabetes related complications generally do not appear until the second decade of hyperglycemia and as duration increases the prevalence of both microvascular and macrovascular complications increase. Vitamin D deficiency also tend to increase with increase in duration of diabetes. It is evident in our study as the duration of DM increases mean value decreases. The mean value of vitamin D is 22.49 ± 6.4 in patients with duration of DM ≤ 5 years and a significantly low value of 13.07±3.27 in patients with duration of DM ≥ 20 years The relation between vitamin D deficiency and duration of DM was statistically significant with r value of -0.39 and p value of .005.

HbA1C and vitamin D

The mean HbA1c in our study was 7.7 ± 1.3 The mean vitamin D values decreases with increase in HbA1c, which is 21.87±6.09 in patients with HbA1c range of 6.5 – 7.5 and 17.58 ±7.05 in patients with HbA1c ≥ 8.5. In our study the relation between these two variables was statistically insignificant with r value of -0.387 and p value of 0.06.

In a study done by Green RT et al[10] in African American Type 2 Diabetes patients revealed that Vitamin D supplementation was inversely associated with HbA1c (r = -.286, P = .031). Significant improvements in HbA1c are obtained with enhanced Vitamin D supplementation as part of drug regimen over time.

Although, it is difficult to identify the reasons for such variation in prevalence rates among various populations, race, age, method of detecting diabetic retinopathy, health-care facilities, and other risk factors could have contributed to the differences.

Vitamin D and diabetic retinopathy

In our study their is a statistically significant realtion between vitamin D levels and presence of diabetic retinopathy(p-0.04) with mean vitamin D value of 17.17 ± 6.02 in patients with diabetes retinopathy. this result compares well with other studies.

Out of 12 patients with retinopathy 9 had NPDR and 3 had PDR, the mean value of vitamin D in patients having PDR is 13.067 ± 3.26 and with NPDR is 18.544 ± 6.23 and on applying ANOVA the p value is 0.05 (significant) which shows that with increase in severity of retinopathy the vitamin D deficiency is increasing in other way the vitamin D levels decease as the severity of retinopathy increases. Aksoy et al.[19] also showed that the mean vitamin D3 concentrations fell with increasing severity of diabetic retinopathy. Suzuki et al.[9] showed that the existence of PDR was significantly associated with a decrease in serum vitamin D concentrations. Even in a study on type 1 diabetes, Kaur et al.[20] found that retinopathy prevalence was higher in cases with vitamin D deficiency versus sufficiency.

Glycemic control and Diabetic Nephropathy

The importance of glucose as a factor in the progression of diabetic kidney disease, as initially suggested from epidemiologic and preclinical studies, was clearly demonstrated in the Diabetes Control and Complications Trial (DCCT) study in patients with T1DM. In both the primary and secondary prevention aim of the study, any decrease in HbA1c was strongly associated with a reduction in the risk of development of microalbuminuria as well as a decrease in the risk of progression to overt nephropathy. The follow-up Epidemiology of Diabetes Interventions and Complications(EDIC) study has confirmed long lasting benefits of this therapeutic approach.

The UKPDS clearly demonstrated a role for intensified glycemic control in newly diagnosed T2DM subjects when treatment led to a reduction in HbA1c from 7.9 to 7.0%. The ADVANCE study has demonstrated that a further reduction of HbA1c to an average of 6.5% was associated with a further reduction in renal events, as assessed by the development and progression of microalbuminuria. Thus, despite the on going controversy as to the appropriate HbA1c target to reduce macrovascular disease as a result of the recent findings from the ACCORD study, no such controversy as to a possible deleterious effect of intensified glycemic control has been reported with respect to nephropathy. It remains to be determined how useful intensification of glycemic control is in the setting of overt nephropathy as a last-ditch strategy to delay the onset of ESRD.

In the present study of 50 patients 14 had diabetic nephropathy 10 patients (71.4%) with diabetic nephropathy had HbA1C more than 7.5%, 4 patients (28.6%) with diabetic nephropathy had HbA1C <7.5%, average HbA1C for those with positive MICRAL TEST is 9.0, (SD : 1.7), compared to HbA1C of 7.21% with negative MICRAL TEST. Diabetic nephropathy is more common in patients with HbA1C more than 7.5% than in patients with HbA1C <7.5% It shows that poor glycemic control is associated with increased risk of diabetic nephropathy, which is statistically significant. (P-value < 0.002).

Hypertension and diabetic nephropathy

A sustained reduction in Blood Pressure(BP) appears to be the most important single intervention to prevent progressive nephropathy in T1DM and T2DM. For example, in the UKPDS, a reduction in BP from 154 to 144 mm Hg was associated with a 30% reduction in microalbuminuria. In particular, the risk of progressive diabetic nephropathy continues to decrease, with BP reductions into the normal range and below, meaning that the lowest achievable BP is associated with the best clinical outcomes. There is good evidence that tight BP control, no matter how it was achieved, is associated with a significant reduction in the risk of microalbuminuria (primary prevention). In this present study 10 out of 14 patients with diabetic nephropathy had hypertension as a risk factor (71%).

Vitamin D and Diabetic Nephropathy

The incidence of nephropathy was higher in the patients with

type 2 diabetes whose 25-OH vitamin D concentrations were <20 ng/mL compared with patients whose 25-OH vitamin D concentrations were ≥20 ng/mL. This was consistently found in most of the studies and our study had similar result where the mean value in patients with nephropathy is 19.021 ± 6.8206 and 21.078 ± 6.3519 in patients with out nephropathy. vitamin D3 treatment is not associated with significant adverse effects, including gastrointestinal adverse effects, and fluctuation of blood pressure. Vitamin D3 can ameliorate proteinuria and protect the kidney from injury in patients with diabetic nephropathy. This renoprotective effect is independent of blood pressure and glucose reduction and does not increase adverse effects over controls, even in combination therapy with angiotensinconverting enzyme inhibitors or angiotensin receptor blockers. In the NHANES study, insulin resistance, kidney function, and vitamin D status of 14,679 patients were assessed, and vitamin D deficiency was reported to be associated with increased risks of microvascular andmacrovascular complications in patients with type 1 as well as type 2 diabetes. In that study, 25-OH vitamin D concentrations were lower in patients with diabetes mellitus and nephropathy compared to patients without nephropathy.[21]

Diabetic neuropathy

Diabetic neuropathy is one of the commonest long term complications of diabetes mellitus. In our study neuropathy was present in 20% of patients.

Glycemic control and diabetic neuropathy

The DCCT Research Group[22] reported significant effects of intensive insulin therapy on prevention of neuropathy. The prevalence rates for clinical or electrophysiologic evidence of neuropathy were reduced by 50% in those treated by intensive insulin therapy during 5 years. At that stage of the study, only 3% of the patients in the primary prevention cohort treated by intensive insulin therapy showed minimal signs of diabetic neuropathy, compared with 10% of those treated by the conventional regimen. In the secondary prevention cohort, intensive insulin therapy significantly reduced the prevalence of clinical neuropathy by 56% (7% in intensive insulin therapy group versus 16% in conventional therapy group). In the UKPDS, control of blood glucose was associated with improvement in vibration perception. Similar to what was found in the DCCT, despite loss of diabetes control, with time nerve function improved in the formerly well-controlled group in what has now come to be known as legacy effect or good metabolic memory.[21]

In this present study, of the total 50 patients studied 10 had diabetic neuropathy(DN), 9 patients(90%) with DN had HbA1C more than 7.5%, 1 patient with DN had HbA1C <7.5%, which shows that poor glycemic control is associated with increased risk of diabetic neuropathy, statistically significant ($P < 0.001$).

Vitamin D and diabetic neuropathy

The prevalence of vitamin D deficiency in patients having diabetic neuropathy in our study is 70% with mean vitamin D value of 17.260 ± 6.7233 which compares well with other studies

Lee and Chen in their study on use of vitamin D as analgesic for neuropathic pain found that all patients were vitamin D insufficient and mean vitamin D level was 18 ng/ml. Soderstorm et al.[23] Demonstrated vitamin D insufficiency is associated with the adjusted composite measure of neuropathy. Shebab et al.[24] showed that the onset of neuropathy can be delayed by vitamin D treatment. A meta-analysis of three studies with adjusted estimates showed that vitamin D deficiency was independently associated with increased risk of DPN in patients with type 2 diabetes.

All microvascular complications and vitamin D

In our study prevalence of microvascular complications is 40%. Single microvascular complications (retinopathy or neuropathy or nephropathy) was present in 20% of cases while the combination of all three was present in 12% of cases. Overall 70% of cases having neuropathy, 75% of cases having retinopathy and 51.1% of cases having nephropathy were deficient in vitamin D. Among diabetics having no microvascular complications, 56.7% of cases were having vitamin D deficiency. On applying ANOVA test vitamin D deficiency was not found to be separately associated significantly with neuropathy, retinopathy and nephropathy individually. The mean vitamin D levels were found to be 21.68 ± 6.44 (no microvascular complication), 17.26 ± 6.72 (neuropathy), 17.17 ± 6.02 (retinopathy), 19.02 ± 6.82(nephropathy), 17 (neuropathy with retinopathy), 25 ± 5.6 (neuropathy with nephropathy), 21 (retinopathy with nephropathy) and 15.2 ± 6.6 ng/ml (neuropathy with retinopathy with nephropathy). This decrease in level of vitamin D was associated significantly with the presence of multiple microvascular complications (ANOVA, $P = 0.02$). There was a significant difference in the vitamin D levels of classes having no microvascular complication and those having multiple microvascular complications, neuropathy with retinopathy with nephropathy ($P = 0.02$). Thus, lower vitamin D levels were found to be significantly associated with increased chances of having multiple microvascular complications.

Macrovascular complications

Peripheral Vascular Disease

Among the macrovascular complications of diabetes mellitus peripheral vascular disease (PVD) could be considered, as most of the interest in research and care has been cornered by coronary artery and cerebrovascular diseases. The advent of Doppler ultrasound has provided an easy means for investigating PVD. In our study we found 4% of patients suffering from PVD which was similar to the study conducted by Ramachandran et al prevalence of peripheral vascular disease was 4% in South Indian diabetic subjects.[11] In study of RP Agrawal et al[14] it is 28%. Much higher prevalence in study was attributed to different genetic constitution and poor glycaemia.

Literature search for articles on the prevalence of vitamin d deficiency in peripheral vascular disease of T2DM in India for comparison are very few. Mean vitamin D value

in cases having PVD in our study is 18.2 ± 2.4 and out of 2 patients having PVD, both of them had vitamin d deficiency. prevalence of CVD in our study is 4%.

Cerebrovascular Disease

Glycemic control and Cerebrovascular disease

Although it is clear that diabetes increases the risk of stroke, it has proven difficult to determine whether controlling glucose effectively reduces this risk. In our study the patients with CVD had poor glycemic control with HBA1C ranging from 7.7 to 10.4

Cerebrovascular disease and viamin D

Vitamin D is another independent risk factor for cerebrovascular disease. In large population-based prospective study in Copenhagen, an increase risk of symptomatic ischemic stroke was observed with decreasing plasma 25(OH)D concentrations. Prevalence of vitamin D deficiency in CVD in our study is 100% with mean value of 13.5±4.31 The high prevalence of vitamin D deficiency in our subjects is reflective of the generalized high prevalence rates of hypovitaminosis D in India.

Targher G et al [25] in their study had prevalace of 34% and analyzed the IMT of the carotid artery in patients with T2DM, and the researchers demonstrated that vitamin D deficiency has a strong association with increased IMT and atherosclerosis development. The lower prevalence in their study was because they have taken the reference value of <37.5 ng/l as vitamin d deficiency which was way higher than the current standard of ≤ 20.In meta analysis they concluded that safe and cost-effective interventions to improve vitamin D status (e.g., supplements, sun exposure, or diet) can be scalable at the population level and may provide complementary benefits to prevent cerebrovascular, coronary and mortality events.

Coronary Artery Disease

CAD is one of the leading cause of death in patients with Type 2 DM accounting for 50-70% of all Deaths. Patients with Type 2 DM have the same risk of myocardial infarction as patients who have already suffered a heart attack, leading many clinicians to consider type 2 DM to be a cardiovascular equivalent. The prevalence of cad is 20% in our study.

Coronary artery disease and vitamin D

Framingham Offspring Study reported that subjects with a severe Vitamin D deficiency (and no prior diagnosis of cardiovascular disease) experienced a hazard ratio of 1.80 for developing their first CV event 5 years after their follow -up compared to subjects with higher levels of Vitamin D.In the National Health and Nutrition Examination Study (NHANES) 2001 to 2004, the prevalence of coronary heart disease (angina, myocardial infarction) was more common in adults with 25OHD levels <20 ng/mL compared with ≥30 ng/ml.In our study 7 0ut of 10 patients with CAD have vitamin D deficiency the mean value of vitamin d in patients with CAD is 19.31±6.27.

CONCLUSION

Vascular complications are a major cause of morbidity and mortality in T2DM. Assessment for vascular complications must be done at the time of diagnosis and during follow up in all patients. Once complications develop, in addition to strict control of hyperglycemia, steps have to be taken to prevent or retard further progression of these complications.

vitamin D deficiency (<20 ng/ml) in type 2 diabetes is associated with any of the microvascular complications, i.e. neuropathy, retinopathy, and nephropathy and type 2 diabetics with decreasing vitamin D levels have significantly increasing prevalence of combination of microvascular complications. The vitamin 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.

REFERENCES

1. Kasper,Fauci, Hauser et al. Dabetes mellitus. Harrisons Principles of internal Medicine 19th edition 2015;417:2401-2407.
2. Holick MF, Binkley NC, Bischoff-Ferrari HA, Gordon CM, Hanley DA, Heaney RP et al. Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2011;96:1911-30.
3. Tahrani AA, Ball A, Shepherd L, Rahim A, Jones AF, Bates A. Theprevalence of vitamin D abnormalities in South Asians with type2 diabetes mellitus in the UK. IntJ Clin Pract. 2010;64:351-5.
4. Baeke F, Gysemans C, Korf H, Mathieu C. Vitamin D insufficiency: implications for the immune system. PediatrNephrol 2010; 25:1597–1606
5. Bajaj S, Singh RP, Dwivedi NC, Singh K, Gupta A, Mathur M. Vitamin D levels and microvascular complications in type 2 diabetes. Indian J Endocr Metab 2014;18:537-41.
6. Jung Chan-Hee, Kim Kyu-Jin, Kim Bo-Yeon, Kim Chul- Hee, Kang Sung Koo, Mok Ji-Oh, Relationship between vitamin D status and vascular complications in patients with type 2 diabetes mellitus, Nutrition Research 2015.
7. Gaurav Modi, Smita Bahediya, Ashish Sharma Vitamin D levels and diabetic microvascular complications, International journal of medical science and education 2016:3;
8. Scragg R, Sowers M, Bell C, Third National Health and Nutrition Examination Survey. Serum 25-hydroxyvitamin D, diabetes, and ethnicity in the Third National Health and Nutrition Examination Survey. Diabetes Care 2004;27:2813-8.
9. Suzuki A, Kotake M, Ono Y, Kato T, Oda N, Hayakawa N, et al. Hypovitaminosis D in type 2 diabetes mellitus: Association with microvascular complications and type of treatment. Endocr J 2006;53:503-10.
10. Green RT, Gambhir KK, Nunlee-Bland G, Odonkor WA, Ganta VA. Maintenance of long-term adequate levels of vitamin d lowers HbA1c in African American patients with type 2 diabetes. Ethn Dis. 2014;24:335-41.
11. Ramchandran A, Snehalatha C, Satyavani K, Latha E, Sasikala R, Vijay V. Prevalence of vascular complications and their risk factors in type 2 diabetes.

Journal of Assoc Physicians India 1999; 47: 1152- 6.
12. Usluogullari et al. BMC Endocrine Disorders 2015;15:33.
13. Knuiman MW, Welborn TA, McCann VJ, Stanton KG, Constable IJ. Prevalence of diabetic complications in relation to risk factors. Diabetes 1986;35:1332-39.
14. RP Agrawal, Vipin Ola, Prashant Bishnoi, Sunil Gothwal, Parmender Sirohi,Ritvik Agrawal Prevalence of Micro and Macrovascular Complications and their Risk Factors in Type-2 Diabetes Mellitus. Journal of the association of physicians of India 2014;62:44-48.
15. Deepa DV, Kiran BR, Gadwalkar srikanth R. Macrovascular and Microvascular Complications in Newly Diagnosed Type 2 Diabetes Mellitus Indian Journal of Clinical Practice 2014;25:
16. Rema M, Premkumar S, Anitha B, Deepa R, Pradeepa R, Mohan V.Prevalence of diabetic retinopathy in urban India: The Chennai Urban Rural Epidemiology Study (CURES) eye study, I. Invest Ophthalmol Vis Sci 2005;46:2328-33.
17. Pemlatha G, Rema M, Mohan V. Complications of diabetes mellitus at diagnosis in South Indian type 2 diabetic patients. Int J Diab Dev Ctries 1998;18:1-4.
18. Weerasuriya N, Siribaddana S, Dissanayake A, Subasinghe Z, Wariyapola D, Fernando DJ. Long-term complications in newly diagnosed Sri Lankan patients with type 2 diabetes mellitus. QJM 1998;91:439-43.
19. Aksoy H, Akçay F, Kurtul N, Baykal O, Avci B. Serum 1,25 dihydroxy vitamin D (1,25(OH) 2D3), 25 hydroxy vitamin D (25(OH) D) and parathormone levels in diabetic retinopathy. Clin Biochem 2000;33:47-51.
20. Kaur H, Donaghue KC, Chan AK, Benitez-Aguirre P, Hing S, Lloyd M,et al. Vitamin D deficiency is associated with retinopathy in children and adolescents with type 1 diabetes. Diabetes Care 2011;34:1400-2.
21. Sadosky A, McDermott AM, Brandenburg NA, Strauss M. A review of the epidemiology of painful diabetic peripheral neuropathy, postherpetic neuralgia, and less commonly studied neuropathic pain conditions. Pain Pract. 2008;8:45-56.
22. Diabetes Control and Complications Trial Research Group. The effect ofintensive treatment of diabetes on the development and progression of longterm complications in insulin-dependent diabetes mellitus. N Engl J Med 1993;329:977-986.
23. Soderstrom LH, Johnson SP, Diaz VA, Mainous AG, 3rd. Association between vitaminD and diabetic neuropathy in a nationally representative sample: results from 2001-2004NHANES. Diabet Med 2012;29:50-5.
24. Shehab D, Al-Jarallah K, Mojiminiyi OA, Al Mohamedy H, Abdella NA. Does Vitamin D deficiency play a role in peripheral neuropathy in Type 2 diabetes? Diabet Med 2012;29:43-9.
25. Targher G, Bertolini L, Padovani R, Zenari L, Scala L, CigoliniM, et al. Serum 25-hydroxyvitamin D3 concentrations andcarotid artery intima-media thickness among type 2 diabetic patients. Clin Endocrinol (Oxf). 2006;65:593–7.

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