VITAMIN D3 LEVEL IN TYPE 2 DIABETES MELLITUS AND ITS CORRELATION WITH HbA1c LEVEL- A CROSS-SECTIONAL STUDY

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ABSTRACT

BACKGROUND

The role of vitamin D in type 2 diabetes is suggested by a seasonal variation in glycaemic control. It was reported in patients with type 2 diabetes being worse in winter, which might be due to hypovitaminosis D as a result of reduced exposure to sunlight.

Aims and Objectives-

(I) To estimate the plasma vitamin D3 level in type 2 diabetes mellitus.

(II) To find out association between vitamin D3 and HbA1c level.

(III) Correlation between serum vitamin D3 level and diabetic cardiovascular complications.

MATERIALS AND METHODS

A cross-sectional study was conducted among 100 type 2 diabetes patients who were selected from medicine ward and diabetes clinic. The descriptive statistics like percentages, mean and median were calculated. The inferential statistics like Chi-square statistics and Spearman's correlation were performed for analysis of data.

RESULTS

HbA1c was increased in majority of patients (71.0%). Majority of the respondents were having low vitamin D levels. There was gross scattering of the dots indicating that poor correlation between HbA1c and Vitamin D levels. The Spearman's Rho was found to be only 0.092 (poor correlation) and this finding was not significant ($p = 0.361$). There was poor correlation between HbA1c and Vitamin D3 levels and Vitamin D3 level was not correlated with age and hypertension.

CONCLUSION

The 25-(OH) D3 concentrations were low in 90% of the diabetic patients. There was an inverse association between the serum concentration of 25-(OH) D3 and type 2 diabetes, thereby suggesting a protective role of vitamin D against the development of the disease.

KEY WORDS

Diabetes Mellitus Type 2, Vitamin D3, HbA1c and Correlation.

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BACKGROUND

Diabetes Mellitus is a heterogeneous group of metabolic disorders characterised by chronic hyperglycaemia with disordered metabolism of carbohydrate, fat and protein due to deficiency of insulin secretion and inadequate insulin action or both.⁽¹⁾ It is broadly classified into two groups, type 1 and Type 2. The type 1 diabetes mellitus is due to deficiency of insulin, which may be complete or near to total and type 2 diabetes mellitus is a result of some heterogeneous group of disorders having variable decrease of insulin-resistant impaired insulin secretion and increased glucose production.⁽²⁾ Vitamin D3 or cholecalciferol is formed in the skin by ultraviolet radiation. External supplementation of vitamin D is necessary when low levels of vitamin D are found, such as during periods with little sun and when the body is totally covered and the intake of vitamin D in the diet

is low. Vitamin D has two intracellular effects: it binds to the intranuclear vitamin D receptor, which modulates gene expression and it has an effect through the regulation of extracellular and intracellular calcium. Vitamin D3 or cholecalciferol is formed in the skin by ultraviolet radiation from sunlight.⁽³⁾ Diabetic patient's condition deteriorates in winter that might be due to low Vitamin D level due to low exposure to sunlight.⁽⁴⁾ There was an estimate of 380 million people likely to be affected with diabetes worldwide by the year 2025. In India, 41 million individuals are affected and likely to rise up to 70 million by the year 2025. Vitamin-D directly or indirectly improves insulin exocytosis via activating calcium-dependent endopeptidases. Vitamin D improves glucose tolerance and prevents type 2 DM as an efficient antioxidant. Vitamin D mediates non-calcaemic functions and regulator of cellular proliferation, differentiation and replication, and mediator of autoimmune reactions in different organs and biological systems. Our view of the physiological role of vitamin D has broadened following the discovery of receptors for 1 alpha 25-dihydroxy vitamin D3 in tissues with its direct role in calcium and bone metabolism.⁽⁵⁾ A large proportion of population has low vitamin D levels, which are generally defined as a serum 25-(OH) vitamin D less than 20 or 30 ng/mL. Modern society are lastly dependent on consumption of vitamin D milk or other supplements to have normal vitamin D levels, even though

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exposure to sunlight stimulates vitamin D production from the skin. The relationship of vitamin D deficiency to the development of diabetes mellitus and complications due to diabetes has broad interest to scientists over the past decades.⁶ The suggested relationship between type 2 diabetes mellitus and vitamin D deficiency has been extensively reported. Diabetes is associated with complications such as cardiovascular disease renal impairment and peripheral neuropathies. When patients were given 1-alpha vitamin D and the Vitamin D analogue paricalcitol it was noted that the mortality rate for the cardiovascular diseases was significantly reduced.⁷ It has been observed that vitamin D with calcium supplementation produces a significant decrease in fasting glucose and insulin resistance in patients with impaired fasting glucose. Some investigators have advocated the HbA1c as a diagnostic test for DM. Measurement of glycated haemoglobin is the standard method for assessing long-term glycaemic control. When plasma glucose is elevated over a period of time, there is increase in non-enzymatic haemoglobin glycation. This change reflects on the glycaemic history over the period of 2-3 months as RBC has lifespan of about 120 days. With this view, the present work was done and evaluated with the serum vitamin D and HbA1c level in 100 cases of type 2 diabetic patients from diabetes clinic and medical ward.

Objectives

1. To estimate the plasma vitamin D3 level in type 2 diabetes mellitus,
2. To find out association between vitamin D3 and HbA1c level in type 2 diabetes mellitus.
3. To find out correlation between serum vitamin D3 level and diabetic cardiovascular complications.

MATERIALS AND METHODS

A cross-sectional study was conducted among 100 type 2 diabetic patients attending Medicine Department, RIMS Hospital, Imphal, Manipur during 2011 to 2013 for duration of 2 years. Sample size (n): $Z_{1-\alpha/2}p(1-p)/d^2$ where 'p' is 0.5 (Expected proportion of 50% of diabetes population having low Vitamin D3 level) with precision (d) 0.10 at 95% confidence interval and 5% level of significance. The sample size is 100. The cases were selected from medicine ward and diabetes clinic, irrespective of sex, age and socio-economic status. Any patient having phenotype of hyperglycaemia irrespective of age, sex and socio-economic status and symptoms of diabetes along with (i) Random blood glucose concentration > 11.1 mmol/L (200 mg/dL), (ii) Fasting > 7 mmol/L (126 mg/dL), (iii) Postprandial > 11.1 mmol/L (200 mg/dL). Patient suffering from critical illness, chronic liver disease, TB, chronic kidney disease, malignancy, hypertension and hypoparathyroidism and any chronic infection was excluded from the study. A detailed personal history of each case regarding age, sex, address, religion, duration of diabetes, family history of diabetes, dietary habits were recorded in a pre-designed proforma, especially mean for the study. Then general physical examination of each case regarding height, weight, blood pressure, pulse rate, abdominal girth, BMI, cyanosis, jaundice, pallor, lymphadenopathy and systemic examination of CVS, respiratory system, CNS and abdomen were carried out.

The following Investigations were included for the Study

I. Blood Sugar: a) Random, b) Fasting, c) PP and Serum Vitamin D3. Estimation by glucose oxidase and peroxidase

method. Estimation of 25-OH Vitamin D: Elisa test principles of the test. This Elisa test kit is designed for the in vitro determination of 25-OH vitamin D in human serum or plasma samples. The descriptive statistics like percentages was calculated. The inferential statistics like Chi-square statistics and Spearman's correlation were applied for analysis of data. The p-value < 0.05 was considered significant. The informed consent was obtained from the participants before conducting the study. The ethical approval was obtained from the Institutional Ethics Committee before conducting the study.

RESULTS

The study conducted in Department of Medicine, RIMS, Imphal, Manipur from October 2011 to September 2013 included 100 cases of type 2 Diabetes Mellitus from Diabetes clinic or admitted in Medicine ward. One third (33%) of the respondents were from age group of 45 to 54 years with a median of 55 years and age ranges from 35 years to 93 years. Majority of the respondents were females, which accounts for 55% of cases. Table 3 and Figure 3 shows that majority of the respondents were Hindu (71.0%) followed by Christian (18.0%) and Muslim (11.0%). Nearly, half of the respondents (47%) had diabetes for more than 1 year to five years with a median duration of 2 years. The minimum was diabetes just detected (0 years) to 18 years. Majority of the respondents had a non-vegetarian diet (85.0%). More than half of the respondents were hypertensive as shown in table (Table 1). Most of the respondents used oral hypoglycaemic, which accounted for 89%. Majority of the respondents were overweight (71.0%) and 19% of them were obese. The median BMI was 26.6 kg/m² with range from 21 to 38.6 kg/m² as shown in Table 2. HbA1c was increased in majority of patients (71.0%). Majority of the respondents were having low vitamin D levels as shown in Table 3. Vitamin D levels in diabetes had no relation with the presence of hypertension. Vitamin D levels in diabetes had no relation with the increase in creatinine level (Table 4). There was gross scattering of the dots indicating that poor correlation between HbA1c and Vitamin D levels. And also the Spearman's Rho was found to be only 0.092 (poor correlation) and this finding was not significant (p= 0.361) (Fig. 1).

Variables		Number (N)	(%)
Age (Years)	<45	16	16.0
	45-54	33	33.0
	55-64	26	26.0
	≥65	25	25.0
Sex	Male	45	45.0
	Female	55	55.0
Religion	Hindu	71	71.0
	Muslim	11	11.0
	Christian	18	18.0
Duration of Diabetes	51 years	31	31.0
	1-5	47	47.0
	5-10	18	18.0
	>10	4	4.0
Dietary Habit	Vegetarian	15	15.0
	Non-Vegetarian	85	85.0
Hypertension	Present	54	54.0
	Absent	46	46.0

Table 1. Socio-Demographic Profile of the Diabetes Patients

Variables		Number (N)	Percentage (%)
Drugs	Oral hypoglycaemic drugs	89	89.0
	Insulin	1	1.0
	Both oral hypoglycaemic and insulin	9	9.0
BMI	< 25.0	10	10.0
	25-29.99	71	71.0
	30.0	90	19.0

Table 2. Distribution of subjects according to Drug used and BMI Status

Variables		Number (N)	Percentage (%)
HbA1c level	Normal (6.5%)	29	29.0
	Increased	71	71.0
Vit D3 Level	Low (30 ng/mL)	90	90.0
	Normal	10	10.0

Table 3. Laboratory findings of the Study Subjects

Variables		Vitamin D3 Level		P-value
		Low, N (%)	Normal, N (%)	
Hypertension	Present	47	7	0.33
	Absent	43	3	
Creatinine	Normal	86	8	0.10
	Increased	4	2	

Table 4. The Association of Vitamin D3 with Hypertension and Serum Creatinine

Figure 1. Scattered diagram showing the relation between HbA1c and Vitamin D3 Level

DISCUSSION

Diabetes mellitus is one of the most prevalent non-communicable diseases showing alarming rise in its incidence in the developing countries like India. Type 2 diabetes mellitus is recognised as a worldwide public health problem due to the high medical and socioeconomic costs that result from complications associated with the disease. The present study on serum Vitamin D3 level in type 2 diabetes mellitus and its correlation with HbA1c level as carried out in the Department of Medicine, Regional Institute of Medical Sciences and Hospital, Imphal in collaboration with the Department of Biochemistry during the period from August 2011 to August 2013. The study sample consisted of 100 type 2 diabetes mellitus patients selected randomly from diabetes clinic and medicine ward. In present study, most of the patients were in the age group of 45 - 64 yrs. and the male-to-female ratio was 1: 2:1 and Hindus were 71%, Muslims were 11% and Christian were 18%. Out of 100 patients 89% were on oral hypoglycaemic, 1% were on insulin and 10% were on both oral hypoglycaemic and insulin. The duration of the diabetes among study population, most of them were having DM 1 - 5 yrs., median 2 yrs. The median BMI was 26.6 kg/m².

The rural and urban distribution of respondent's ratio was 1:1. According to various references, Vitamin D has a potential influence on glucose homeostasis as suggested by the following factors-

1). Effect of vitamin D on insulin secretion, pancreatic 13 cell express with 1-alpha hydroxylase which is responsible for an active vitamin D3 synthesis and also by increasing the insulin response to the glucose stimulation, but not affecting the basal insulin secretion and sensitivity is influenced by vitamin D mediated intracellular calcium secretion that enhances the binding of the calcium binding protein to the IRS-1 stimulating tyrosine phosphorylation and PI3 kinase activation and thus promoting insulin secretion and sensitivity is influenced by vitamin D mediated intracellular calcium secretion. The insulin secretion thus enhances the binding of the calcium binding protein to the IRS-1, stimulating tyrosine phosphorylation and P13 kinase activation and thus promoting insulin secretion.⁸

2). Effect of vitamin D on the insulin sensitivity: - Type 2 diabetes mellitus, a state of chronic systemic inflammation has been found to increase the insulin resistance. Type 2 was found to be associated with an increase in the level of the tumour necrosis factor "a" and "b," the "c" reactive protein the plasminogen activator inhibitor 1 and IL-6. Vitamin D also suppresses the antigen-presenting production of IFN γ and IL-2 among other cytokines. These cytokines have role to activate macrophages and cytotoxic T-cell, which ultimately leads to pancreatic islets destruction. By the modulation of the immune and the inflammatory processes, vitamin D may also decrease insulin resistance and increase the insulin secretion in type-2 DM, which are the two characteristic defects in this condition. From the above discussion, it is clear that vitamin D has a significant role to play in the molecular mechanisms of the synthesis, secretion and the peripheral sensitivity of insulin.⁹ Hence, hypovitaminosis D may be associated with insulin resistance and beta cell dysfunction. In our study, we observed that 90% of type 2 diabetic individuals have lower vitamin D level (< 30 ng/mL). Song et al¹⁰ in their study found an inverse and significant association between circulating 25-(OH) D level and risk of type 2 diabetes across a broad range of blood 25-(OH) D levels in diverse population. Thus, the present study with similar finding in the previous studies show that there is significant lower circulating 25-(OH) D in type 2 diabetes. Hurskainen AR et al¹¹ in their study found that low serum 25-(OH) D is associated with impaired glucose metabolism. Thus, the present study with similar findings in the previous studies show that there is significant lower circulating 25-(OH) D in type 2 diabetes. Scragg R et al¹² in their study found that low serum 25-(OH) D is associated with impaired glucose metabolism. The present study with similar findings in the previous studies shows that there is significant lower circulating 25-(OH) D in type 2 diabetes. Isaia G et al¹³ in their study found that 25-(OH) D levels were significantly lower in diabetic patients than in control subjects and the prevalence of 25-(OH) D deficiency was significantly higher in diabetic patients than in control subject. Shoaib A et al¹⁴ in their subject found that low serum 25-(OH) D is associated with impaired glucose metabolism. The cross-sectional studies have demonstrated that lower serum 25-(OH) D levels are associated with impaired glucose tolerance and diabetes. Thus, the present study with similar findings in the previous

studies shows that there is inverse and significant association between circulating 25-(OH) D levels and risk of type 2 diabetes. In our study, we observed that vitamin D levels were not correlated with age and hypertension ($p= 0.33$). Joergensen C et al¹⁵ in their study found that vitamin D level were not correlated with HTN. Thus, the present study with similar findings in the previous studies shows that vitamin D level was not changed with age and HTN. In our study, we observe that there is poor correlation between HbA1c level and vitamin D levels, ($p= 0.361$). Parameasvari PJ et al¹⁶ in their study found there exists a statistically insignificant correlation between HbA1c and Vitamin D3 for all 34 patients, ($p= 2.78$). Thus, the present study with similar findings in the previous studies shows that there is poor correlation between HbA1c level and vitamin D levels. Pilz S et al¹⁷ in their study observed non-significant trend towards an inverse association of 25-(OH) D with prospective changes in HbA1c that deserves further investigation. Thus, the present study with similar findings in the previous studies shows that there is poor correlation between HbA1c level and vitamin D levels.

CONCLUSION

The 25-(OH) D3 concentrations were low in 90% of the diabetic patients. There was an inverse association between the serum concentration of 25-(OH) D3 and type 2 diabetics, thereby suggesting a protective role of vitamin D against the development of the disease. There was poor correlation between HbA1c and vitamin D level and Vitamin D level was not correlated with age and hypertension.

Limitation and Strength

This study cannot be generalised due to small sample size and also because the study was limited to a single hospital.

Recommendation

Further study is recommended involving more subjects and covering both urban and rural population.

Ethical Clearance

Approved from the Institutional Ethics Committee of RIMS, Imphal, Manipur, India.

REFERENCES

- [1] Bennett PH, Knowler WC. Definition, diagnosis and classification of diabetes mellitus and glucose homeostasis. In: Kahn RC, Weir GC, King GL, et al. eds. Joslin's diabetes mellitus. 14th edn. Philadelphia: Lippincott Williams & Wilkins 2005: p. 331-40.
- [2] Power AC. Diabetes Mellitus. In: Fauci AS, Braunwald E, Kasper D, et al. eds. Harrison's Principles of internal medicine. 18th edn. New York: McGraw-Hill 2012: p. 2275-304.
- [3] Krans HMJ. Baseline serum 25-hydroxyl vitamin D in predicting glycemic status and insulin levels. F1000 Med Rep 2009;1: pii: 85.
- [4] Mathieu C, Gysemans C, Giulietti A, et al. Vitamin D and diabetes. Diabetol 2005;48(7):1247-57.
- [5] Seshadri KG, Tamilselvan B, Rajendra A. Role of vitamin D in diabetes. J Endocrinol & Metab 2011;1(2):47-56.
- [6] Ortelepp JR, Metrikat J, Albrecht M, et al. The vitamin D receptor gene variant and physical activity predicts fasting glucose levels in healthy young men. Diabetes Med 2003;20(6):451-4.
- [7] Zittermann A. Vitamin D and disease prevention with special reference to cardiovascular disease. Prog Biophys Mol Biol 2006;92(1):39-48.
- [8] Danescu LG, Levy S, Levy J. Vitamin D and diabetes mellitus. Endocrine 2009;35(1):11-7.
- [9] Kolb H, Mandrup-Poulsen T. An immune origin of type 2 diabetes? Diabetologia 2005;48(6):1038-50.
- [10] Wolford JK, Gruber JD, Ossowski VM, et al. A C-reactive protein promoter polymorphism is associated with type 2 diabetes mellitus in Pima Indians. Mol Gent Metab 2003;78(2):136-44.
- [11] Hurskainen AR, Virtanen JK, Tuomainen TP, et al. Association of serum 25-hydroxyvitamin D with type 2 diabetes and markers of insulin resistance in a general older population in Finland. Diabet Metab 2012;28(5):418-23.
- [12] Scragg R, Holdaway I, Singh V, et al. Serum 25-hydroxy vitamin D3 levels decreased in IGT and diabetes mellitus. Diabetes Res Clin Pract 1995;27(3):181-8.
- [13] Isaia G, Giorgino R, Adami S. High prevalence of hypovitaminosis D in female type diabetic population. Diabetic Care 2001;24(8):1496-9.
- [14] Shoaib A, Stig EB, Berge GN. Low 25-hydroxyvitamin D and risk of type 2 diabetes: a prospective cohort study and meta-analysis. Clin Chemistry 2013;59(2):381-91.
- [15] Joergensen C, Gall MA, Schemedes A, et al. Vitamin D levels and mortality in type 2 diabetes. Diabet Care 2010;33(10):2238-43.
- [16] Parameasvari PJ, Revathy C, Shanti B. A cross sectional study on vitamin D3 level in type 2 diabetes mellitus patients from Chennai, India. Dabetologia 2012;(45):584-7.
- [17] Pilz S, van den Hurk K, et al. Vitamin D status, incident diabetes and prospective changes in glucose metabolism in older subjects: the Hoorn study. Nutr Metab Cardiovasc Dis 2012;22(10):883-9.