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Research Article

STUDY OF VITAMIN-D AND HOMOCYSTEINE IN TYPE-2 DIABETES

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ABSTRACT

Diabetes mellitus is the most common endocrine disorder in developed countries and also in developing countries like India. It has been hypothesized that vitamin D levels and homocysteine levels may contribute in the pathogenesis of diabetes. The aim of our present study is to evaluate the role of vitamin D and homocysteine in type-2 diabetes. We tried to assess 25 hydroxy vitamin- D Levels by CLIA method and homocysteine by ELISA method. For this, we have taken 50 cases of type-2 diabetic patients and 75 patients as controls. A significant decrease in the levels of vitamin-D and significant increase in the levels of homocysteine were observed. This suggests that vitamin-D and homocysteine may play a role in development of type-2 diabetes mellitus.

Keywords: Vitamin- D, Homocysteine, Diabetes mellitus.

INTRODUCTION

Diabetes mellitus comprises a group of common metabolic disorders that share the phenotype of hyperglycemia. It is the most common endocrine metabolic disorder, affecting about 170 million people worldwide.[1]The prevalence of Type-2 diabetes has been increasing nationally and worldwide, and is associated with considerable morbidity and mortality. Epidemiological data suggest that nine of ten cases of Type-2 diabetes mellitus could be attributed to habits and forms of modifiable behavior.[2].

The most important and major function of vitamin D is to maintain calcium and phosphorus homeostasis and promote bone mineralization. Vitamin D insufficiency has long been suspected as a risk factor for type 1 diabetes based on animal and human observational studies[3].There is accumulating evidence to indicate the role of vitamin D deficiency in the development of type-2 diabetes. Evidences indicate that circulating concentrations of vitamin D may be inversely related to the prevalence of diabetes[4,5], to the concentration of glucose[5-7], and to insulin resistance[5,7,8]. In addition, vitamin D deficiency may be a risk factor for the metabolic syndrome[7,9]. Recently, low levels of vitamin D have been associated with increased risk of cardiovascular disease[10] as well as all-cause[11] and cardiovascular mortality[12] in the general population.

Homocysteine is an intermediary aminoacid formed during the conversion of methionine to cysteine. Elevated total plasma level of aminoacid Homocysteine has been identified as an independent risk factor of arteriosclerosis involving coronary, cerebral ,and peripheral arteries. High levels of Homocysteine causes lipid peroxidation, vascular endothelial injury, impaired vasomotor regulation, pro thrombotic surface, and therefore atherothrombogenesis.[13].Hyperhomocysteinemia is suggested to be an independent risk factor for premature vascular disease[14],myocardial infarction[15], and stroke[16].Furthermore, raised Homocysteine levels have recently been suggested as a risk factor for non-arteritic anterior ischemic optic neuropathy[17] and retinal vascular occlusive disease with thromboembolism.[18].

The aim of our present study is to evaluate the role of vitamin D and homocysteine in development of type 2 diabetes by estimating the status of vitamin D and homocysteine levels in type 2 diabetes as early identification paves the way for early intervention, thereby contributing to desirable reduction in complications among diabetes patients.

MATERIALS AND METHODS

The present study was conducted in the department of biochemistry, Saveetha Medical college, Chennai and S.V.Medical college,Tirupati.50 diagnosed cases of diabetes mellitus belonging to age group of 35-70 years were included in this study. 75 age matched subjects who have no history of diabetes mellitus were taken as controls. All the subjects were not having any complications of diabetes mellitus and they had no prior history of metabolic bone disease, vitamin D deficiency, parathyroid disease, malabsorption and other diseases like liver diseases, psychiatric illness, chronic alcohol abuse, anticonvulsant and immunosuppressive therapy, postmenopausal hormone replacement. Informed consent was obtained from all the subjects. Due permission was obtained from Ethical clearance committee for this study.

5ml of fasting blood samples were collected by venipuncture and for the separation of sera, blood was centrifuged at 3000rpm for 5min. 25-hydroxy vitamin D levels were estimated by fully automated Chemi Luminescent Immune Assay(C.L.I.A) method. Serum total homocysteine levels were determined by Enzyme linked immunosorbent assay(ELISA) kit .All the results were expressed as mean ± SD and statistical comparisons were done using student t-test using the SPSS package.

RESULTS

Table 1: Comparison of levels of vitamin-D and homocysteine in cases and controls.

Parameters	Type-2 diabetics(n=50) Mean ± S.D	Controls (n=75) Mean ± S.D	p value
Total 25-hydroxy vitamin D (ng/ml)	8.87±0.11	31.66±0.13	<0.001 (highly significant)
Homocysteine (ng/ml)	18.13±2.62	7.96±2.46	<0.001 (highly significant)

There was a significant decrease in the levels of vitamin-D in type-2 diabetic patients when compared with controls. There was a significant increase in the levels of homocysteine in type-2 diabetic patients as compared to controls.

DISCUSSION

Diabetes mellitus comprises a group of common metabolic disorders that share the phenotype of hyperglycemia. Several distinct types of diabetes mellitus exist and these are caused by a complex interaction between the genetic factors[19]. Hyperglycemia due to insulin resistance is characterized by dyslipidemia and inflammation[20]. Vitamin D can be obtained from dietary sources of vegetable(D2 or ergocalciferol) or animal origin(D3 or cholecalciferol). The best food sources are fatty fish or their liver oils. Vitamin D3 itself is biologically inert and requires two successive hydroxylations, one in the liver and one in the kidney. The main function of vitamin D is facilitating intestinal calcium absorption. The mechanisms by which vitamin D may affect the risk of type 2 diabetes are not clear. Vitamin D deficiency was linked to impaired glucose tolerance(IGT) and type 2 Diabetes in human[7] and these observations were confirmed in animal models, which demonstrated that pancreatic insulin secretion is inhibited by vitamin D deficiency[21]. Both insulin resistance and impaired pancreatic beta cell function have been reported with vitamin D insufficiency[5,7]. The active role of vitamin D in the functional regulation of endocrine pancreas mainly the beta cells was shown by the receptors for 1,25 dihydroxycholecalciferol found in beta cells[22] and the finding of impaired insulin secretory capacity in mice lacking a functional vitamin D receptor[23].

The mechanism by which 1,25 dihydroxycholecalciferol might act on insulin secretion is suggested by the significant rise in cytosolic Calcium levels observed following 1,25(OH)2D3 stimulated secretion of insulin by islet cells. Controversy remains as to whether an influx of external calcium via voltage dependent calcium channels is solely responsible for this rise, or whether the mobilization of calcium from intracellular organelles and the activation of release potentiating systems via protein kinase C and protein kinase A pathways are also involved.[24,25].Vitamin D supplementation improved insulin release in some[26,27] short term randomized trials. Vitamin D may have a beneficial effect on insulin action either directly, by stimulating the expression of insulin receptor and thereby enhancing insulin responsiveness for glucose transport[28],or indirectly via its role in regulating extracellular calcium and ensuring normal calcium influx through cell membrane and adequate intracellular cytosolic calcium pool. Changes in calcium in primary insulin target tissues may contribute to peripheral insulin resistance via impaired insulin signal transduction, leading to decreased glucose transporter-4 activity[29]. It is currently recognized that type 2 diabetes is associated with systemic inflammation[30,31]. Systemic inflammation may be primarily due to insulin resistance, but elevated cytokines causes cell dysfunction by cell apoptosis. Vitamin D may improve insulin sensitivity and promote cell survival by directly modulating the generation and effects of cytokines.[32].

Homocystenemia has been established as a risk factor for cardiovascular disease and occurs with high prevalence in patients with type 2 diabetes, obesity and metabolic syndrome. 31% of type 2 diabetic patients have homocysteine concentrations above > 15mmol/L.[33] Many studies found significant elevation of plasma homocysteine levels in type 2 diabetes[34,35,36].In some studies there were no significant differences in fasting plasma homocysteine levels between type 2 diabetic patients without microalbuminuria and healthy control subjects.[37]. Hyperhomocystenemia may lead to any of the above metabolic disorders by elicitation of oxidative stress [38], systemic inflammation[39], and or endothelial dysfunction[40]. These factors are known to promote insulin resistance and beta cell dysfunction, two important underlying causes of type-2 diabetes.[41]. Some studies suggested contribution of variants in homocysteine metabolism pathway genes in susceptibility to obesity,type-2 diabetes, or related traits[42,43]. In a developing Country like India Obesity and Malnutrition are two ends of spectrum, obesity being an emerging issue which needs closed monitoring.[44]

In conclusion, the present study revealed that an increase in the levels of homocysteine and decrease in the levels of vitamin-D in type-2 diabetes patients when compared with controls suggesting the role of vitamin-D level and homocysteine levels in the

pathogenesis of diabetes and further extensive studies are required in future to establish these parameters as biomarkers in the development of diabetes to prevent the mortality and morbidity of diabetes.

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