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Association of Vitamins with Type 2 Diabetes Mellitus

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Introduction

The cases of DM are increasing rapidly at an alarming rate all over the globe. About 415 million adults are suffering from the disease all around the world according to the International Federation of Diabetes. It is also estimated that by the year 2040 the number of people suffering from diabetes will reach around 642 million.[1] The number of adults with diabetes has quadrupled to 422 million since 1980 according to the first global report on Diabetes by World Health Organization.[2] Type 2 diabetes mellitus is a serious problem of public health in India associated with dietary shift, genetic susceptibility and lifestyle changes.[3] According to a study it has been found that diabetes is gaining the status of epidemic in India with more than 62 million people diagnosed with the disease.[4,5]

It is found that obesity is one of the major risk factors for diabetes. India has lower obesity rates compared to western countries still the prevalence of diabetes in India is higher, which suggests that diabetes may be diagnosed at a much lower body mass index. Diabetes is now being found to be associated with a spectrum of complications. India is a vast and diversified country according to geography, socio-economic levels and ethnic nature, so despite high prevalence there is small number of studies investigating the precise status of disease.[6]

Type 2 Diabetes is a multifactorial disease which is associated to energy metabolism, particularly carbohydrate and fat management in the organism. However, micronutrients are involved as either cause or effect of this chronic pathology. The imbalance between free radical formation and their control by natural oxidants results in serious consequences of the disease. Thus, anti-oxidizing plays a crucial role in development and complications of disease. Other non-antioxidant vitamins have also been shown to have relationship with diabetes. Vitamins and minerals play an important role in glucose metabolism, so understanding the impact of vitamin and mineral deficiencies and the potential utility of supplementation is relevant to the prevention and/or management of type 2 diabetes mellitus (DM).Vitamin A plays a crucial role in various metabolic processes cellular differentiation and growth, playing an important role in immune system, fetal development, sight, taste, hearing, appetite. Retinol is the most active form which has an important function as antioxidants helping to maintain homeostasis when subjected to various forms of stress. Vitamin B6status is not clearly associated to the development of type 2 diabetes mellitus there is evidence that its deficiency may be effecting negatively the progression of some of its complications once the disease is present. Vitamin B12 is a coenzyme involved in the synthesis of methionine, pyrimidine and purine bases. Its deficiency is involved in cancer, vascular diseases and some birth defects, while a consequent hyperhomocysteinemia, also related to folic acid deficiency; it has been identified as a risk factor for hypertension and atherosclerosis. type 2 diabetes mellitus is an oxidative stress disease; vitamin B12 and folic acid deficiencies in diabetic subjects have been found associated to oxidative stress, in relation to a resulting hyperhomocysteinemia. This association shows that deficiency in Vitamin B12 should be considered as a risk factor for complications of diabetes. Vitamins C and E concentrations as well as antioxidants have been found reduced in diabetic patients with respect to healthy controls. New cases of type 2 diabetes mellitus have been found to increase lipid peroxidation and decrease antioxidant enzymes as well as vitamins C and E during the first two years of the disease .The main cause of increased requirements of vitamin C in type 2 diabetes mellitus is the high levels of oxidative stress caused by hyperglycemia. Plasma vitamin C concentrations have been inversely correlated to glycosylated hemoglobin and fasting and postprandial blood glucose and oxidative stress. Various studies have associated vitamin K intake with insulin sensitivity, glucose metabolism and thus with diabetes. A lower risk for diabetes mellitus was observed with increased vitamin K intakes. Rees et al. in a systematic review of studies that evaluated associations of vitamin K deficiency and type 2 DM. There is enough scientific evidence to recommend the supplementation of vitamin B12 in those patients with type 2 diabetes mellitus.[7]

Vitamin B1 (Thiamine) is an essential cofactor in carbohydrate metabolism, low levels of which has an impact on glucose homeostasis. According to Thornalley et al (2007) levels of thiamine were 75% less in people with type 2 diabetes. It has been found that there is deficiency of thiamine in individuals suffering with the disease, Page et al (2011).Vitamin D deficiency affects glucose metabolism which increases insulin resistance and glucose intolerance. There was strong association between type 2 diabetes and low levels of serum vitamin D according to a meta analysis (Song et al, 2013). The data revealed significant linear association between 25-hydroxyvitamin D and diabetes in the range of serum levels 20-160 nmol/L.[8]

Material and Methods

Present study was conducted in Dept. of Medicine in collaboration with Dept. of Biochemistry. A total of 100 patients were enrolled in the study of which 64 were male and 36 were female. 100 subjects were taken as a control group from 30 to 65 years age group who were not suffering from the diabetes and their HbA1c level is <6.5% and not on hyperglycemic drugs. The diagnostic criteria for type 2 diabetes were defined as a glycohemoglobin (HbA1c) ≥6.5%, fasting blood sugar ≥126 mg/dl, or glucose ≥200 mg/dl 2 hours after a 75-g oral glucose load, and patients on anti hyperglycemic drugs. We excluded patients with liver or renal disease, pregnant women, and using antioxidants or using ant vitamin supplements since last 6 months. Age group of patient selected was 25 to 65 years. Written consent was obtained from each patient to participate in the study.

Blood collection: Fasting blood samples were collected in a tube with anticoagulant, centrifuged and serums were separated. Serum levels of vitamin B-12 were measured by electro-chemi-luminescence immunoassay. Levels of vitamin D3 were measured by radioimmunoassay (RIA). Levels of HbA1c were measured by high-performance liquid chromatography (HPLC). A simple colorimetric method for plasma vitamin A and Vitamin E is evaluated, which does not require expensive equipment. Estimation of ascorbic acid or vitamin c was done by titration. Vitamin B1 and Vitamin K was estimated by Spectrophotometric method.

Data Analysis: Data were expressed as mean ±SD. Mean values were assessed for significance by unpaired student –t test. A statistical analysis was performed using the Stastical Package for the Social Science program (SPSS, 21.0). Frequencies and percentages were used for the categorical measures. Probability values $p < 0.01$ were considered statistically significant.

Observation and Result

Table 1: Shows Levels of HbA1C, Serum vitamins in DM patients and Control group

Tests	Diabetes (n=100)	Control group (n=100)	P value
HbA1C (%)	8.1 ± 0.92	4.8± 0.72	**p < *0.01***
Vit D_3 (ng/ml)	15.24± 4.43	25.28± 4.74	**p < *0.01***
Vit B_{12} (pmol/L)	384± 312.11	416 ± 254.24	**p < *0.01***
Vit A (mg/L)	0.58 ± 0.17	0.90 ± 0.37	**p < *0.74***
Vit E (µg/mL)	8.31± 3.72	11.36 ± 4.17	**p < *0.01***
Vit C (mg/dl)	0.46± 0.10	1.13 ± 0.61	**p < *0.01***
Vit B_1 (µg/dL)	2.73 ± 0.93	4.53 ±1.47	**p < *0.01***

Level of HbA1C was higher in diabetes mellitus patients (8.1 ± 0.92 %) compare to normal subjects (4.8± 0.72). A Vit D3 level was 15.24± 4.43 ng/ml in DM patients and in control group 25.28± 4.74 ng/ml shows concentration of Vit D decreased found in DM patients.. About 31 (31%) patients had serum vitamin B12 level less than 150 pg/ml while 40 (40%) had an intermediate level between 150 and 350 pg/ml. resulting in a total of 71% of the patients were diagnosed with a metabolic B12 deficiency. According to Pawlak the cut-off point of serum vitamin B-12 was set at 250 pmol/L based on the medians of vegetarians and the definition of vitamin B12 deficiency (<150 pmol/L) and borderline deficiency (<200 pmol/L).

Discussion

There has been no known link between DM and vitamin A. The some researchers believe that the purpose, in DM patients, is that vitamin A plays an important role for the development of beta-cells in the early stages of life, but also for a proper function during the remaining life especially during pathophysiological conditions, i.e some inflammatory conditions.[9] Individuals with diabetes mellitus have been considered a group in risk of presenting marginal nutritional state or deficient in many related micronutrients and composites, such as vitamins A.[10] In our study we found that the level of Vit A in DM patients was 0.58 ± 0.17 and in control group 0.90 ± 0.37 shows the concentration of Vit A was decreased in DM.

A studies in 1991 reported that serum vitamin A levels were elevated in children and adults in T2D, such as obesity and impaired glucose tolerance.[11-13]

The present study showed that the diabetic had a lower vitamin B-12 level (384± 312.11). Vitamin B-12 could be a useful potent antioxidant, as it can stimulate methionine synthase activity and through a glutathione sparing effect, can modify signaling molecules to decrease oxidative stress[14,15] and it also act as an anti-inflammation agent.[16] In the present study it was found that diabetic patients with lower vitamin B-12 level had a significantly higher concentration of blood glucose. Metformin drug is the first line treatment for diabetes and it's reported that the potentially decrease vitamin B-12 status.[17] Veg in die may be one of the major factor for vitamin B-12 deficiency in diabetic patients.

Vit D3 levels were decreased found in diabetes mellitus type 2 patients (15.24± 4.43) than in a control group (25.28± 4.74). The relationship between vitamin D and diabetes mellitus type 2 has been observed by Palomer X et. al.[18] Also it has been observed that Vitamin D is related to glucose metabolism and the development of diabetes mellitus type 2 and the metabolic syndrome.[19] In study conducted by Pittas AG et. al founded that higher plasma Vit D3 was associated with a lower risk of incident diabetes in high-risk patients.[20] Also it has been shown that ingestion of vitamin D may be related with a higher risk for the development of diabetes mellitus type 2 and the metabolic syndrome.[21]

A study by Chiu et.al shows vitamin D deficiency was found to be related to a higher risk for insulin resistance and the metabolic syndrome.[22] These findings suggests the therapeutic implications of vitamin D, in patients with diabetes mellitus type 2, normal levels of vitamin D in the blood may facilitate glucose control and optimal levels of vitamin D may retard the clinical course.

Ascorbic acid (Vit C) act as a co-factor in many reactions, it acts as a potent antioxidant, in collagen, neuropeptide and carnitin synthesis, it increases iron absorption, inhibit histamine release and stimulate the immune system. The main reason of increased requirements of vitamin C in type 2 DM is the high levels of oxidative stress and it is caused by hyperglycemia.[23]

In our study it is found that the Vitamins C and E levels have been decreased in diabetic patients as compare to healthy controls group (0.46± 0.10, 1.13 ± 0.61) (8.31± 3.72, 11.36 ± 4.17) respectively , similar findings observed by Odum E.P et. al.[24]

Plasma vitamin C concentrations have been inversely correlated to HbA1c and fasting and blood glucose level.[25] Diabetes has also been associated to periodontal disease and vitamin C supplementation together with dental maneuvers has been shown to improve chronic periodontitis in newly diagnosed type 2 diabetic subjects.[26] Vitamin C has also been shown to reduce anxiety levels but not stress and depression scores in diabetes.[27]

Thiamine, Riboflavin, Niacin, Panthotenic acid, Pyridoxine, Biotin, Cobalamin and Folic acid are usually called as B vitamins, and most of them have been linked to type 2 diabetes mellitus.

Thiamine (Vit B1) acts as a coenzyme in the transferase reactions like transfers aldehyde groups and glycation, as well as in neuro-transmission and neuronal conductivity, and may have effects on the development of various diabetic complications.[28]

Decreased levels of thiamine have been found in type 2 diabetic patients.[29] In this comparative study it is found that, thiamine was lower in DM patients, with a progressive decrease with albuminuria. On the basis of our findings we concluded that vitamins exert important effects on risk of diabetes mellitus as well as its progression and complications. It is necessary to undertake dietary evaluations to identify specific intake deficiencies and establish recommendations of vitamins. We observed that the potential links between vitamins C and D in reversing defects in glucose homeostasis and the prevention of type 2 diabetes. Some research studies suggest an association between vitamin C deficiency and diabetes. An association between vitamin D and insulin resistance has been well described; however, the role of vitamin C and D supplementation in diabetes and its prevention requires further controlled trials.

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