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Vitamin A, C and E Status in Type II Diabetes Mellitus Patients of Sub-Himalayan Region.

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ABSTRACT

Background: Vitamin A, vitamin C, and vitamin E are an integral part of non-enzymatic antioxidant defense system in humans. The present study was designed to estimate and investigate the role of vitamin A, C and E levels in patients with type 2 diabetes mellitus (T2DM). **Methods:** The study design involved 200 subjects viz. 100 healthy controls and 100 T2DM cases. Glycosylated hemoglobin (HbA1c) levels were estimated in whole blood sample and serum obtained was analyzed for quantitative estimation of vitamin A, C and E by enzyme linked imunosorbent assay (ELISA). **Results:** A significant increase ($p < 0.005$) was observed in the mean HbA1c levels in patients with T2DM as compared to healthy controls. On the contrary, a significant decrease ($p < 0.005$) was witnessed in the serum vitamin A, vitamin C, and vitamin E. A negative correlation was seen between HbA1c and vitamin A ($r = -0.327$); HbA1c and vitamin C ($r = -0.174$); HbA1c and vitamin E ($r = -0.226$). **Conclusion:** Reduced levels of serum vitamin A, C and E with poorly controlled HbA1c were observed inT2DM patients. Hence supplementation of these vitamins along with periodic estimation should be done in T2DM for risk prediction in diabetes and to prevent diabetic complications.

Keywords: Vitamin A, Vitamin C, Vitamin E, Glycosylated hemoglobin, Type 2 diabetes mellitus.

INTRODUCTION

Diabetes mellitus (DM) is a group of metabolic disorders characterized by hyperglycemia and insufficiency in production or action of insulin produced by the pancreas.[1] According to International Diabetes Federation (IDF), 40 million people are living with DM in India that is expected to increase to 70 million by 2020.[2] Sedentary lifestyle and unhealthy eating habits are main causes of type 2 diabetes mellitus (T2DM). Moreover, during the developmental phase intrauterine exposures also play a key role in susceptibility to T2DM in the later phases of life.[3] Hyperglycemia may lead to metabolic changes that include polyol pathway influx, formation of advanced glycation end products (AGEs) activation of signaling pathways. This acts as a biochemical trigger for altered redox signaling thereby compromising antioxidant defense system and increased free radical formation viz. reactive oxygen species (ROS) that in turn leads to increased insulin resistance.[1,4]

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Antioxidants are molecules capable of deactivating free radicals and overcome the effects of ROS in several diseased conditions. Humans have evolved highly complex enzymatic and non-enzymatic antioxidant system, that act synergistically and protect the cells and organ systems of the body by neutralizing free radicals.[5] Enzymatic antioxidants are superoxide dismutase, catalase, glutathione reductase and glutathione peroxidase. Non-enzymatic antioxidants are vitamin A, vitamin E, vitamin C, alfa lipoic acid, coenzyme Q10, L-carnitine, albumin, uric acid, and glutathione.[6,7]
The consequences of DM are a result of disparity between free radical production and their control by natural antioxidants.[8] Any alteration in antioxidant levels is a significant biomarker of oxidative stress.[1] However, there are inconsistent reports about individual vitamins and their effect on outcome in T2DM patients. Therefore, the present study was aimed at understanding the role of vitamin A, vitamin C and vitamin E levels in patients with T2DM in a tertiary care centre in Sub Himalayan region of north India.

MATERIALS AND METHODS

The study was conducted at the Department of Biochemistry, Dr. Rajendra Prasad Government

Medical College, Kangra at Tanda, District Kangra, Himachal Pradesh, India. Experimental protocols followed and study design was in accordance with the Protocol Review and Institutional Ethics Committee (No. HFW-HDRPGMC/Ethics/2016, Protocol No. 113/2016).

Patients

In total, 200 adult subjects (both male and female) viz. 100 healthy controls and 100 T2DM coming to central sample collection centre as outpatients or in-patients of the hospital were recruited for the study. After receiving written consent from the subjects demographic, physical and clinical history of subjects was obtained. Subjects were excluded from the study if they suffered from chronic illness such as immunocompromised states, cancer, tuberculosis, pregnant or lactating mothers and subjects who had undergone blood transfusion or donated blood a fortnight before obtaining the blood sample.

Methods

Approximately, 10 ml of whole blood sample was collected via venipuncture from cephalic or median cubital vein. For HbA1c estimation 2 ml of whole blood was collected in ethylene diamine tetra acetic acid (EDTA) tube. HbA1c was estimated using Nyco card (Alere Technologies AS, Oslo, Norway) reader. 8 ml of blood was collected in plain vial and the serum levels of vitamin A, vitamin C and vitamin E were estimated by enzyme linked imunosorbent assay (ELISA) reader using commercially available kits (Qayee Bio-Technology Co., Ltd. Shanghai, China).

Statistical Analysis

Statistical Package for Social Sciences (SPSS) software version 20 was used to analyze the data using independent samples t test between the different groups. Values were expressed as mean ± standard deviation (SD). Values with $p < 0.005$ were considered to be statistically significant and were calculated at 95 % confidence interval. Pearson's correlation coefficient (r) was used for correlation studies.

RESULTS

A significant increase was seen in the mean HbA1c of cases (8.03 ± 1.46) as compared to that of controls (5.49 ± 0.38) [Table 1] and the difference was statistically significant ($p < 0.005$). However, a statistically significant decrease ($p < 0.005$) was observed in the mean serum vitamin A value of cases (212 ± 55.97) as compared to controls (278.72 ± 86.66) [Table 1]. The mean serum vitamin C value of controls was 281.59 ± 56.44 (mean ± SD) as compared to cases where the mean value of serum vitamin C was 245.46 ± 64.67 (mean ± SD) [Table 1]. There was a statistically significant difference in the serum vitamin C values of controls and cases ($p < 0.005$). Similarly, a decrease was observed in the mean serum value of vitamin E in cases (31.85 ± 8.01) as compared to controls (40.07 ± 13.07) [Table 1]. A statistically significant difference was seen in the serum Vitamin E values of controls and cases ($p < 0.005$).

A negative correlation was observed between HbA1c and vitamin A levels (r = -0.327) [Figure 1]. Moreover, with higher HbA1c values a subsequent decrease was observed in vitamin A values. Similarly, a negative correlation was seen amongst levels of HbA1c and vitamin C levels (r = -0.174) [Figure 2]. An inverse relationship was observed between HbA1c and vitamin C values. Likewise, a negative correlation was observed between levels of HbA1c and vitamin E levels (r = -0.226) [Figure 3]. It was observed that with higher HbA1c values there was a consequent decrease in the values of vitamin E.

Table 1: Mean values of HbA1c, Vitamin A, Vitamin C and Vitamin E in Controls and Cases.

Test Parameter	Controls (mean±SD)	Cases (mean ± SD)	p value
HbA1c (%)	5.49 ± 0.38	8.03 ± 1.46	< 0.005
Vitamin A (mg/dl)	278.72 ± 86.66	212.53 ± 55.97	< 0.005
Vitamin C (mg/dl)	281.59 ± 56.44	245.46 ± 64.67	< 0.005
Vitamin E(µg/dl)	40.07 ± 13.07	31.85 ± 8.01	< 0.005

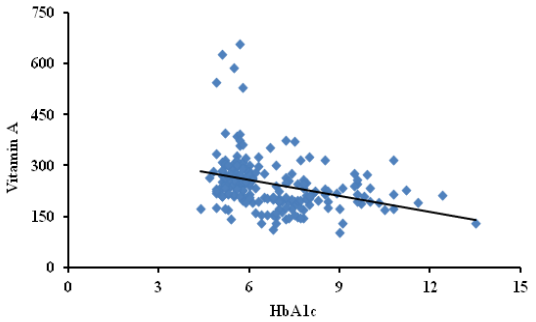

Figure 1: Scatter plot showing negative correlation between HbA1c and Vitamin A (r = - 0.327).

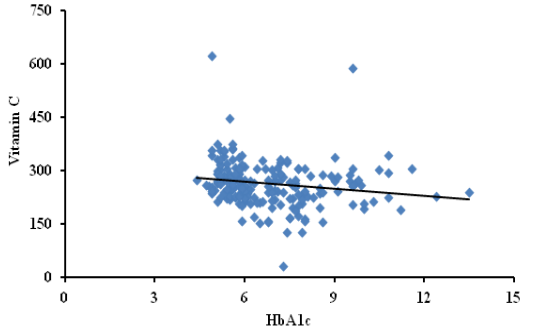

Figure 2: Scatter plot showing negative correlation between HbA1c and Vitamin C (r = - 0.174).

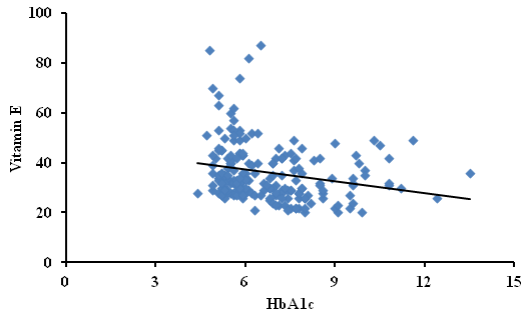

Figure 3: Scatter plot showing negative correlation between HbA1c and Vitamin E (r = - 0.226).

DISCUSSION

The present study exhibited poorly controlled HbA1c values in T2DM patients (cases) as compared to healthy controls with a statistically significant difference between the two groups. The mean serum levels of vitamin A were significantly lower in T2DM patients as compared to the control group. The results are in line with a recent study where, Malgorzata et al found a significant decrease in vitamin A levels of diabetics as compared to controls.[9] Moreover, the present study also revealed a significant negative correlation between HbA1c and vitamin A levels. Similarly, negative correlation (r = -0.314) was observed by Usoro et al,[10] between HbA1c and serum retinol levels in diabetic patients. The diabetic population also exhibited a significant diminution in serum retinol levels as compared to healthy controls. Additionally, the results of the present study are in line with the population-based study carried out by Terry et al,[11] where serum carotenoids were inversely associated with T2DM. Furthermore, hyperglycemia is also associated with increased the risk of vitamin A deficiency in diabetic patients.[12]

Vitamin C has been proven to be one of the most potent antioxidants. The results of the present study demonstrated a significant decline in vitamin C levels in T2DM group as compared to the healthy group along with an inverse relationship between HbA1c and vitamin C levels. Ahmad et al observed a significant decrease in vitamin C levels in patients with T2DM as compared to healthy controls.[13] Moreover, a significant reduction was witnessed in vitamin C levels in diabetic patients as compared to the control group followed by a negative correlation between plasma vitamin C and HbA1c levels in a study carried out by Sawant et al.[14] The main cause of diminution in vitamin C in T2DM can be attributed to high levels of oxidative stress caused by hyperglycemia.[15]

Vitamin E imparts stability to the biological membranes through its antioxidant activity.[16] In the present study, mean serum vitamin E levels were significantly reduced in T2DM cases as compared to healthy controls. Additionally, a negative correlation was also observed between HbA1c and vitamin E levels in the present study and the results are in line with previous studies. In a study carried out by Odum et al,[17] on Nigerian patients with T2DM a significant decline was observed in the vitamin E levels as paralleled to healthy controls. In an another study carried out by Sawant et al,[14] serum vitamin E levels were found to be significantly reduced in diabetic neuropathy patients with an inverse correlation amid plasma vitamin E and HbA1c levels. Low levels of α-tocopherol have been associated with increased risk of diabetes in the general population. Moreover, in a case control study led by Goud et al,[18] on 20 controls and 20 T2DM patients. Patients with T2DM had lower mean value of vitamin E as compared to controls with p value less than 0.0001. The effect of vitamin E on risk of diabetes and its complications is perhaps due to its role as antioxidant and a diminution in plasma tocopherol has been observed in diabetic subjects with longer spell of the disease.[19]

CONCLUSION

It can be concluded from the present study that reduced serum levels of vitamin A, vitamin C and vitamin E with poorly controlled HbA1c levels suggest for an increased oxidative stress that may initiate adverse changes in T2DM patients. Vitamin A, C and E are listed among the non-enzymatic mechanisms counteracting this phenomenon. Hence supplementation of these vitamins along with periodic estimation should be done for risk prediction and prevention of diabetic complications.

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