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Remedial Role of Vitamin-E in Type-2 Diabetes Mellitus Patients

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SUMMARY
Diabetes is accompanied by an increased oxidative damage to all the biomolecules.It will be helpful to find out the role of Vitamin-E in preventing the development of diabetic complications.
Background: The oxidative damage of biomolecule within the cell membrane has occurred through reactive oxygen species propagates chain reaction of lipid peroxidation.It is checked by a complex network of antioxidant defense and repair systems which are synthesized with the human body.Vitamin-E acts as a chain breaking inhibitor of lipid peroxidation.

Methods
i.Hexokinase method
Ii.Enzymatic method
Iii.Vitamin-E (α-tocopherol) method
Results: The present study specified correlation in glucose,malondialdehyde and cholesterol as compared to control group and T2 DM group based on statistical analysis.In the present study,control group and study group values of biochemical parameters significantly increases glucose as mean >>5.01(0.03)<< in control group and >>6.02(0.04)<< in T2DM group($p<0.001$).Both groups include total number of 200 patients. Mean values of cholesterol were significantly increased >>7.08(0.06)<< as compared to control group >>6.02(0.04)<< ($p<0.001$).The level of vitamin E increases significantly with mean value of >>12.5(0.10)<< in control group as compared >>9.5(0.08)<< to T2DM group($p<0.001$).
Conclusion: It has to be concluded that intake of vitamin E could contribute to the prevention of type-2 diabetes mellitus due to increase in concentration of glucose,cholesterol and decrease in concentration of vitamin E.

Abstract
The oxidative damage of biomolecule within the cell membrane has occurred through reactive oxygen species propagates chain reaction of lipid peroxidation.It is checked by a complex network of antioxidant defense and repair systems which are synthesized with the human body.Vitamin-E acts as a chain breaking inhibitor of lipid peroxidation. Diabetes is accompanied by an increased oxidative damage to all the biomolecules.It will be helpful to find out the role of Vitamin-E in preventing the development of diabetic complications.This study was conducted in CSSH,Meerut in the year 2008.100 controls and 100 T2DM patients of age 48-68 years were included for the study.
Key words: CVD-Cardiovascular disease,T2DM-Type-2 Diabetes Mellitus,RCTs-Randomized controlled trials,
Apo-AI-Apolipoprotein AI, Apo-AV-Apolipoprotein AV, Apo-AII-Apolipoprotein AII, Apo-E-Apolipoprotein E, Apo-B-Apolipoprotein B,HDL-High density lipoprotein &APOA5-Apolipoprotein gene A5

I. INTRODUCTION

Diabetes mellitus, a chronic metabolic disorder, is associated with an increased risk of diferent comorbidities including cardiovascular disease (CVD), chronic kidney disease, retinopathy, and mortality as well [1]. Hyperglycemia, which is among the main signs of diabetes, has been shown to be involved in the development of vascular complications and subsequent disorders [2]. Prior studies have proved that controlling glycaemia is the best approach to prevent subsequent disorders among patients with diabetes [3]. Recently, it has been shown that supplementation with antioxidants, such as vitamin E, may ameliorate endothelial cell dysfunction in patients with diabetes [4, 5].There is evidence of a positive association between reduced levels of vitamin E and risk factors of type 2 diabetes mellitus (T2DM) including insulin resistance and hyperglycemia [6]. Additionally, a prior meta-analysis of prospective cohort studies showed that a higher intake of foods rich in vitamin E (nuts, seeds, liquid oil, and raisin) was associated with a reduced risk of hyperglycemia and diabetes [7]. There is also further evidence indicating the benefcial efects of adherence to vitamin-E-rich diets on glycemic control in diabetic patients [8]. In contrast to that meta-analysis, findings from randomized controlled trials (RCTs) investigating the efect of vitamin E supplementation on glycemic control and insulin resistance in diferent types of diabetes are conficting. Some studies showed that vitamin E supplementation improves glycemic

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indices and insulin resistance in patients with T2DM from Western and Asian countries [9-12], while other studies from these regions did not report such a significant effect on patients with diabetic nephropathy [13–15] and T2DM patients [16–18].As the main apolipoproteins involved in α-tocopherol circulation, it is worth considering Apo-AI and Apo-AV, which belong to a gene cluster, Apo-AII, Apo-E, and Apo-B. The gene encoding for Apo-AI is clustered on chromosome 11 with other apolipoproteins (Apo-AIV, Apo-AV, and Apo-CIII) [19]. Apo-AI is the main protein component of nascent and mature HDL; it is synthesized in the liver (80%) and small intestine (10%), and as a cofactor for lecithin cholesterol acyltransferase, it supports cholesterol efflux from tissues [20].Obese and diabetic individuals have lower plasma levels of Apo-AV in comparison with healthy subjects [21,22], which may be because insulin is a negative regulator of the APOA5gene. Furthermore, a number of studies provide evidence the interaction between genetic variations associated with APOA5 in the modulation of lipid metabolism and an increased risk of obesity and metabolic syndrome (for reviews, see Guardiola et al. (2017) and Girona et al. (2018) [23,24]).In the present study,main emphasize is on the remedial role of vitamin-E and its prevention in complications of Type-2 Diabetes Mellitus.

II. MATERIAL AND METHODS

Quantitative analysis of blood glucose-Hexokinase method

Principle-

The enzyme hexokinase (HK) catalyzes the reaction between glucose and adenosinetriphosphate (ATP) to form glucose-6-phosphate (G-6-P) and adenosine diphosphate (ADP). In the presence of nicotinamide adenine dinucleotide (NAD), G-6-P is oxidized by the enzyme glucose-6-phosphate dehydrogenase (G-6-PD) to 6-phosphogluconate and reduced nicotinamide adenine dinucleotide (NADH). The increase in NADH concentration is directly proportional to the glucose concentration and can be measured spectrophotometrically at 340 nm.

Quantitative analysis of cholesterol

Principle-Cholesterol is measured enzymatically in serum or plasma in a series of coupled reactions that hydrolyze cholesteryl esters and oxidize the 3-OH group of cholesterol. One of the reaction byproducts, H_2O_2 is measured quantitatively in a peroxidase catalyzed reaction that produces a colour. Absorbance is measured at 500 nm. The colour intensity is proportional to cholesterol concentration. The reaction sequence is as follows:

cholesteryl ester hydrolase
Cholesteryl ester + H_2O ----------> cholesterol + fatty acid

cholesterol oxidase
Cholesterol + O_2 ----------> cholest-4-en-3-one + H_2O_2
peroxidase
$2H_2O_2$ + 4-aminophenazone + phenol ----------> 4-(p-benzoquinone monoimino)-phenazone + 4 H_2O
Cholesterol Reagent, buffer(pH 6.8) & sodium cholate.

Quantitative analysis of Vitamin-E

Principle

A small volume (100 µL) of serum is mixed with an ethanol solution containing two internal standards- retinyl butyrate and nonapreno-β-carotene (C45). The micronutrients are extracted from the aqueous phase into hexane and dried under vacuum. The extract is redissolved in ethanol and acetonitrile and is filtered to remove any insoluble material. An aliquot of the filtrate is injected onto a C18 reversed phase column and isocratically eluted with a mobile phase consisting of equal parts of ethanol and acetonitrile. Absorbance of these substances in solution is linearly proportional to concentration (within limits), thus spectrophotometric methods are used for quantitative analysis. Three wavelengths, approximately corresponding to absorption maxima namely 300, 325 and 450 nm are simultaneously monitored and chromatograms are recorded. Quantitation is accomplished by comparing the peak height of the analyte in the unknown with the peak height of a known amount of the same analyte in a calibrator solution. Calculations are corrected based on the peak height of the internal standard in the unknown compared with the peak height of the internal standard in the calibrator solution. Retinol and the retinyl esters are compared with retinyl butyrate at 325 nm, α- and γ-tocopherol are compared with retinyl butyrate at 300 nm, and the carotenoids are compared with C45 at 450 nm.

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III. RESULT

Table I
Demographic data

Mean age		Cases	Control
58 ± 12	Males	54	46
53 ± 10	Females	52	48
Hypertensive	Yes	70 %	30 %
	No	30 %	70%
Smokers	Yes	70 %	30 %
	No	30 %	70 %
Alcoholics	Yes	70 %	30 %
	No	30 %	70 %

Table II:-

Subject	No.of patients	Glucose (mg/dL)	Cholesterol (mg/dL)	Vitamin-E (µmol/L)	P value
Control	100	5.01± 0.03	6.02 ± 0.04	12.5 ± 0.10	p<0.001
T2DM	100	6.57± 0.05	7.08 ± 0.06	9.5 ± 0.08	p<0.001

The present study specified correlation in glucose,cholesterol & vitamin E as compared with control group and T2 DM group based on statistical analysis.In the present study,control group and study group values of biochemical parameters significantly increases glucose as mean >>5.01(0.03)<< in control group and >>6.02(0.04)<< in T2DM group(p<0.001).Both groups include total number of 200 patients. Mean values of cholesterol were significantly increased >>7.08(0.06)<< as compared to control group >> 6.02(0.04)<< (p<0.001).The level of vitamin E increases significantly with mean value of >>12.5(0.10)<< in control group as compared to T2DM group >>9.5(0.08)<<(p<0.001).

IV. DISCUSSION

In the previous findings,There is evidence of a positive association between reduced levels of vitamin E and risk factors of type 2 diabetesmellitus (T2DM) including insulin resistance and hyperglycemia [25]. It has been proposed that vitamin E inhibits glucose oxidation which is a necessary step for further metabolic functions [26]. Additionally, a prior meta-analysis of prospective cohort studies showed that a higher intake of foods rich in vitamin E (nuts, seeds, liquid oil, and raisin) was associated with a reduced risk of hyperglycemia and diabetes [27]. Tere is also further evidence indicating the benefcial efects of adherence to vitamin-E-rich diets on glycemic control in diabetic patients [28].Previous study has mentioned fasting glucose (mmol/l) 5.68 ± 0.03 ,total cholesterol (mmol/l) 5.71 ± 0.05 &α-tocopherol OR(95% CI)[a] 0.53 (0.34, 0.77)[29] , by using comprehensive metabolomics profiling, we have identified a novel multivariate panel of metabolic markers consisting of glucose,cholesterol&α-tocopherol.These metabolic markers significantly improved the prediction of progression towards type 2 diabetes, showing the added value of screening metabolites along with clinical risk factors. Statistical association testing and machine learning-based predictive modelling identified metabolic changes that preceded type 2 diabetes. Statistical tests identified 34 significant metabolites, yet multivariate predictive models required only five metabolites for the optimal prediction of progression to type 2 diabetes. While the metabolite features identified using both approaches are well supported in type 2 diabetes literature, our novel contribution was in systematically assessing the predictive performance of the biomarker panel in type 2 diabetes risk prediction.Similar results have been previously reported in an African-American population [30].In the present study,control group and study finding reviewed similar results.

V. CONCLUSION

It is concluded that different metabolic profiles are initiated towards type-2 diabetes

mellitus. In this study, biochemical parameters such as glucose,cholesterol and α-tocopherol were found to accurately predict type 2 diabetes mellitus. It enhances association of glucose,cholesterol and vitamin E with progression to type 2 diabetes mellitus.It ensured a possible mechanism by which interventions such as vitamin E supplementation could contribute to the prevention of type 2 diabetes.

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