Original article

Changes of Plasma Total proteins, Albumin and Fibrinogen in Type 2 Diabetes mellitus- A Pilot study.

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Abstract

Introduction: Type II diabetes is characterized by insulin resistance and/or abnormal insulin secretion. It has been hypothesized that atherosclerotic cardiovascular disease and type 2diabetes arise from a "common soil" and chronic inflammation may be such a candidate**.** Inflammatory markers, such as high white cell count, high fibrinogen, or low albumin**.**. In type 2 diabetic patients, post absorptive albumin synthesis and its response to insulin were normal, where as fibrinogen synthesis was increased, irrespective of metabolic control. Fibrinogen, serum Total protein of long term type-2 diabetics was significantly elevated. However there is little information about plasma total proteins, albumin, globulins and fibrinogen in type 2 diabetes. The present study was planned to assess the levels of plasma total proteins, albumin and fibrinogen in first time diagnosed type 2 diabetes cases.

Materials and Methods: In our study 50 first time diagnosed type 2 diabetics who attended Dr. Pinnamaneni Siddhartha Institute of Medical Sciences, Research Foundation & general hospital and fifty age, sex matched controls were recruited. From the subjects, venous blood samples were collected and used for estimation of plasma glucose, Total proteins, Albumin, fibrinogen. We used graph pad prism version 3.0 software. Unpaired" t" test has been used. Between cases and control group "p" value <0.05 is considered statistically significant.

Results & Conclusion: In our study of type 2 diabetics plasma albumin levels were decreased compared to controls and plasma fibrinogen, total protein levels were statistically significantly increased compared to controls.

Key words: Diabetes mellitus, fibrinogen, coronary artery disease

INTRODUCTION: Diabetes mellitus has long been considered a disease of minor significance to world health, but is now developing into one of the main public health challenges for the 21st century. The past two decades have seen an explosive increase in the number of people diagnosed with diabetes mellitus worldwide. This diabetes mellitus epidemic relates particularly to type II diabetes, which is taking place both in developed and developing countries. Diabetes mellitus can be divided into two principal forms, type 1diabetes and type 2 diabetes(T**2**D). Type II diabetes is characterized by insulin resistance and/or abnormal

insulin secretion. Individuals with type II diabetes are not dependent on exogenous insulin, but may require it for control of blood glucose levels if this is not achieved with diet alone or with oral hypoglycemic agents[1]. It has been hypothesized that atherosclerotic cardiovascular disease and type 2 diabetes arise from a "common soil" [2, 3] and chronic inflammation may be such a candidate [4]. Inflammatory markers, such as high white cell count, high fibrinogen, or low albumin [5].

In type 2 diabetes, fibrinogen production is increased both in the post absorptive state and in response to hyperinsulinemia. In type 2 diabetic patients, post absorptive albumin synthesis and its response to insulin were normal, where as fibrinogen synthesis was increased, irrespective of metabolic control [6]. Fibrinogen , serum Total protein, of long term type-2 diabetics were significantly elevated[7].In patients with non insulin dependent diabetes mellitus, high plasma levels of C-reactive protein and fibrinogen are present[8]. However there is only little information about plasma total proteins, albumin, globulins and fibrinogen in type 2 diabetes. So the present prospective study intended to assess the levels of plasma total proteins, albumin, fibrinogen and total antioxidant levels in first time diagnosed type 2 diabetes cases.

MATERIALS AND METHODS: In our study 50 first time diagnosed type 2 diabetic cases who attended Dr. Pinnamaneni Siddhartha Institute of Medical Sciences a Research Foundation & general hospital and 50 age, sex matched controls were also recruited. Our study is approved by institutional ethical committee.

1..First time diagnosed cases of type 2 diabetes mellitus who were having Fasting > 126 mg/dl & Post prandial > 200 mg/dl are included in our study.1.Patients who are on Drugs.2.Patients who are suffering from any other illness.3.Pregnant women excluded from our study.

Sample collection: After obtaining informed consent from the subjects, venous blood samples were collected after an overnight fast , under aseptic precautions, 6-8 of blood was collected in clean sterile heparin tubes, the samples were centrifuged and plasma was separated for estimation of plasma glucose Total proteins, Albumin, fibrinogen . Aliquots were stored at 2-8 ^{o} C. Samples were analyzed on the same day or within one week. Plasma glucose both fasting and postprandial were estimated by glucose oxidase and Peroxidase method Trinder's method,(Erba Mannheim), estimation of plasma total proteins by Biuret modified(TRANSASIA BIO-MEDICALS LTD), plasma albumin by Bromocresol Green(SPAN DIAGNOSTICS LTD), Fibrinogen by Biuret, (modified)[9] reaction. Results are shown in table No:1

Statistical Analysis: Data entry was done and statistical analysis was done by using graph pad prism. Unpaired" t" test has been used to find the significance of the study characteristics (frequency) between cases (study group) and control group. "p"value <0.05 is considered statistically significant.

DISCUSSION: Total number of subjects selected in our study 100 both cases and controls. Out of 50 Type 2 diabetes cases studied men are 26 and women are 24 in number. In our study diabetic women are more in numbers than diabetic men. Out of 50

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controls studied men are 24 and women are 26 in number. All patients in our present study were normoalbuminuric and without detectable micro- and macro vascular complications. The use of plasma protein data to aid in the diagnosis of various diseases and provide supportive pathophysological information has increased markedly over the past decade. Of the more than 100 plasma proteins which have been characterized from a basic biochemical standpoint, relatively few have well documented clinical significance.[10,11,12,13,14] These are, for the most part, the higher-concentration proteins which are within analytical limits of detection by current techniques. Profile studies have led to an increased understanding of protein physiology in healthy individuals and helped characterize the complex relationships of proteins in basic pathological processes.

Discussion of patterns frequently observed in disease states will include the inflammatory process, rheumatic diseases, liver diseases, protein losing disorders, plasma cell dyscrasias, pregnancy, and genetic protein deficiencies. A variety of measures of inflammation predicted later type 2 diabetes in the Atherosclerosis Risk in Communities (ARIC) Study [15] including raised fibrinogen, white cell count, Sialic acid, and orosomucoid, as well as lower serum albumin. Such inflammatory markers are known to have positive cross-sectional associations with BMI.

During insulin deficiency, there is significant decrease in fractional synthetic rate of albumin and concomitant significant increase in fibrinogen. These data indicate a differential effect of insulin deficiency on the fractional synthetic rate of two hepatically synthesized plasma proteins [16]. Boulge D et al showed Albumin level is *low and* CRP is *elevated* in diabetics with persistent ischemic foot ulcers.[17] Laurel C.B et al [10] observed significant decrease in albumin in diabetes mellitus may be due to insulin deficiency and significant decrease in the fractional synthetic rate of albumin. In our study of type 2 diabetic population plasma albumin levels were decreased compared to controls and in accordance with the above studies.

The acute phase proteins CRP,[18,10] α1-acid glycoprotein[10,11] plasminogen [12] complement C3,[13] ceruloplasmin,[14,19] haptoglobin,[10] and serum amyloid A[11] are modestly *elevated* in DM, while albumin is *decreased*,[10] suggesting chronic inflammation. Several acute-phase proteins have also been shown to be altered in serum from subjects with T2DM, connecting the disease to a low grade inflammatory process [20, 21, 22].

Plasma glucose concentrations were also increased in the patients, as expected. Hyperglycemia has been previously shown to activate the coagulative cascade [23], thus increasing thrombin formation and fibrinogen degradation products, which, in turn, may stimulate hepatic fibrinogen synthesis[24]. A positive correlation between plasma glucose and fibrinogen concentration has been reported in large epidemiological studies [25]. Increased plasma glucose contributes to the hyperfibrinogenemia of type 2 diabetes. This hypothesis is consistent with previous findings of less pronounced increments in plasma fibrinogen concentration in type 2 diabetic patients studied under conditions of good metabolic control [26]

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as well as with the observation of acute reductions of fibrinogen synthesis in type 1 diabetes after normalization of plasma glucose[27]. Laurel C.B et al[28] showed that significant increase in fibrinogen levels in diabetes mellitus and apo A-1[29, 30] is *decreased* in DM. Both are associated with increased cardiovascular risk.[19] Clinic-based studies reported that plasma fibrinogen levels were higher in diabetic patients than in controls [31] and in diabetic patients with microalbuminuria than in diabetic patients with normoalbuminuria.[31, 32, 33] In Our study of type 2 diabetic cases plasma fibrinogen levels were statistically significantly increased compared to controls and our study in accordance with the above studies.

Plasma fibrinogen, serum total proteins, of long term type-2 diabetics were significantly elevated[7].In our study plasma total protein levels were statistically significantly increased compared to controls. Our study is in accordance with the above study.

Conclusion: All patients in our present study were normoalbuminuric and without detectable micro- and macro vascular complications. In our study Plasma total proteins and fibrinogen levels were statistically significantly increased. Increased fibrinogen may be due to increased plasma glucose. Plasma albumin levels were statistically significantly decreased. May be due to significant decrease in fractional synthetic rate of albumin thou none of the patients were positive for urine albumin. These diabetic patients should be followed up to prevent complications of diabetic nephropathy and other complications. Higher fibrinogen is seen in patients with coronary artery disease than without the disease. So these diabetic patients should be followed up and reduce the fibrinogen levels to prevent complications like coronary artery disease and diabetic nephropathy. Fibrinogen level can be reduced considerably by life style interventions that also affect levels of established risk factors (such as regular exercise, smoking cessation, and moderate alcohol consumption).

Table No:1 showing plasma glucose, total proteins, albumin, fibrinogen & total antioxidant levels

Parameter	Controls (n=50) Mean ±SD	Cases (n=50) Mean ±SD	P-value
PLASMA Glucose Fasting	80.100–+7.399	158.54±42.524	<0.0001
PLASMA glucose PgBS	118.38–+14.000	285.92±52.845	<0.0001
PLASMA TOTAL PROTEIN	7.672–+0.3071	7.464±0.2961	<0.0007
PLASMA ALBUMIN	4.492–+0.4040	3.990±0.3726	<0.0001
PLASMA FIBRILOGEN	0.2314–+0.008636	0.33241±0.02557	<0.0001

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