Turkish Journal of Endocrinology and Metabolism, (1998) 4 : 209-212 **ORIGINAL ARTICLE**

The Level of Antithrombin III (AT III) in Turkish Diabetics

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A natural anti-coagulant AT III plays a defensive role against intravascular coagulation and regulates blood hemostasis. Diabetes is associated with hyper-coagulable state. The level of blood AT III levels in the Turkish diabetic population have been studied. 100 diabetic patients (2 type 1, 75 type 2) and 20 healthy control wese included in the study. AT III levels were 34.75 mg/dl in healthy control, and 41.89 mg/dl in the diabetic group ($p<0.0001$). There was no difference between type 1 and type 2 diabetics ($p=0.16$).

This study showed that serum AT III levels increased in both type 1 and type 2 diabetics. The level of AT III did not have any correlation with duration of diabetes, blood glucose, HbA1c, lipid levels and diabetic complications ($p>0.05$). Treatment type (diet, oral anti-diabetics and insulin) did not affect AT III levels ($p>0.05$).

KEY WORDS Antithrombin III, diabetes mellitus

Introduction

Antithrombin III (AT III) is a natural anti-coagulant. It plays a defensive role against intravascular coagulation and regulates blood hemostasis. Its molecular weight is 65 kilodalton. AT III is a single chain glycoprotein composed of 425 amino acids. It is a member of the serin protease inhibitor super-family. It is synthesized in the liver. AT III inactivates thrombin and the rest of the serin proteases (factor XIIa, XIa, Xa, IXa). AT III deficiency may cause thromboembolic events. AT III deficiency may be hereditary or acquired. Decreased synthesis and excretion, drugs or increased AT III utilization may be the causes of acquired AT III deficiency (1-7). AT III increases in hepatocellular carcinoma and is accepted as a tumor marker (8-10).

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Coagulation and fibrinolysis defects, micro and macroaangiopathies are frequently seen in diabetes mellitus. Several studies suggest that diabetes is associated with a hypercoagulable state (11-13). What is the level of AT III in diabetes mellitus in Turkish diabetes? Is there any relation between blood AT III levels and diabetic complications? It was aimed to give the answers to these questions in this study.

Material and Methods

One hundred diabetic patients and 20 healthy volunteers were included in this study. 75 of the diabetic patients were type 2 and 25 of them were type 1.

Fifty six of te diabetic patients were female (13 type 1, 43 type 2), and 44 of them were male (12 type 1, 32 type 2). The mean age in type 1 was 29±11.02 years and in type 2 was 56.45±10.04 years. Diabetes age was 9.17±8.54 years for type 1 and 10.56±8.16 years for type 2 diabetic patients (Table 1).

Table 1. Demographic data of the study group.

Study group	Type 1 DM	Type 2 DM	Controls
n	25	75	20
Sex (m/f)	12/13	32/43	12/8
Mean age (years)	29±11.02	56.45±10.01	30.65±06.45
Diabetes age (years)	9.17±8.54	10.56±8.16	-

All patient's histories were taken and a thorough physical examination including arterial blood pressure, neurological and retinal assessment were performed. They were screened for micro and macroangiopathic complications. Serum creatinine, ions, transaminases, bilirubin, cholesterol, tryglycerides, urea, complete blood count, APTT and PT were studied. Abdominal ultrasonography was performed if needed. Healthy volunteers were included in the study as controls. Exclusion criteria were abnormal laboratory results including liver function tests, having a diabetic as a first degree relative, being pregnant or using oral contraceptives.

All subjects' biochemical and urinary examination and AT III levels were assessed on the same day. AT III assays were performed by using Behring Nephelometer 100 Analyzer.

Statistical methods: Student's t-test and Mann-Whitney U test used for statistical analyses. Values were expressed as mean SE.

Results

Diabetic complications are demonstrated in Table 2.

Table 2. Diabetic complications of the study group.

Type of Complication	Type 1	Type 2
Retinopathy	3 (12 %)	49 (65 %)
Neuropathy	4 (16 %)	45 (60 %)
Nephropathy	1 (4 %)	20 (27 %)
Diabetic foot	2 (8 %)	10 (13 %)
No complication	20 (80 %)	20 (27 %)

AT III levels were 34.75±04.02 mg/dl in the healthy controls and 41.89±05.20 mg/dl in the diabetic group. AT III levels in type 1 and type 2 diabetic groups are shown in Table 3.

Table 3. AT III levels in all groups (*** p<0.0001) (p is the difference between study group and controls)

Group	Type 1 DM	Type 2 DM	Control
AT III (mg/dl)	43.±04.63***	41.40±05.35***	34.75±04.02

Results showed a significant increase of AT III in the diabetic subjects as compared to healthy controls (p<0.0001). On the other hand, there was no difference between type 1 and type 2 diabetics (p=0.16).

The level of AT III did not have any correlation with the duration of diabetes, blood glucose, HbA1c, lipid levels and diabetic complications (p>0.05). Treatment type (diet, oral antidiabetics and insulin) did not affect AT III levels (p>0.05).

Discussion

This study showed that serum AT III levels increased in both type 1 and type 2 diabetics. Serum AT III levels did not correlate with diabetes age, metabolic control, diabetic complications or the type of treatment. In the study by Fuller et al although there were clotting factor differences between those with and without microvascular disease they were independent of age, sex, duration and type of diabetes, smoking and blood pressure (14).

In the literature AT III levels are usually decreased or not changed when blood glucose levels increase. Studies by Ceriello A. et al in 1987 (15, 16), 1989 (17) and 1990 (18, 19) al showed that AT III levels either did not change or decreased in diabetics or in normals with induced hyperglycemia. AT III activity in all these studies was inversely correlated with blood glucose levels. In the present study, blood AT III levels were evaluated and they were found significantly higher than in controls both in type 1 and type 2 diabetics. Meade et al also showed higher levels of AT III and increased risk of arterial disease (20). Meade et al reported that these apparently contradictory results could be explained by postulating that in some circumstances low AT III levels are of direct causal significance while in others raised levels represent a compensatory response.

When studies on specific races are considered, decrease in AT III activity was reported by Blavy et al (21) in the Ivory Coast diabetic population and by Thian et al (22) in Senagalese diabetics compared to normal controls of each communities. In the study from the Ivory Coast, contray to Turkish people, the serum AT III levels were significantly decreased in the diabetic group of this population.

Morangi et al, (23) reported that AT III levels of 79 diabetic (Type 1 and 2) patients were not different from those of the controls and no correlation existed with HbA1c.

On the contrary, Donders et al (24) from Netherlands showed that Hb1Ac values correlated with AT III levels.

Myrup et al, (25) from the Steno Diabetics Center classified their diabetic patients according to their albumin excretion rate. No difference in the level of AT III was seen between the groups.

There is one study from Australia presented by Lee et al, (26) which found increased AT III levels in diabetic patients with evidence of renal damage. Fuller et al (14), also found that AT III values were raised in those with microvascular disease. In the present study there was no correlation between the AT III levels of diabetics with or without nephropathy.

In conclusion, this study showed that serum AT III levels increased in both type 1 and type 2 diabetics. The level of AT III did not have any correlation with duration of diabetes, blood glucose, Hb1Ac, lipid levels and diabetic complications ($p>0.05$). Treatment type (diet, oral anti-diabetics and insulin) did not affect AT III levels ($p>0.05$).

Does AT III protect the diabetics from hypercoagulability? The aim of the next study will be to answer this question.

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