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PLASMA GLYCOPROTEINS IN DIABETES

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SUMMARY

Serum levels of glycoproteins-fibrinogen, α_1 acid glycoprotein, α_2 macroglobulin, B_2 glycoprotein 1 and haptoglobin were estimated by immunodiffusion technique in three groups of subjects: (A) Non-diabetic controls (B) Newly detected diabetics and (C) diabetics with clinically manifest microangiopathy.

Significant elevations in fibrinogen and haptoglobin were present in group B and C, the elevation being higher in group C. Levels of α_1 acid GP and B_2 GP 1 were significantly elevated only in group C. The concentration of α_2 MG was higher in females compared to males and this variation was present in all three groups. Newly detected diabetics had lower concentration of α_2 MG. There was no significant increase of this parameter in diabetics with microangiopathy.

Thus enhanced synthesis of fibrinogen, haptoglobin, α_1 acid glycoprotein and B_2 glycoprotein-1, appear to be related to microvascular complication in diabetes while α_2 macroglobulin does not appear to bear any relationship.

INTRODUCTION

Widespread changes are seen in the protein fractions of plasma in diabetes mellitus.[1] These changes occur due to the deficiency of active insulin. The production of several glycoproteins are enhanced and some of these are the so called 'acute-phase reactants' i.e., proteins which are synthesised in greater quantities during an acute stress. Recent studies have implemented that changes in the concentration of these glycoproteins affect the haemodynamic properties by increasing the plasma viscosity and erythrocyte aggregation.[2] These changes have been found to contribute to the development of microangiopathic changes in diabetes.

It has been proposed that Acute phase reactants such as fibrinogen, α_1-acid glycoprotein (α_1-A.G.), haptoglobin and other glycoproteins like α_2-macroglobulin (α_2-M.G.) and B_2 glycoprotein-1 (B_2-GP_1) play a role in the development of microvascular sequelae of diabetes.[2-7] In this study, we have tried to evaluate the relation of these glycoporoteins to the microangiopathic complications in our diabetic patients.

MATERIAL AND METHODS

Three groups of individuals were selected for this study. In Group A, there were 18 healthy, normal subjects with no family history of diabetes. Group B consisted of 23 newly detected diabetics without any clinical evidence of microangiopathy. Group C consisted of 24 individuals with definite retinopathy and/or nephropathy. None of the study subjects had any acute infection at the time of the study. In Group C, duration of diabetes varied from 3 years to 20 years and majority of them had diabetes of long duration.

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Fibrinogen was estimated by the adoption of Biuret method described by Varley.[8] α_1-acid glycoprotein, α_2-macroglobulin, B_2-glycoprotein 1 and haptoglobin were estimated by immunodiffusion technique using the Beringwerk plates (Hoechst, W. Germany).

The data for α_2-MG for male and female patients were analysed separately in all three groups, as the concentration of this protein is known to be higher in females.

RESULTS

Table 1 presents the results of the study in the three different study groups.

TABLE 1

Glycoprotein	(A) Controls (n = 18)	(B) Diabetics without complication (n = 23)	(C) Diabetics with complication (n = 24)
Fibrinogen mg% ± SD	214.2 ± 46.4	298 ± 118.3 P<0.01	373 ± 166.3 P<0.001
α_1 acid glycoprotein mg% ± SD	64.1 ± 19.2	61.5 ± 28.5 N.S.	99.7 ± 40.4 P<0.001
B_2 glycoprotein—1 mg% ± SD	21.8 ± 3.9	24.1 ± 4.7 N.S.	27.4 ± 5.9 P<0.001
Haptoglobin mg% ± SD	120.7 ± 56.7	163.8 ± 49.8 P<0.01	193.4 ± 76.9 P<0.001
α_2 Macroglobulin mg% ± SD	207.6 ± 37.2 (12)	192 ± 38.6 N.S. (17)	233.2 ± 53 N.S. (17)
Male			
Female	251.1 ± 21.0 (6)	204.2 ± 16.2 P<0.001 (6)	266.3 ± 66 N.S. (7)

It was noticed that the concentrations of fibrinogen and haptoglobin were significantly elevated in Group B and C compared to the controls, but the levels of both the parameters were highest in those with complications. Levels of α_1 acid glycoprotein and B_2 G.P. 1 were significantly elevated only in Group C.

Concentration of α_2 M.G. was found to be higher in females than in males in all the three groups. In the newly diagnosed diabetics, there was a lowering in the concentration of this protein, the change being significant in the female diabetics. The diabetics in Group C showed no significant difference from the control group in the level of α_2 MG.

DISCUSSION

The rates of synthesis of different glycoproteins are varied in diabetes, and the elevated concentrations of some of them are known to be detrimental to the blood flow properties.[2] Positive correlation has been demonstrated between the concentrations of glycoproteins like haptoglobin, α_1 AG and B_2 GP 1 and fibrinogen and the increasing viscosity of plasma.[2, 4, 5, 9] It has also been shown that the long term blood flow changes are closely associated with diabetic microangiopathy. The elevated levels of these glycoproteins also favour erythrocyte aggregation.[10]

The fact that the concentrations of these parameters are high even in the newly detected diabetics indicates that these changes may be early markers of the changes in microcirculation. An earlier study by us has indicated that the

increased synthesis of some of the plasma protein fractions are reversible with control of hyperglycemia.[11] Higher levels of these parameters in diabetics with established microvascular complications, probably, reflects the effect of prolonged hyperglycemia.

Elevated levels of α_2 MG in diabetes has been demonstrated by some workers[6, 7] but we have not noticed any significant elevation in α_2 MG in diabetics with or without microangiopathy. Our findings of a slightly decreased level of α_2 MG in new diabetics with non-significant elevation in diabetics with microangiopathy are similar to those of McMillan[2, 9] and contradicts the proposition of Brownlee.[6] It has been postulated by Brownlee[6] that increased concentration of α_2 MG may be the chief factor responsible for the capillary basement membrane thickening in diabetics. α_2 MG is supposed to inhibit the enzymes which normally degrade the membranes, thus leading to thickening of the basement membrane. However, this hypothesis does not appear feasible in view of the fact that α_2 MG synthesis is enhanced only in diabetics with established complications and basement membrane thickening can be present even in diabetics with short duration of the disease.[12] Moreover, McMillan's studies and the present study show that the females who have a higher concentration of α_2 MG do not show greater risk of microangiopathy.

Thus, it is concluded that enhanced synthesis of fibronogen, α_1 AG, B_2-GP_1 and haptoglobin may be directly related to the development of microangiopathic changes in diabetes while α_2 MG has no significant role in the pathogenetic process.

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