PLASMA GLYCOPROTEINS IN DIABETES

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SUMMARY

Serum levels of glycoproteins—fibrinogen, α1 acid glycoprotein, α2 macroglobulin, B1 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 α1 acid GP and B1 GP 1 were significantly elevated only in group C. The concentration of α2 MG was higher in females compared to males and this variation was present in all three groups. Newly detected diabetics had lower concentration of α2 MG. There was no significant increase of this parameter in diabetics with microangiopathy.

Thus enhanced synthesis of fibrinogen, haptoglobin, α1 acid glycoprotein and B1 glycoprotein-I, appear to be related to microvascular complication in diabetes while α2 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, α1-acid glycoprotein (α1-A.G.), haptoglobin and other glycoproteins like α2-macroglobulin (α2-M.G.) and B1 glycoprotein-I (B1-GP 1) play a role in the development of microvascular sequelae of diabetes.3-7 In this study, we have tried to evaluate the relation of these glycoproteins 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.
Fibrinogen was estimated by the adoption of Biuret method described by Varley. \(^6\) \(\alpha_1\)-acid glycoprotein, \(\alpha_2\)-macroglobulin, \(B_2\) glycoprotein 1 and haptoglobin were estimated by immunodiffusion technique using the Bieringwerk plates (Hoechst, W. Germany).

The data for \(\alpha_2\)-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>
<thead>
<tr>
<th>Glycoprotein</th>
<th>(A) Controls (n = 18)</th>
<th>(B) Diabetics without complication (n = 23)</th>
<th>(C) Diabetics with complication (n = 24)</th>
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<tbody>
<tr>
<td>Fibrinogen mg% ± SD</td>
<td>214.2 ± 46.4</td>
<td>298 ± 118.3</td>
<td>373 ± 165.3</td>
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<tr>
<td>(\alpha_1) acid glycoprotein mg% ± SD</td>
<td>64.1 ± 19.2</td>
<td>61.5 ± 28.5 P&lt;0.01</td>
<td>98.7 ± 49.4 P&lt;0.001</td>
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<tr>
<td>(B_2) glycoprotein-1 mg% ± SD</td>
<td>21.8 ± 3.9</td>
<td>24.1 ± 4.7 N.S.</td>
<td>27.4 ± 5.9 P&lt;0.001</td>
</tr>
<tr>
<td>Haptoglobin mg% ± SD</td>
<td>120.7 ± 56.7</td>
<td>163.8 ± 49.8 P&lt;0.01</td>
<td>193.4 ± 76.9 P&lt;0.001</td>
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<tr>
<td>(\alpha_2) Macroglobulin mg% ± SD</td>
<td>207.6 ± 37.2 (12)</td>
<td>182 ± 38.6 N.S. (17)</td>
<td>233.2 ± 53 N.S. (17)</td>
</tr>
<tr>
<td>Male</td>
<td>251.1 ± 21.0 (6)</td>
<td>204.2 ± 18.2 N.S.</td>
<td>256.3 ± 66 N.S.</td>
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<tr>
<td>Female</td>
<td></td>
<td>P&lt;0.001</td>
<td></td>
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</tbody>
</table>

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 \(\alpha_1\) acid glycoprotein and \(B_2\) G.P. 1 were significantly elevated only in Group C.

Concentration of \(\alpha_2\) 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 \(\alpha_2\) 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, \(\alpha_2\) AG and \(B_2\) GP 1 and fibrinogen and the increasing viscosity of plasma. \(^2\) \(\&\) \(^6\) \(\&\) \(^9\) 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. Higher levels of these parameters in diabetics with established microvascular complications, probably, reflects the effect of prolonged hyperglycemia.

Elevated levels of α₂-MG in diabetics has been demonstrated by some workers⁵-⁷ but we have not noticed any significant elevation in α₂-MG in diabetics with or without microangiopathy. Our findings of a slightly decreased level of α₂ MG in new diabetics with non-significant elevation in diabetics with microangiopathy are similar to those of McMillan⁸ and contradicts the proposition of Brownlee⁹. It has been postulated by Brownlee⁹ that increased concentration of α₂-MG may be the chief factor responsible for the capillary basement membrane thickening in diabetics. α₂-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 α₂-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 α₂-MG do not show greater risk of microangiopathy.

Thus, it is concluded that enhanced synthesis of fibrinogen, α₁ AG, β₂-GP, and haptoglobin may be directly related to the development of microangiopathic changes in diabetes while α₂-MG has no significant role in the pathogenetic process.

REFERENCES