FIBRINOGEN AND MUCOPROTEIN LEVELS IN DIABETICS AND THEIR RELATIONSHIP TO METABOLIC CONTROL

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INTRODUCTION :

Glycoproteins are considerably increased in diabetics due to an activation of metabolic pathways independent of insulin. The elevated levels of glycoproteins alter several tissue funtions and also the haemostatic properties of the system. (McMillan, 1975a). Fibrinogen is one of the important glycoproteins, governing the coagulation of blood. Mucoproteins are glycoproteins with more than 4 per cent hexosamine content and their concentration in blood also reflect changes in glycoprotein metabolism.

This paper deals with a study of the levels of these two important proteins in diabetes. Follow-up studies of the patients were also conducted to evaluate the influence of diabetic control on these parameters.

MATERIAL AND METHODS :

A group of 144 diabetics admitted for control of diabetes at the Diabetes Research Centre, Madras, were taken up for study. All patients were subjected to a complete clinical examination including direct ophthalmoscopy after mydriasis. Kidney functions tests including 24 hour proteinuria and creatinine clearance were done in all cases. Blood sugar estimations were carried out using the Ortho-Toluidine method. (Hyvarinen and Nikkila, 1962). Serum proteins, albumin and fibrinogen were measured using adoption of the Biuret method described by Varley (1963). Mucoprotein levels were estimated by the method of Winzler et al (1963). The patients were grouped according to the presence of diabetic complications.

Patients were put on a Restricted Calorie High Carbohydrate, High Protein, Low Fat diet. Diabetes was controlled where necessary with oral drugs or insulin.

Follow-up of 46 patients were possible for a period of 1 to 6 months, during which all the biochemical parameters were repeated.

The follow-up data was analysed with respect to the degree of diabetic control. The following criteria were adopted by us in grading the diabetic control.

Degree of Control	P.P.B.S. mg/ 100 ml
Excellent	< 150 mg
Good	< 180 mg
Fair	< 200 mg
Poor	> 201 mg or more

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For excellent control, the fasting blood sugar should be below 120 mg/100 ml.

RESULTS :

The initial data was analysed in separate groups according to the presence and type of diabetic complications. (Table 1).

The total concentration of serum proteins was nearly normal in all groups of diabetics, but the level of albumin was low in majority of them indicating an elevation in globulin fractions.

The concentrations of fibrinogen and mucoproteins were significantly high in all the diabetics.

During the follow-up studies, only a mild increase in albumin levels was noticed; but the levels of fibrinogen and mucoproteins decreased significantly with control of blood sugar. Good correlation was noted between the degree of diabetic control and the reduction in fibrinogen and mucoprotein levels. The fall in mucoprotein concentration was more marked than fibrinogen. Both the parameters showed no reduction in patients showing poor diabetic control. Table 2 shows the results on follow-up.

DISCUSSION :

Marked elevation in glycoproteins like fibrinogen and mucoproteins was seen in all diabetics irrespective of the presence of vascular complications. However, in those with vascular complications mucoproteins were very significantly raised.

Changes in glycoproteins like fibrinogen have been demonstrated even in early diabetics, (McMillan, 1975a) and probably these changes precede the clinical manifestations of the microvascular changes. McMillan (1975b), Merril (1969) and Fahraens cited by Kieding (1955) have shown that fibrinogen is of major importance in increasing erythrocyte aggregation and altering blood proper-

TABLE 1

THE PROTEIN PARAMETERS IN DIABETICS IN RELATION TO COMPLICATIONS

Study group	Total Protein gms/100 ml ± SD	Albumin gms/100 ml ± SD	Fibrinogen gms/100 ml ± SD	Mucoprotein gms/100 ml ± SD
Controls (n=18)	6.7±0.32	3.5±0.22	214.2± 46.2	225.0± 32.8
Diabetic with complication (n=75)	6.9±1.4 P<0.01	3.2±0.9 P<0.01	398.0±106.5 P<0.001	444.3±220.5 P<0.001
Neuropathy (n=20)	6.9±1.2 N.S.	2.8±0.6 P<0.001	422.6±145.4 P<0.001	518 ±189.8 P<0.001
Retinopathy (n=21)	6.6±0.8 N.S.	2.9±0.8 P<0.001	419.0±160.4 P<0.001	470.6±263.9 P<0.001
Nephropathy (n=15)	6.4±1.3 N.S.	2.4±0.5 P<0.001	373.4±220.6 P<0.05	477.2±223.5 P<0.001
Mixed complications (n=4)	6.9±1.1 N.S.	2.8±0.2 P<0.001	352.5±142.4 N.S.	507.5±109.3 P<0.001
Other complications (n=9)	7.9±0.9 N.S.	3.1±0.5 N.S.	328.5±157.6 P<0.05	625 ±329.9 P<0.05

TABLE 2

THE POST PRANDIAL BLOOD SUGAR AND PROTEIN PARAMETERS BEFORE AND AFTER TREATMENT

Degree of response	PPBS mg/100 ml ± SD	Total protein gms/100 ml ± SD	Albumin gms/100 ml ± SD	Fibrinogen mg/100 ml ± SD	Mucoprotein mg/100 ml ± SD
Excellent & Good Response					
Initial (n=24)	323.7±118.5	6.4±0.8	2.8±0.6	409.3±186.3	527.6±107.7
Follow-up	130.6± 18.6	6.2±0.72	3.1±0.9	309.5±152.8	354.8±169.4
	P<0.001	N.S.	N.S.	P<0.05	P<0.001
Fair Response					
Initial (n=11)	358.2±129.7	6.8±0.6	2.9±0.7	422.3±132	565.5±74
Follow-up	181.4±22	6.6±0.5	3.1±0.6	296.5±173.9	374 ±161.5
	P<0.001	N.S.	N.S.	P<0.05	P<0.001
Poor Response					
Initial (n=11)	340 ± 98.6	6.7±0.6	3.1±0.6	408.9±125.6	446.8±72
Follow-up	265 ± 54.5	6.5±0.6	3.2±0.9	408.9±111	437.7± 68.6
	P<0.05	N.S.	N.S.	N.S.	N.S.

ties contributing significantly to the deterioration of microcirculation. The decreased level of fibrinolytic activity in diabetics (Fearnley et al, 1963; Almer, Pandolfi and Nilson, 1975; Bedi et al, 1977) and the increased level of fibrinogen favour the formation of fibrin clots which further impede the microcirculation.

There are also evidences to show that there is an accelerated rate of fibrinogen degradation to low molecular weight fractions in diabetics. This qualitative difference may account for the elevated levels as well as the deleterious influence on microcirculation (Pulini et al, 1977).

Though elevated levels of mucoproteins occur in inflammatory and other degenerative conditions also, it is a common feature of diabetes mellitus. Marked elevation of mucoproteins in diabetics have also been reported by Keiding and Tuller (1955), and Pathak et al (1977).

In this study, it was noted after metabolic control of diabetes was achieved, the initial elevated levels of fibrinogen and mucoproteins showed a significant reduction, though not to normal levels.

The positive correlation observed between the control of diabetes and reduction in fibrinogen and mucoprotein suggest that the synthesis of these proteins depend on the severity of diabetes. In the presence of insulin deficiency, the protein precursors are shunted through the pathways not requiring insulin, like those of glycoprotein (John and Miller, 1969). The tendency for the protein-bound hexoses to rise with blood sugar and also to reverse in early stages of diabetes has been reported. (Bradley, 1971).

The significance of this study lies in the observation that the abnormal concentrations of fibrinogen and mucoproteins, which may play some role in causation of vascular complications of diabetes, can be decreased to some extent by control of diabetes and hence stresses the need for sustained and effective chemical control of diabetes.

SUMMARY

Changes in different fractions of plasma proteins are known to occur in diabetes. Albumin and fibrinogen are important in controlling the haemodynamic properties of the body. Alterations in mucoproteins are known to affect the cellular functions in diabetics, in several ways. This paper deals with a study of levels of total protein, albumin, fibrinogen and mucoproteins in diabetic patients conducted at the Diabetes Research Centre, Madras.

A total numbar of 144 diabetics were studied. Patients were divided into different groups according to the presence or absence of vascular complications of diabetes. Patients with complications showed lower albumin levels compared to those without complications. The levels of fibrinogen and mucoproteins were elevated in all groups of diabetics irrespective of the presence of complications. These changes were evident even in diabetics with short duration of the disease.

Follow-up studies were possible in 46 patients. The follow-up period ranged from 1 month to 9 months. Serum albumin levels showed only slight improvement with control of hyperglycaemia whereas the levels of fibrinogen and mucoprotein showed marked reduction with control of diabetes. In diabetics with poor control, the concentration of both these parameters did not reduce.

Thus, it was noticed that the changes in plasma proteins may occur even early in diabetes and may be the early markers of associated vascular complications. These changes can be controlled, to some extent, by good control of hyperglycaemia.

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