ORIGINAL ARTICLE

Glycosylated Haemoglobin and Coagulation Profile in Diabetes Mellitus

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ABSTRACT

The present study was designed to find out HbA1 levels and coagulation profile parameters like prothrombin time (PT), activated partial thromboplastin time (APTT) and thrombin time (TT) in diabetic patients. For this purpose 50 cases of noninsulin dependent diabetes mellitus (NIDDM) and 30 controls with equal male to female ratio were taken. The coagulation parameters (PT, APTT, TT) did not show significant difference with control. HbA_1 levels were significantly raised in diabetic patients when compared with control group.

Key words: HBA_1, coagulation parameters

INTRODUCTION

Diabetes mellitus is a chronic disorder of carbohydrate, fat and protein metabolism. A defective or absent insulin secretory response which translates into impaired carbohydrate use and resulting hyperglycemia is the charcteristic feature of diabetes mellitus[1].

Normal glucose haemostasis is tightly regulated by three inter-related processes, glucose production in the liver, uptake and utilization by the peripheral tissues (mostly muscles) and insulin secretion by the pancreas[2].

Most of the available experimental and clinical evidence suggest that the complications of diabetes mellitus are a consequence of metabolic derangements mainly hyperglycemia[3]. The discrete pathogenetic mechanism for the long term complications of diabetes mellitus has gradually focused on three promising targets a) Non-enzymatic glycolysation of proteins. b) Altered microvascular hemodynamics and c) Abnormal polyol-inositol metabolism[4]. The non-enzymatic glycolysation of proteins result in the formation of "Schiff bases" which are reversible early glycolysation products of glucose with proteins. These early glycolysation products due to long term hyperglycemia undergo a slow series of chemical rearrangements to form irreversible advanced glycolysation end products (AGE). These irreversible AGE products facilitate cross linking of etravasated plasma proteins (e.g. LDL & IgG) to matrix components and also of insoluble matrix components (collagen peptides from cross linking) to each other. These irreversible AGE products are thus responsible for the vascular and nephrotic complications associated with long term diabetes mellitus[5]. In some body tissues (nerves, occular lens, kidney and blood vessels) that do not require insulin for glucose transport, hyperglycemia leads to an increase in sorbitol (a polyol) and fructose. In turn increased osmolarity causes water influx and osmotic cell injury results. Sorbitol accumulation is also associated with a decrease in myoinositol content, phosphoinositide metabolism, diacylglycerol, protein kinase c and Na+, K+ ATPase activity. This pathway may contribute to the occular and neurological changes associated with diabetes mellitus [4].

Diabetes mellitus has definite effects on the antithrombin III activity and glycosylated haemoglobin due to hyperglycaemia. Haemoglobin Alc is produced via a postsynthetic glycolysation of haemoglobin A [6]. Haemoglobin Alc reflects blood glucose control over the previous one to two months (Fraser et al, 1979). The use of glycohaemoglobin testing for routine diabetes care provide an objective measure of a patients risk for developing diabetic complications and result of this test can alert patients and clinicians to the need for change in the treatment [7].

MATERIAL & METHODS

A total of eighty subjects were included in the study. They were divided in two groups. Group I consisted of fifty (50) cases of noninsulin dependent diabetes mellitus NIDDM with equal male to female ratio. Group II consisted of thirty healthy subjects.

Collection of Blood

1. 4.5 ml of blood was put into plastic test tubes containing 0.5 ml of 3.13 % aqueous trisodium citrate dehydrate salt (1:10 dilution). Immediately after proper mixing platelet poor plasma (PPP) was separated by centrifuging blood at 4000 rpm for 15 minutes. Prothrormbin time (PT), activated partial thromboplastin time (APTT) and thrombin

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time (TT) were performed within 2 hours of collection.

2. One ml of blood was added in a plastic test tube containing 1.5 mg dipotassium anhydrous ethylene diamine-tetra acetic acid (EDTA) salt. This specimen was used for hemolysate preparation for the estimation of glycosylated haemoglobin (HbA1). This part of the sample was stored at 4^0C temperature for a maximum of eight days till analysed.

RESULTS

The detailed results of PT, APTT, TT and HBA_1C are given in tables 1 - 4

Table 1: Comparison of Prothrombin Time (PT) in patients with Diabetes Mellitus (Group I) and Control subjects (Group II)

PT (Sec)	Group I (Subjects with Diabetes Mellitus)	Group II (Control)
Mean ± SD	13.6 ± 1.85	12.8±1.06
Range	13 – 16	12.3–13.3
Total Subjects	50	30

Statistical Analysis: I Vs II p >0.05 (Non Significant)

Table 2: Comparison of Activated Partial Thromboplastin Time (APTT) in patients with Diabetes Mellitus (Group I) and Control subjects (Group II)

APTT (Sec)	Group I (Subjects with Diabetes Mellitus)	Group II (Control)
Mean ± SD	28.7 ± 3.4	28.01 ± 2.4
Range	23 – 36.9	23 – 32
Total Subjects	50	30

Statistical Analysis: I Vs II p >0.05 (Non Significant)

Table 3: Comparison of Thrombin Time (TT) in patients with Diabetes Mellitus (Group I) and Control subjects (Group II)

TT (Sec)	Group I (Subjects with Diabetes Mellitus)	Group II (Control)
Mean ± SD	15.1 ± 3.45	14.8±2.56
Range	5 – 19	7 – 17
Total Subjects	50	30

Statistical Analysis: I Vs II p >0.05 (Non Significant)

Table 4: Comparison of HbA_1 in patients with Diabetes Mellitus (Group I) and Control subjects (Group II)

HbA_1 (%)	Group I (Subjects with Diabetes Mellitus)	Group II (Control)
Mean ± SD	10.13 ± 2.04	6.5 ± 0.751
Range	6.5 – 14.5	6.0. – 8.3
Total	50	30

Statistical Analysis: I Vs II p <0.05 (Significant)

DISCUSSION

Prothrombin time (PT): Prothrombin time in various groups of diabetics were compared with those of controls. No significant difference was found between them. This finding was in agreement with different studies [10]. This test was originally thought to measure prothrombin, but is now known to depend also on reactions with factor V, VII and X, and the fibrinogen concentration of plasma [8]. There have been fewer reports of factor VII activity in diabetic patients, and the results are inconclusive. Fuller et al (1979)[9] reported higher mean factor VII concentrations in diabetic patients. Reports concerning other coagulation factors involved in the extrinsic pathway are scanty. Fuller et al (1979)[9] reported normal concentrations of factor II in diabetic subjects but increased concentrations of factor V only in those patients with retinopathy. The same research also showed significantly increased concentrations of factor X in insulin-dependent diabetic men. There is general agreement that fibrinogen concentrations in diabetic patients are significantly increased as compared to the normal controls[9 10]

Activated partial thromboplastin time: The difference in APTT between diabetic and control subject was nonsignificant. These results were in agreement with those of Jones and Peterson (1981) [10]. This clotting assay, like PT, failed to detect the hypercoagulable state of diabetes because this test depends not only on the contact factors and on factors VII and IX, but also on the reactions with factor V, X, prothrombin and fibrinogen[8].

Thrombin time (TT): The difference in TT between diabetics and control was nonsignificant and this finding was in agreement with Jones and Peterson (1981) [10]. This clotting assay like PT and APTT is also insensitive in detecting the hypercoagulation state of diabetes mellitus. This test depends upon the concentration reaction of fibrinogen [8]. There is general agreement that fibrinogen concentrations in diabetic patients are significantly increased above those in normal controls[9,10]

Glycohaemoglobin (HbA_1): HbA_1 levels in diabetic patients (Group I) were compared with that of controls (Group II). HbA_1 levels were significantly raised in diabetic patients as compared to control subjects. This finding was consistent with the results of Brooks et al (1983) [11] and patrassi et al (1985) [12], who also observed raised levels of HbA_1 in their studies.

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