IBN AL- HAITHAM J. FOR PURE & APPL. SCI. VOL.23 (2) 2010

Determination of Adenosine Deaminase Activity in type 1 and type 2 Diabetes Mellitus

H. Mossa and Z. Hussein
Department of Biology, Collage of Education Ibn-Al-Haitham
University of Baghdad

Abstract

Serum adenosine deaminase (ADA) activity was determined in 30 blood sample of type 1 diabetic individuals 30 blood sample for the type 2 and 15 normal children as a control for type 1 15 normal adults as control for type 2. The mean ADA activity and specific activity in type 1 was (8.85± 5.55 U/mg of protein) which is compared with control (32.11± 1.54 U/mg of protein) while in type 2 was (48.46±11.91 U/mg of protein) is compared with control (5.18± 2.27 U/mg of protein). We conclude that the altered blood level of ADA activity may help in predicting immunological dysfunction in diabetic individuals and also has a prognostic value.

Introduction

Diabetes mellitus is a group of devastating metabolic disease caused by insufficient insulin synthesis, increased insulin destruction or in effective insulin action. All of its metabolic effect result when the body's cells fail to acquire glucose from the blood. The metabolic imbalances that occur have serious, but not life-threatening, consequences (Figure 1). In insulin dependent diabetes mellitus (IDDM), also called type 1 diabetes, inadequate amount of insulin are secreted because the B-cells of the pancreas were destroyed. Because IDDM usually occurs before the age of 20, it has (until recently) been referred to as juvenile-onset diabetes. Non insulin dependent diabetes mellitus (NIDDM), also called type 2 or adult-onset, is caused by the insensitivity of target tissues to insulin. Although these forms of diabetes share some features, they differ significantly in other. The most obvious symptom of diabetes in hyperglycemia (high blood glucose levels), is caused by adequate cellular uptake of glucose. Because the kidneys capacity to reabsorb glucose from the urinary filtrate is limited, glucose appears in the urine (glucosuria). Glucosuria results in osmotic diuresis, a process in which an excessive loss of water and electrolytes (Na^-, K, and Cl^-) is caused by the presence of solute in the filtrate. With out insulin to regulate level metabolism, its three principal target tissues (liver, adipose tissue, and muscle) fail to absord nutrient appropriately. Instead, there tissues function as if the body were undergoing starvation.

Insulin- Dependent diabetes

In most cases of insulin-dependent diabetes the insulin produced B-cells have been destroyed by the immune system. Although the symptom of IDDM often manifest themselves abruptly, it now appears that B-cell destruction is caused by an inflammatory process over several years. The symptom are not obvious until virtually all insulin producing capacity is destroyed. As in other inflammatory and autoimmune processes, B-cell destruction is initiated when an antibody bind to cell surface antigen. Auto antibodies to insulin and the tyrosine phosphotase. IA-2 have been detected. The most acute symptom of type 1 diabetes is ketoacidosis. Elevated concentration of ketones in the blood and low blood PH a long with hyperglycemia cause excessive water losses, ketoacidoses and dehydration, it left untreated, can lead to coma and death. Certain HLA antigens are found in a large majority of type 1 diabetes.

Non-insulin-dependent diabetes

Non-insulin-dependent diabetes is a milder disease them the insulin dependent form. Its onest is slow, often occurring after the age of 40. Individual with type 2 diabetes have normal or often eveated blood levels of insulin. Type 2 patients are resistant to insulin. The most common cause of insulin resistance is the down-regulation of insulin receptor. Approximately 85% of type 2 diabetics are obese. Treatment of NIDDM usually consists of diet controland exercise. In same cause oral hypoglycemic drugs are used. When the failure of type 2 diabetic patients to control hyperglycemia is accompatied by other medical condition (e.g infection) a serious metabolic state referred to as hyperosmolar hyperglycemic nonketosis (HHNK) can result. Because of the additional metabolic stress, insulin resistance in exacerbated, and blood glucose level would rise[1].

Adenosine deaminase (ADA),as an enzyme that is involved in nucleic acid metabolism [2]. Its main biological activity is defected in T lymphocyte function[3]. So it was considered as good marker of cell mediated immunity [4], and it has acrucial role in lymphocyte proliferation and differentiation [5]. It has been reported that adenosine deaminase is a good marker for insulin function [6,7]. But its connection with immune system was not yet established in diabetic subject. Even through there are some reports available on ADA levels in diabetic subject there are all inconclusive and controversial [8]. We have undertaken apreliminary study to determine its blood activity and to highlight its role in type 1 and type 2 diabets mellitus.

Material and Methods

There were 30 blood samples for adult patients form (both sex) who had a history of not less than six years of diabetes mellitus (sample were collected from AL-Yarmuk hospital). They were aged 20 to 50 years. All of them were in the category of type 2 diabetes mellitus. None of subject have a history of infection or other factor (like drugs) at the time of the study. And there were 30 blood samples of patients with type 1 diabetes mellitus and there were in range of 5 to 16 years (samplewere collected from AL-Yarmuk hospital).Non of the subjects have ahistory of infection or other element at the time of study. A group of 15 healthy adult individuals were served as control and 15 healthy children served as control for type 1.

ADA activity was determinded according to the Giusti method (9). The total activity was defined as the amount of enzyme required to release 1 mol of ammonia per minute from adenosine at standard assay condition and it was expressed as U/ml. The specific activity was expressed as U/mg of protein. The statistical analysis was performed by using T - test to compare the mean value of ADA in patients with control.

Results

Adenosine deaminase activity was significantly **($p<0.01$)** decreased in patients with type 1 symptom, it was (8.85± 5.55 U/mg of protein) as compared with control (32.11 ± 1.54 U/mg of protein). While specific activity in patients (2.01± 1.25 U/mg of protein) as compared with control (9.44 ± 0.78 U/mg of protein). The results in patient with type 2 show a significant increased level in ADA activity, it was (48.46 ± 16.91 U/mg of protein) in patient as compared with control (5.18 ± 2.27 U/mg of protein). While the specific activity levels in patients were (2.01± 1.26 U/mg of protein) as compared with control which were (9.44 ± 0.78 U/mg of protein). The activity and specific activity of patients and control for type 1 and type 2 were shown in table 1.

Discussion

Enzyme is useful in modern medical practice for several reasons. Enzyme assays provide important information concerning the presence and severity of disease. In addition, enzyme often provide a means of monitoring patients response to therapy. Genetic

predisposition to a certain disease may also be determined by measuring specific enzyme activities [1].

Adenosine deaminase is an enzyme necessary for the normal catabolism of purine. ADA catalyses the conversion of adenosine and deoxyadenosine to inosine and deoxyinosin. Experimental evidence indicates that adenosine, in increased amount, may result in increased cAMP activity. which is known to be associated with the inhibition of lymphocyte functionso immunodeficiency may result as consequenes of ADA defect [10]. In this study we observe that there were significant decreases in the ADA levels in type 1 individuals while there were elevated levels of ADA activity in type 2 individuals. In regard to type 2 our finding is similar to result reported by [6,11]. The decreased level of ADA activity in type 1 may result fromthe detect in the action of insulin that is required for the function of lymphocyte. It is also thought that in diabetic individuales, insulin may be a good target for killing by antibody dependent cellular cytotoxicity response [12], that has control over T-lymphocyte function[8]. The increased level of ADA in type 2 may releated to the elevated level of insulin in blood, insulin has a modulating action on immune response [13]. So according to this study we can conclude that there were immunological disturbances associated with this disease, and the altered level of ADA may help in establishing this enzyme as a good marker for assessing CMI in diabetes individuals. However, this study has a few limitation, further studies of ADA in lymphocyte DM individuals is required.

Refrences

1- Trudy Mckee,and Tames R. Mckee,(2003) Biochemistry . 3rd ed., : 550-554.

2- Amja, P.O.,Ekanem, E.A., Short Term.(2005) Glucose load and serum Adenosine Deaminase Activity in Diabetic Nigerians. *Journal of Medical Lab*. Oratory science; 14:1.

3- Mishra, O.P.; Gupta, B.L.; Ali, Z.; Nath, G.and Chandra, L. (1994) Adenosine deaminase Activity in typhoid fever. TNDIAN PEDIATRICS: 31:1380-1383.

4- Bayhanha, M.F.; Pego, A. Lima, M.A.etal.(1990) Serum and pleural adenosine deaminase correlation with lymphocyte population. *Chest* ; 87: 605-610.

5- Sullivan, J.L.; Osborne, W.R.A.;Wedgwood, R.J.(1977) Adenosine deaminase activity in lymphocytes. *Br. J. Hematol.* 37:157-158.

6- Kurtul, N.; Penu, S.; Akarsu, E.; Kocogla, U.; Akosoy, Y.and Akosoy, H.(2005) Adenosine deaminase activity in the serum of type 2 diabetic patients, *Acta. Medic* (Hradec Kralove), 48(1):63.

7- Hoshino, T.; Yamada, K.and Masuoka, K. et al. (1994) Elevated adenosine deaminase activity in serum of patients with diabetes mellitus. Diabetes *Res Clin Pract*; 25: 97-102.

8- Frankie, B. and Abass, E. (2003) Activated T-lymphocyte in type 2 diabetes: implications from in vitro studies. *Curr. Drug Targets*, 4:493-503.

9- Giusti, G. Adenosine deaminase. In: Bergmeyer, H. U. (Ed.) Methods of Enzyme Analysis.(1981). 2nd ed. *Academic Press.*, 2:1092-1099.

10- Daniel, D.;Stites,John D.;Stobo, J.,Vivian Wells (1987) Basic and clinicl immunology, 6th ed.,:339-340.

11- Casanueva, V.; Ximena, C.;Cavicchioli, G.;Oelkev, M.; Cofre, J.and Chiang, M.I.(1992) Serum adenosine deaminase in the early diagnosis of typhoid fever. *Pediatr. Intec. Dis. J.*,11:828-830.

12- Foveny, J.J., K., Totpal, E., Thassz, ,T, Garan (1984).

13- Ivan, M., Roitt and Peter, J., Delves (2004) 10th ed.: 214-215.

Table (1): Adenosine deaminase activity in serum of diabetes patients type 1 and type 2.

Age (both sex)		Number	ADA activity U/mg of protein	Specific activity U/mg of protein
5-13	control	15	32.11 ± 1.54	9.44 ± 0.78
5-13	patients	30	8.85 ± 5.55*	2.01 ± 1.26*
20-50	control	15	5.18 ± 2.27	7.66 ± 0.48
20-50	patients	30	48.46 ± 11.91*	46.19 ± 16.55*

***Significant (p<0.01)**

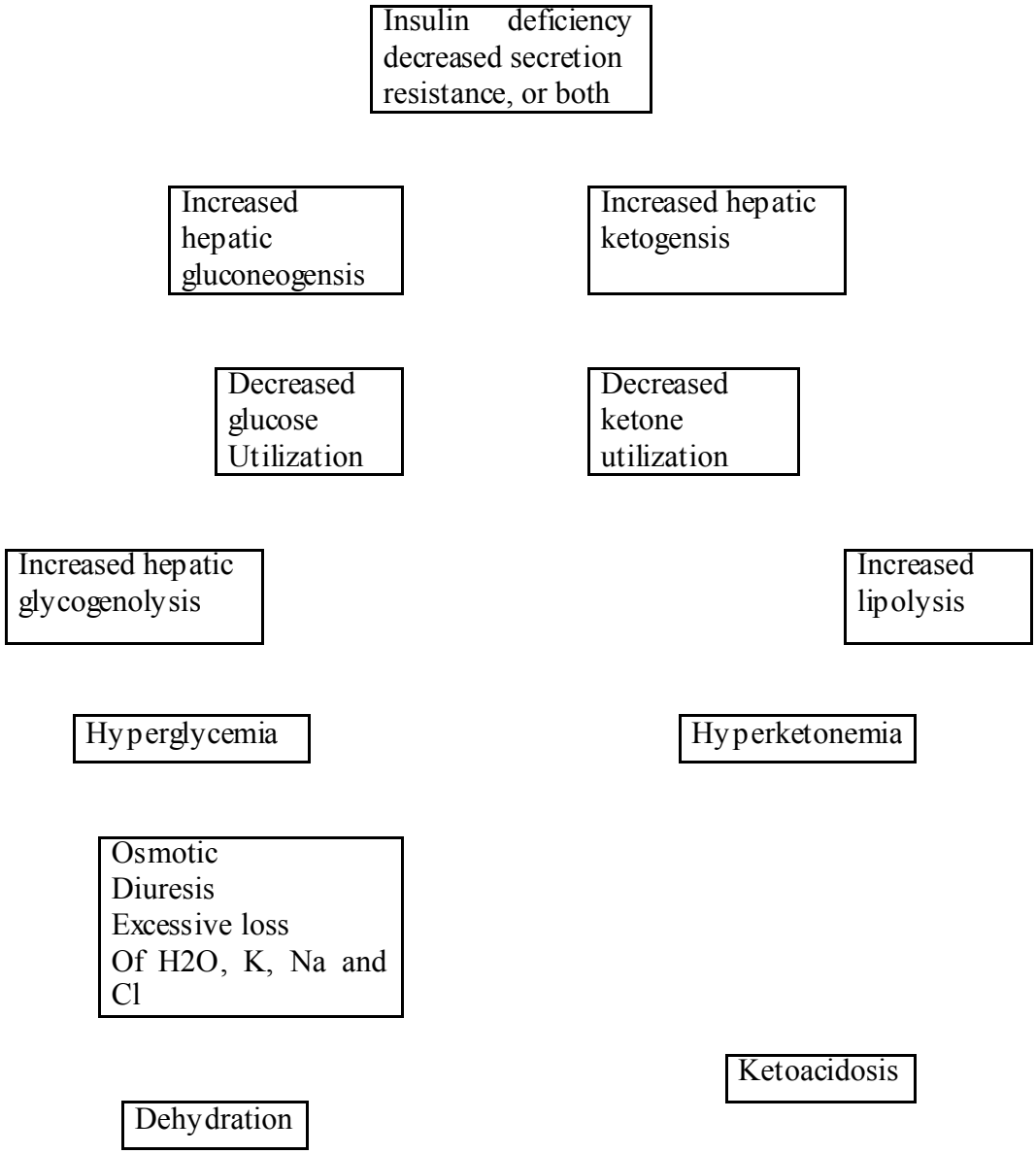

Fig .(1) The metabolic consequences of insulin deficiency or resistance

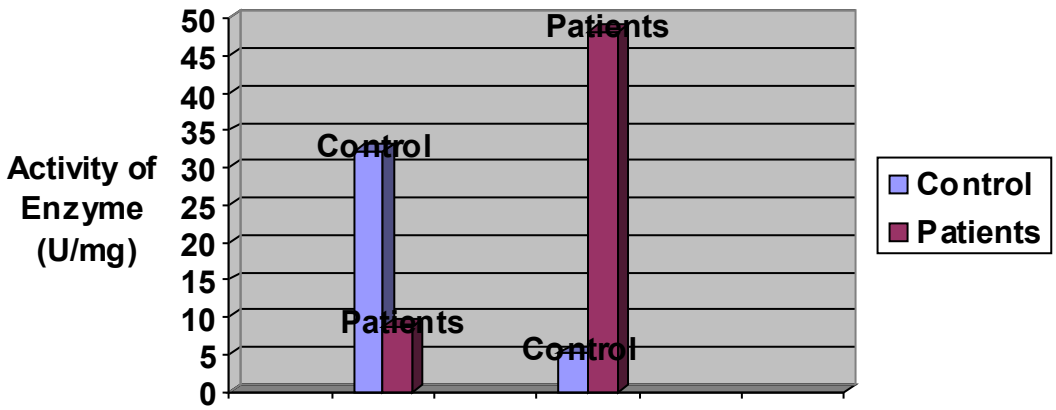

Fig.(2) Activity and specific activity for patients and controls

قياس فعالية انظيم ادينوسين دي امينيز في مرضى السكري من النوع الثاني

حازمة موسى وزهراء حسين

قسم علوم الحياة ، كلية التربية ابن الهيثم ،جامعة بغداد

الخلاصة

قيست فعالية الانظيم المزيل لمجموعة الامين من الادينوسين (ADA) في مرضى السكر النوع الاول (IDDM) والنوع الثاني (NIDDM) وذلك بأخذ عينات دم من ثلاثين مصاباً بالنوع الاول وثلاثين مصاباً بالنوع الثاني وقورنت هذه العينات مع عينات الاشخاص السليمين لكل نوع . وقد اظهرت النتائج وجود ارتفاع كبير في فعالية الانظيم في مرضى النوع الثاني مقارنة بالسيطرة، في حين وجد انخفاض معنوي في عينات النوع الاول مقارنة بالسيطرة.

هدفت الدراسة الى تحديد فعالية هذا الانظيم لدى مرضى السكر حيث ان للADA دور رئيس في انقسام وتمايز الخلايا التائية التي هي اساس المناعة الخلوية. كما ان الانسولين يعد محور للفعالية المناعية لذا حددنا هذا النوع من الامراض كهدفآ لدراسة فعالية انظيم ADA .

ومن خلال النتائج يمكننا الاستنتاج ان هناك اختلافآ في مستوى فعالية ADA في كل من الاشخاص المصابين بالنوعين الأول و الثاني مقارنة بالسيطرة . ان هذا الاختلاف قد يعد مؤشرآ فعالآ لحصول اظطراب مناعي لدى هؤلاء المرضى.