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Oxidative Status in Diabetic Patients

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Abstract

Diabetes mellitus is a group of metabolic disorders of carbohydrate metabolism in which glucose is deficient therefore resulting to hyperglycemia. The prevalence of type 2 diabetes mellitus increases with age and approximately half of all cases occur in individuals older than 55 years.Patients with diabetes suffer from cardiovascular disease and wasting.One explanation for this high incidence of cardiovascular disease and wasting amongst diabetics invokes the molecular similarity of glucose and vitamin C which resulted in competition for membrane transport between glucose and ascorbic acid.It was based on these observations that we assessed the association of some biochemical variables Aspartate transaminase and lactate Dehydrogenase (AST and LDH) with indicators of oxidative damage such as Vitamin C and Uric acid. Our goals were to assess the antioxidant status of these subjects, ascertain whether Diabetes was associated with lower plasma concentrations of these key antioxidants. Sixty five diabetic patients and apparently twenty healthy subjects were studied. The Lactate Dehydrogenase, Aspartate transaminase, Ascorbic acid and uric acid were determined using standard biochemical methods. The statistical analysis used was the one-way analysis of variance ANOVA .The result showed a significant increase in the levels of Aspartate transaminase and lactate Dehydrogenase (AST and LDH) in diabetic patients on drugs and those not on drugs compared to control($P < 0.05$).Though, this increase was very obvious in diabetic patients on drugs. On the other hand, there was a remarkable increase in the level of uric acid in diabetic patients not on drugs.But when the level of Ascorbic acid was compared in diabetic patients on drugs and those not on drugs with healthy individuals, there was a remarkable reduction Ascorbic acid in diabetic patients on drugs compared to diabetic patients not on drugs. ($P<0.05$). From the result of the study we are recommending vitamin C supplements along side with the diabetic drugs to boost the immune system.

Key words: Diabetes, Lactate Dehydrogenase (LDH), Aspartate transaminase (AST), Ascorbic acid (vitamin C) and uric acid.

Introduction

Diabetes mellitus is a group of metabolic disorders of carbohydrate metabolism in which glucose is deficient therefore resulting to hyperglycemia.Some individuals may experience acute life- threatening hyperglycemic episode such as keyoacidosis or hypersmolar coma. As the disease progresses, individuals are at increased risk for the development of specific complications including retinopathy leading to blindness, renal failure, neuropathy (nerve damage) and atherosclerosis[35, 23]. The latter condition may result in stroke, gangrene or coronary artery disease. The prevalence of diabetes mellitus increases with age and approximately half of all cases occur in individuals older than 55 years[1]. Type 2 diabetes comprises approximately 90% of all individuals with diabetes. Though, these individuals have minimal symptoms and are not prone to ketosis and do not depend on insulin to prevent ketonuria. Insulin concentrations may be normal, decreased or increased and most people with this form of diabetes have impaired insulin action[15]. Obesity is commonly associated with the condition and weight lossalone frequently ameliorate the hyperglycaemia. However many individuals with type 2 diabetes may require dietary

manipulation, an oral hypoglycemic agent or insulin to control hyperglycemia.One explanation for this high incidence of cardiovascular disease amongst diabetics invokes the molecular similarity of glucose and vitamin C.It should be recalled that in diabetes there is an insufficient level of the hormone insulin to take up glucose from the blood cells.Therefore the diabetic may have extremely high glucose levels in the blood and urine.His or her cells may actually be starved for glucose which need insulin to transport glucose into the cell. Since vitamin C is structurally very similar to glucose, one of the transport mechanisms of vitamin C into the cells has been suggested to be via insulin transport mechanism.If as in diabetes glucose concentration is very high,then vitamin C will be wiped out completed by glucose and will simplily not get into the cells[18]. As stated by[27] who were investigating competition for membrane transport between glucose and ascorbic acid" the results of their study were consistent with the hypothesis that chronic hyperglycemia may be associated with intracellular deficits of leukocyte AA, an impaired acute inflammatory response , altered susceptibity to infection and faculty wound repair in patients with diabetes" this cellular deficiency in vitamin C with its concomitant effects- increased cholesterol levels, increased atherosclerosis and degeneration of heart and arterial tissues .Contribute to the complications experienced by diabetic patients[10, 3, 4, 24, 13]. Vitamin C is said to be a potentizer of insulin in that less insulin is needed to control blood sugar when vitamin C is given in combination. Diabetes had been considered to be associated with oxidative stress. It has been suggested that increased free radicals and decline of antioxidant defense mechanism induced diabetic micro and macrovascular complications[11, 21, 15]. It was equally reported that plasma vitamin C decreased remarkably inType 2 diabetic patients when compared to control[22]. However the study[17] revealed conflicting finding that there was no significant difference in the level of plasma vitamin C obtained in diabetic and those of healthy persons so also the study[6]. Though, vitamin C level was much lower in the lymphocytes of subjects with diabetes compared to lymphocytes of healthy persons. On the other hand, Uric acid is by-far the highest concentration antioxidant in human blood[9] and provides over half of the total antioxidant capacity of human serum[2]. Uric acid's antioxidant activities are also complex, given that it does not react with some oxidants, such as superoxide, but does act against peroxynitrite[12, 31] peroxides, and hypochlorous acid.

The effects of uric acid in conditions such as atherosclerosis, ischemic stroke, and heart attacks are still not well understood, with some studies linking higher levels of uric acid with increased mortality[33, 8] and other studies showing no association[31]. As Proctor first noted over two decades ago "the well-established association between high urate levels and atherosclerosis could be a protective reaction (antioxidant) or a primary cause (pro-oxidant)". He stated that uric acid was activated as a defense mechanism against oxidative stress, may act as a pro-oxidant in cases where metabolic derangements shift its production well outside of normal levels. [33, 31, 8].

Lactate dehydrogenase (LDH) is especially concentrated in the heart, liver, red blood cells, kidneys, muscles, brain, and lungs.The Disease of liver, heart, muscle and some form of cancer can be detected using Lactate dehydrogenase. Lactate dehydrogenase concentration also increases during leukemia, renal cell necrosis, hepatic necrosis, carcinomas, muscular dystrophy and many more conditions. Lactate dehydrogenase can be elevated due to vitro haemolysis or delayed separation of plasma from whole blood .This may lead to marked increase of more than 5 times the upper reference limit in adults. Circulatory failure with shock, hypoxia, myocardial infarction and some haemotological disorders may increase the activity of (LDH) up to 20 times the upper reference limits in adults. This may also be found in megaloblastic anaemia, acute leukemia and lymphomas. Smaller increases occur in other disorder or erythropoiesis such as thalasaemia, myelofibrosis and haemolytic anaemia. Renal infarction or occassinally during rejection of a renal transplant. Moderate increase may be seen in viral hepatitis, malignancy or any tissue, skeletal muscle disease, pulmonary embolism and infectious mononucleosis[25]. The work done by[7] it was observed that lactate dehydrogenase was elevated in HIV/AIDS patients. This was attributed to muscle inflammation (myostisis) or breakdown of muscle cell (rhadonyolysis). [20]Reported Cardiomyopathy associated with anti retroviral drugs in HIV patients. Increased activities of Aspartate transaminase (AST) in plasma are of considerable diagnostic help in the recognition of myocardial infarction and other conditions associated with myocardial damages (e.g rheumatic carditis). Increased activity of AST in plasma occurs in patients with muscular dystrophy. [19]Reported that AST levels were raised in HIV patients having cardiomyopathy. This increase was attributed to the wasting away of the heart muscle by HIV infection. It was based on these observations that we assessed the association of some biochemical variables AST and LDH with indicators of oxidative damage such as Vitamin C and Uric acid. Our goals were to assess the antioxidant status of these subjects, ascertain whether Diabetes was associated with lower plasma concentrations of these key antioxidants.

Material and methods

Sixty five diabetic patients and apparently twenty healthy subjects were studied**.** The subjects were within Aba Metropolitan. The blood collected was centrifuged, the serum used for the determination of clinical chemistry parameters such as Ascorbic Acid (vit C), Uric Acid, Lactate Dehydrogenase (LDH) and Aspartate Transaminase

(AST). The Lactate Dehydrogenase and Aspartate Transaminase were determined using the methods[16, 29,] respectively. Ascorbic Acid (vit C) Level was assayed using[30] method. Ascorbic acid in the sample was oxidizes to dinitrophenylhydrozone by reacting with 2,2 dinitrophenyl hydrazine which when dissolved in sulphuric acid produce a red colour which was measured colorimetrically at 500nm. Though serum used for ascorbic acid (VitamineC) and uric acid determinations was deproteinated before been treated with either 2, 4,– Dinitrophenylhydrazine or uricase. Fortress diagnostic kits were used for the determinations. All analysis was based on calorimetric assay. The statistical analysis used was the one-way analysis of variance ANOVA.

Result and discussion

Table-1 Serum Glucose, Uric Acid, Ascorbic Acid Aspartate Transaminase AND Lactate Dehydrogenase Activities in Control, Diabetic Patients NOT on Drugs and Diabetic Patients on Drugs.

Parameters	Control	Diabetic patients' (Not on drugs)	Diabetic patients (On drugs)
Glucose(mmol/L)	5.55± 1.58	8.69± 3.01	6.48±2.69
Serum Uric acid (mg/dL)	4.96± 1.56	8.78. ±4.00**	7.60.± 2.14.*
Ascorbic Acid (umol/L)	52.59± 34.74	18.9. ±4.88**	17.7± 4.18*.
AST (U/L)	17.9± 1.32	21.6 ±2.65*	22.00± 2.85*.
LDH(U/L)	181.4± 18.2	463.9 ±32 .6*	472.86 ± 38.4**

***Significant difference P <0.05**

The result showed a significant increase in the levels of Aspartate transaminase and lactate Dehydrogenase (AST and LDH) in diabetic patients on drugs and those not on drugs compared to control(P <0.05)Table.Though, this increase was very obvious in diabetic patients on drugs. On the other hand, there was a remarkable increase in the level of uric acid in diabetic patients not on drugs.But when the level of Ascorbic acid was compared in diabetic patients on drugs and those not on drugs and with healthy individuals, there was a remarkable reduction of Ascorbic acid in diabetic patients on drugs compared to diabetic patients not on drugs and control. (P <0.05) Table-1.

The increase in activites of Aspartate transaminase and lactate Dehydrogenase (AST and LDH) observed in diabetic patients on drugs and those not on drugs compared to control could be attributed to the effects of the disease and drugs since the two enymes are also located in the hepatocytes where most xenobiotics are metabolized.This observation is also in consonance with the studies[25, 7] where it was observed that lactate dehydrogenase was elevated in HIV/AIDS patients on antiretroviral drugs. Though, this was attributed to muscle inflammation (myostisis) or breakdown of muscle cell (rhadonyolysis). Also[20] reported Cardiomyopathy associated with anti retroviral drugs in HIV patients. Increased activity of AST in plasma occurs in patients with muscular dystrophy and this disorder is one of the complications of diabetes mellitus. Equally,[19]Rreported that AST levels were raised in HIV patients having cardiomyopathy.

The remarkable increase in the level of uric acid in diabetic patients not on drugs could be as a result of uric acid being activated as a defense mechanism against oxidative stress. The level of Ascorbic acid in diabetic patients on drugs was lowest compared to those not on drugs and control.However one would have expected the ascorbic acid level to be lowest in diabetic not on drugs instead of those on drug.We are tempted to suggest that it is probably due to the dual effects of the drugs and disease which readily deplete ascorbic acid in the system. Since vitamin C is an antioxidant it will mop up the free radicals generated either from the disease or drug. [28, 5, 32]From the result of this study and previous studies it can be suggested that lower serum vitamin C level is a feature of diabetes.This low level seem to increase the risk of the disease complication such as retinopathy, neurop athy, nephropathy and eventual death.Again, we are of the Opinion like [26] that measurement of lymphocyte vitamin C concentration will be a better clinical indicator to plasma vitamin C. Since complications of diabetes are as a result of cellular vitamin C deficiency, then treatment aimed at increasing vitamin C levels in diabetics ought to yield beneficial theraperutic effects therefor, we are recommending vitamin C supplements along side with the diabetic drugs to boost the immune system.

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