Research Article
AMERICAN JOURNAL OF PHARMACY AND HEALTH RESEARCH
www.ajphr.com
2014, Volume 2, Issue 7
ISSN:2321–3647(online)

Studies on Some Possible Biochemical Aberrations in Type II Diabetes Mellitus

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ABSTRACT

To evaluate the liver and kidney function status of Type ll Diabetic patients. In the present research work on type II diabetes mellitus, various biochemical parameters have been analyzed in a systematic manner. Blood samples were collected from Sun and Apollo laboratory in Coimbatore. About thirty type ll diabetic patients (age : 40 – 70, 15 males and 15 females) and thirty normal individuals (age 30 – 50, 17 males and 13 females) were selected. Among with elevated blood sugar level, serum creatinine, urea, uric acid and protein were also significantly increased. Significantly increased levels of AST and ALT were observed in diabetic, when compared to normal control. The present study suggests that an elevation of blood glucose level might precede the development of liver diseases and renal problems in patients with type ll diabetes mellitus. In conclusion, the hyperglycemic patients were also observed the elevated levels of liver function enzymes and blood metabolites like urea, creatinine and uric acid.

Keywords: Diabetes mellitus (DM), hyperglycemia, insulin, Asparatate transaminase (AST), Alanine transaminase (ALT), Alkaline phosphatase (ALP), urea, creatinine, and uric acid.

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Received 18 June 2014, Accepted 25 June 2014

Please cite this article in press as: Venkatesh R *et al*., Studies on Some Possible Biochemical Aberrations in Type II Diabetes Mellitus. American Journal of Pharmacy & Health Research 2014.

INTRODUCTION

Diabetes mellitus is regarded as a syndrome, a collection of disorders that have hyperglycemia as the hallmark. Non-insulin dependent diabetes mellitus is now epidemic in many countries undergoing modernization and industrialization. Diabetes is becoming the third killer of mankind, after cancer and cardiovascular diseases, because of its high prevalence, morbidity and mortality.[1] Diabetes mellitus is a common endocrine disorder characterized by hyperglycemia, metabolic abnormalities and long-term complications afflicting the eyes, kidneys, nerves and blood vessels.India, a developing Asian country with fast industrialization and a modern lifestyle is facing a grave problem in having the largest number of people with diabetes which is estimated to reach 80 million by the year 2030, [2-3]. It is close to becoming the diabetic capital of the world. The literature on Indian studies showed a threefold rise in the diabetic prevalence in rural as well as urban areas [4].

Diabetes is a chronic condition which occurs either when the pancreas cannot produce insulin or the body is unable to properly use the insulin that the pancreas does produce. Under normal circumstances, insulin is produced by the pancreas in order to regulate the body's metabolism. When food is digested, it is broken down into glucose. The glucose molecules enter the bloodstream, causing a rise in blood sugar levels. Soon thereafter, the pancreas secretes insulin via the pancreatic beta cells. Insulin is responsible for facilitating the transfer of glucose from the bloodstream to the inside of the body's cells. Once glucose enters the cells it can then be used immediately for energy or stored for later use. It is when the insulin pathway becomes disrupted that diabetes develops [5].

The type ll diabetes mellitus is affected many peoples in india and also its complications cause a heavy economic burden for diabetic patients themselves, their families and society. So in future it is necessary for planning of healthcare, policy and advanced treatments in order to ensure that the burdens of disease are addressed [6]. Most of the literature survey on disorder of glucose metabolism have mentioned that 90-95% of the diabetic cases were type 2 diabetes mellitus. The main causes of type ll diabetes mellitus is obesity, over weight or lack of physical activity inherited from the parents.

Liver plays an important role in the metabolism of carbohydrates, fats and proteins, excretion of bilirubin, alteration of many toxic substances and the storage of essential nutrients such as glycogen. Damage to liver or biliary tract may affect any or all of these functions [7]. Liver is the main organ involved in glucose homeostasis. It is the main site for gluconeogenesis, a process

where glucose is synthesized from lactate, amino acids and glycerol. These are the two important complimentary events that balance the glucose load in our body [8].

At the onset of diabetes mellitus, the kidney begins to grow and glomerular filtration rate increases. Sometime later, structural changes can occur in the glomerulus, which forms the basis for progressive diabetic nephropathy, intrarenal hemodynamic abnormalities, as manifested by glomerular hyperfilteration, are thought to be among the foremost factors responsible for the onset and progression of diabetic glomerulonephropathy [9].

Kidney damage from diabetes is called diabetic nephropathy. The onset of kidney disease and its progression is extremely variable. Initially, diseased small blood vessels in the kidneys cause the leakage of protein in the urine. The progression of nephropathy in patients can be significantly slowed by controlling high blood pressure, by aggressively treating high blood sugar levels [10].

The mode of disposal of nitrogen in the body is through the formation of urea, creatine and creatinine. Liver is the most important organ in the maintenance of blood urea levels through the urea cycle.

Creatinine is formed from creatine. Muscle contains 98% of total body creatinine. Creatinine leaves muscle and enters blood, from where it is eliminated by kidneys. If the kidneys are failing to function normally, the serum creatinine and urea levels increase abnormally. Serum creatinine and urea are well-established markers of Glomerular Filtration Rate (GFR). Increased catabolism of proteins coupled with the diminished ability to excrete the nitrogenous waste might have accounted for the raised urea and creatinine in serum of diabetic patients. Enhanced activities of urea cycle enzymes in diabetic condition might have also lead to increased production of urea nitrogen**.** The main objective of the study is to evaluate the liver and kidney functional status in type ll diabetic patients.

MATERIALS AND METHODS

Collection of serum sample:

Blood samples were collected from Sun and Apollo laboratory in Coimbatore. The blood was obtained by vein puncture and collected in the centrifuge tubes. The medical history and clinical symptoms of the patients by face to face interactions on through prescribed questionare. General health characteristics such as age, sex, smoking status, alcohol consumption, dietary habits etc, were collected and detailed physical examination was also done. In the present research work on type II diabetes mellitus, various biochemical parameters have been analyzed in a systematic manner.

Liver function marker enzymes and blood metabolites:

In the present study liver function marker enzymes and blood metabolites such as Aspartate transaminase, Alanine transaminase and alkaline phosphatase, urea, creatinine, uric acid and total protein were analyzed. Liver function marker enzymes have been analyzed to confirm the non-toxic effect of the drug.

Chemicals:

All the chemicals used in the present study were of analytical reagent grade.

Statistical analysis:

Results are Mean ± SD for 60 samples. Values are expressed as mg / dl. Values that have a different superscript (a,b,c) differ significantly with each other (P<0.05). Data were analyzed using the statistical pack Students't' Test and one way Analysis Of Variance (ANOVA).

RESULTS AND DISCUSSION

Level of Liver function marker enzymes in normal and diabetic patients:

In the present study significantly higher of levels urea, creatinine, uric acid and total protein were noted in diabetic, when compared to normal subjects (P<0.05). In the present study showed that the elevation of blood glucose in type ll diabetic patients also influence the levels of serum creatinine, urea, uric acid and total protein were also significantly increased in diabetic compared with non-diabetic patients. The levels of urea, creatinine, uric acid and total protein in normal and diabetic patients are represented in the table 1 and figure 1.

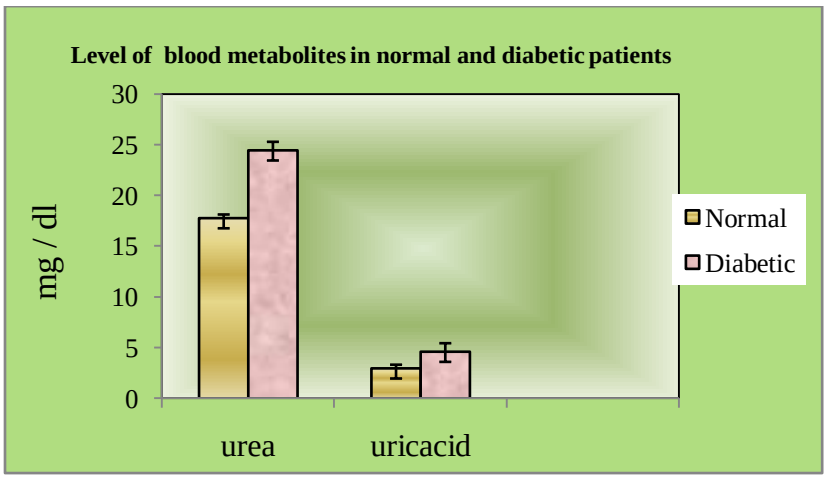

Figure1. Level of blood metabolites in normal and Diabetic patients

Table 1. Level of blood metabolites in normal and diabetic patients

Parameter	Urea	Creatinine	Uric acid	Total protein
Non – Diabetic (n = 30)	17.76 ± 3.26	0.70 ± 0.10	2.96 ± 0.32	6.44 ± 0.62
Diabetic (n=30)	24.44 ± 7.05	0.84 ± 0.10	4.60 ± 0.89	9.52 ± 0.84
't' value	4.633*	5.601*	9.371*	15.791*

Units:

Urea, creatinine, uric acid, – mg / dl; Total protein – g / dl.

Values are mean ± SD ; * - Significant at 5% (t<0.05) ns – not significant

This present finding is in line with the studies of Judykay (2007) and Wagle (2010). The high levels of blood glucose also affects the kidey, so pre – renal problems occur in diabetic patients. Due to kidney failure, cause impaired function of the nephrons, so high creatinine levels noted in diabetic patients. Comparative clinical studies on type ll diabetic patients and creatinine levels were increased in patients compared with non-diabetic male and female persons [11- 12].

Uric acid is a plasma antioxidant, which stabilizes it in plasma and protects it from oxidation [13]. However, the antioxidant property of uric acid has been questioned by recent studies in the exacerbated oxidative state of diabetes and they have demonstrated that uric acid could be related to the development of diabetes. In the present study, we found significantly elevated levels of serum uric acid in the T2DM patients without cardiovascular compilations. Nieto et al., (2000) reported that an increase in the serum uric acid in the T2DM patients might therefore reflect a compensatory mechanism to counter the oxidative stress that occurs in these conditions. However, a high level of uric acid does not confer protection and patients with elevated uric acid levels have a greater risk of developing cardiovascular events [14]. In most cases of diabetes mellitus are able to raise the urea and creatinine are mainly identified as risk markers of kidney disturbances in our sample are characterized by: high urea, creatinine, uric acid, and total protein.

Level of Liver function marker enzymes in normal and diabetic patients:

In the present study significantly increased levels of AST and ALT were observed in diabetic when compared to normal controls. The level of AST, ALT, ALP, Total bilirubin, direct bilirubin and indirect bilirubin in normal and diabetic patients are represented in the table 2 and figure 2.

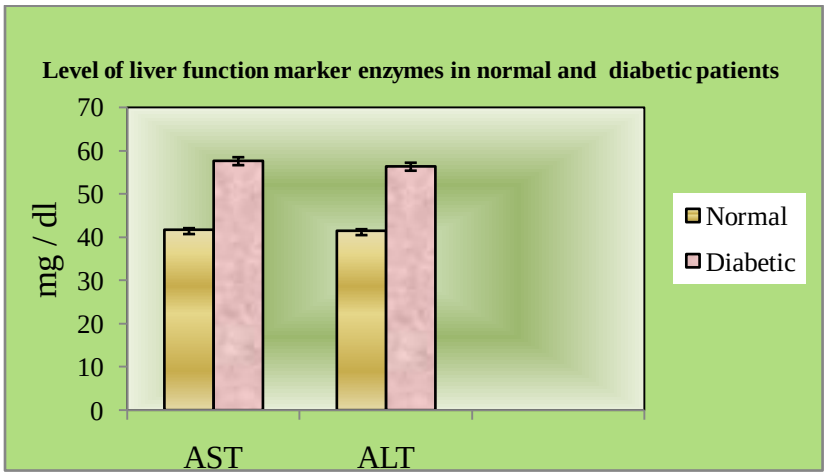

Figure 2. Level of Liver function marker enzymes in normal and Diabetic patients

Table 2. Level of Liver function marker enzymes in normal and diabetic patients

Parameter	AST	ALT	ALP	T.B	D.B	In.B
Non-Diabetic(n=30)	41.67±22.49	41.43±25.80	84.99±14.09	0.89±0.47	0.44±0.38	0.44±0.23
Diabetic(n=30)	57.58±23.58	56.30±32.32	90.13±11.47	1.42±5.96	0.85±0.45	0.59±0.35
't' value	2.611*	1.936*	1.521 ns	0.885 ns	0.817 ns	0.275 ns

Units:
AST- µmoles of pyruvate liberated / L, ALT- µmoles of pyruvate liberated / L
ALP- µmoles of phenol liberated / L,Total, direct, indirect bilirubin – mg / dl
Values are mean ± SD ; * - Significant at 5% ($t<0.05$) ns – not significant

The beta – cells of pancreas were helps to maintain normal blood glucose concentration in the fasting and postprandial states. Loss of insulin in the liver leads to glycogenolysis and an increase in hepatic glucose production. Abnormalities of lipid metabolism and lipolysis in insulin-sensitive tissues such as the liver is an early manifestation of conditions characterized by insulin resistance and are detectable earlier than fasting hyperglycemia. The precise genetic, environmental and metabolic factors and sequence of events is still unknown [15].

Many studies are available in the elevation of liver enzymes in type ll diabetic patients. Recent study in diabetics with hepatitis showed ALT, AST and Gamma Glutamyl transferase (GGT) levels exceeding the upper limit in patients with diabetic and obesity conditions. Elevated enzymes were systematically associated with most parameters of the metabolic syndrome [16].

It is well understood that glucose intolerance is associated with chronic liver disease, particularly cirrhosis and over DM is two to four times more common than in the general population. The relationship between the cause of cirrhosis and the development of glucose intolerance or whether cirrhosis is a prerequisite is unknown, however, it is shown that there appears to be an association between DM and chronic liver disease [17].

This enzyme is less sensitive and specific for liver disease but still should be employed as a screening test because the ALT to AST ratio can often be used to suggest the cause and/or extent of liver disease [18].

CONCLUSION

In conclusion an elevation of blood glucose levels might precede the development of liver diseases and kidney function problems in patients with type ll diabetes mellitus. In conclusion the hyperglycemic patients also observed the elevated levels of liver function marker enzymes and blood metabolites like urea, creatinine and uric acid.

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