Research Article

A study of liver functions in metabolic syndrome and Type 2 diabetes mellitus

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Abstract

Introduction: Diabetes mellitus is a metabolic disease known by chronic hyperglycemia which results from defective insulin action and secretion. Metabolic syndrome consists of a constellation of metabolic abnormalities that confer increased risk of diabetes mellitus. The aim of the present study was to find out if there is any liver function impairment in patients with metabolic syndrome and type 2 diabetes mellitus**. Materials and Methods:** 50 controls, 50 individuals with metabolic syndrome and 50 individuals with type 2 diabetes mellitus were selected by purposive sampling technique. Serum levels of ALT, AST, ALP, total bilirubin and albumin were estimated in controls and cases**. Results:** The mean values of serum ALT,AST,ALP, total bilirubin were significantly increased ($p<0.001$) and serum albumin levels were significantly decreased ($p<0.001$) in cases compared to controls. **Conclusion:** Liver functions are impaired in patients with metabolic syndrome and type 2diabetes mellitus when compared to controls.

Key words: Liver function, Metabolic syndrome, Diabetes mellitus.

Introduction

Diabetes mellitus is a metabolic disease known by chronic hyperglycemia which results from defective insulin action and secretion. World Health Organization projects that number of diabetes will exceed 350 million by 2030. Various studies have documented liver disease as a major cause of mortality in patients with type 2 diabetes. It is well known that liver plays an important role in maintenance of normal glucose levels during fasting as well as in the post prandial period [1].

Metabolic syndrome consists of a constellation of metabolic abnormalities that confer increased risk of diabetes mellitus. The major features of the metabolic syndrome include central obesity, hypertriglyceridemia, low HDL cholesterol, hyperglycemia and hypertension. Central feature of metabolic syndrome is insulin resistance. It results in hypoglycemia and hyperinsulinemia later leading to diabetes mellitus. It contributes to pathogenesis of various diseases like hypertension, atherosclerosis, coronary artery disease and organ dysfunctions [2]. Serum aminotransferases, aspartate aminotransferase (AST), and alanine aminotransferase (ALT) are commonly measured as indirect markers of liver inflammation or injury.

Because ALT is closely related to liver fat accumulation, ALT has also been used as a surrogate marker for nonalcoholic fatty liver disease (NAFLD) in some epidemiologic studies. NAFLD is frequently observed among obese subject and may be involved in the pathogenesis of type 2 diabetes [3].

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Alkaline phosphatase (ALP) is hydrolytic enzyme acting optimally at pH 10. Physiological increases are found during bone growth, while pathological increases are largely associated with hepatobiliary and bone diseases. It has been reported that many diabetics may also exhibit elevated serum alkaline phosphates level [4].

Bilirubin is the end product of heme catabolism in the systemic circulation. It is formed by the action of hemeoxygenase, an enzyme that splits cyclic tetrapyrroleheme into biliverdin, carbon monoxide, and ferrous iron. Biliverdin is subsequently reduced to bilirubin by biliverdin reductase. It is not surprising that bilirubin, has salutary effects in terms of the prevention of diabetes mellitus and its complications.

In addition, bilirubin was also reported to provide protection against metabolic syndrome, and to be negatively associated with overweight and obesity [5].

Serum albumin level is a marker of nutritive conditions, acts as an antioxidant, and is a plasma volume expander. Some studies have reported positive associations between serum albumin levels and metabolic syndrome the latter of which is a clustering of multiple cardiovascular risk factors [6].

The aim of the present study was to find out if there is any liver function impairment in patients with metabolic syndrome and type 2 diabetes mellitus.

Materials and Methods

The present study was conducted in the department of Biochemistry, after obtaining clearance from hospital ethical committee. The study group consisted of 150 individuals who had come to hospital for health check-up during a time period of two years of which, 50 individuals had metabolic syndrome (all patients who fulfil criteria for metabolic syndrome, according to NCEP: ATP III 2001 for metabolic syndrome), 50 individuals had type 2 diabetes mellitus and 50 were controls.

Patients with alcohol abuse were excluded from the study. Informed written consent was obtained from all individual participants included in the study.

Serum levels of ALT and AST were estimated by kinetic UV test IFCC (without PP) .ALP was estimated by photometric UV test IFCC (pNPP). Serum albumin was estimated by photometric colour test BCG. Total bilirubin levels were estimated by photometric colour test diazonium salt. All estimations were done on Olympus AU 400 autoanalyser.

The data was analysed by ANOVA for multiple group comparisons and Pearson's correlation co-efficient for relationship between variables. Statistical analyses were performed with the help of SPSS software. For all statistical analyses the *p* value was considered to be significant at $p < 0.05$ and highly significant for $p<0.001$

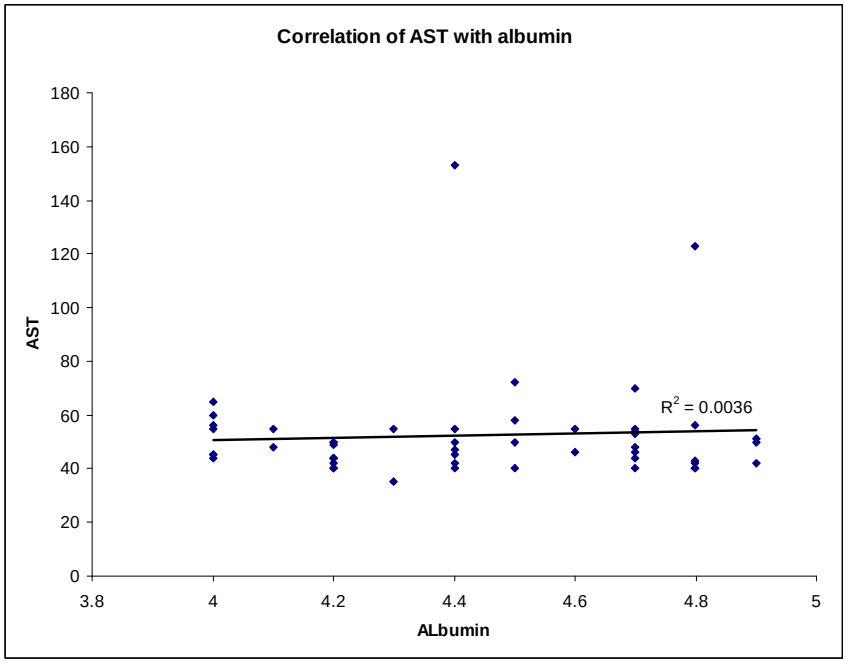
Results

In the present study it was found that serum ALT, AST, ALP , total bilirubin levels were significantly increased and serum albumin levels were significantly decreased in patients with metabolic syndrome and diabetes mellitus when compared to controls. It was found that there is a significant negative correlation of AST and ALP with albumin in patients with metabolic syndrome.

Table 1: Serum liver function tests in controls, metabolic syndrome and diabetic mellitus

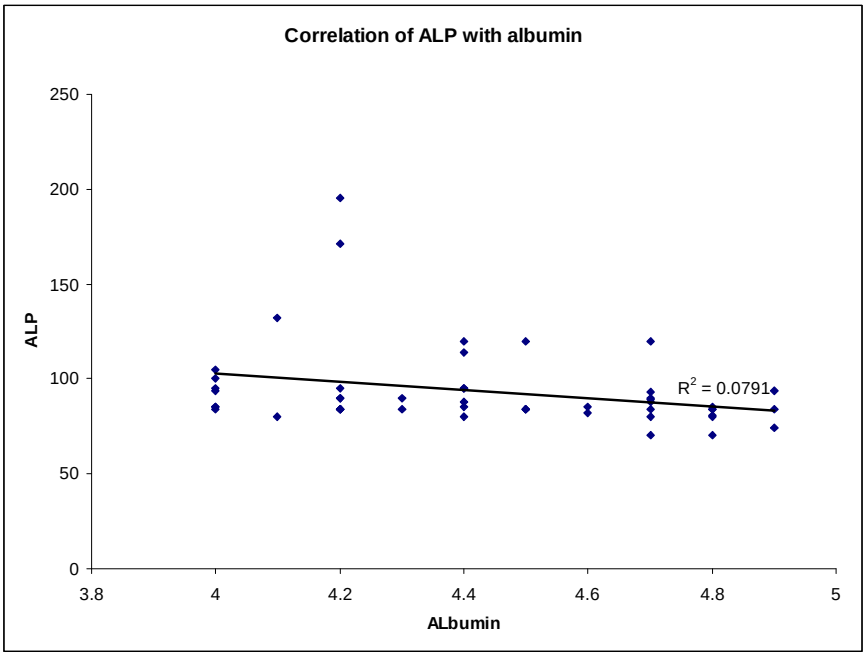
	Control	Metabolic syndrome	Diabetes mellitus	p value
ALT (IU/L)	25.7 ± 8.5	53.7 ± 20.95	57.54 ± 15.18	**<0.001**
AST (IU/L)	24.78 ± 7.66	52.32 ± 19.55	49.54 ± 14.72	**<0.001**
ALP (IU/L)	69.62 ± 8.39	93.54 ± 22.44	99.1 ± 17.86	**<0.001**
Total bilirubin (mg/dl)	0.74 ± 0.22	1.31 ± 0.20	1.60 ± 0.17	**<0.001**
Albumin (g/dl)	5.09 ± 0.58	4.43± 0.29	3.82 ± 0.24	**<0.001**

Figure 1: Shows linear relationship of serum AST with serum albumin in metabolic syndrome.



r = 0.060;**p< 0.001**

Figure 2: Shows linear relationship of serum ALP with serum albumin in metabolic syndrome.



r = -0.2812; **p = 0.048**

Discussion

Metabolic syndrome, characterized as a cluster of metabolic disorders including central obesity, dyslipidemia, hypertension, and glucose intolerance, has been increasing in the developed countries. Subjects with metabolic syndrome are recognized to be at high risk of type 2 diabetes [7]. The metabolic syndrome, in part through glucose intolerance and insulin resistance, is strongly associated with steatosis, fibrosis, and cirrhosis of the liver in severely obese adults [8].

We found that the ALT levels were significantly increased (p<.001) in metabolic syndrome when compared to controls. ALT levels in diabetics were further increased when compared to metabolic syndrome. Increased ALT levels in metabolic syndrome and diabetics are mainly due to liver fat accumulation [9]. ALT is found to be significantly related to liver fat accumulation among the hepatic enzymes. NAFLD is also significantly related to obesity, hypertension, dyslipidemia, and insulin resistance, which are constituent features of the metabolic syndrome. Therefore, NAFLD is considered a hepatic manifestation of metabolic syndrome [7]. Our studies are in accordance with previous studies which also found that serum transaminases are elevated in metabolic syndrome and type 2 diabetes[1,3,6-13].

In our studies serum AST levels were significantly higher in metabolic syndrome and diabetes mellitus when compared to controls. It was also noticed that AST levels are increased in metabolic syndrome when compared to controls. AST is cleared by the liver sinusoidal cells. The increased levels of AST may be due to advancing fibrosis which injures the sinusoidal cells [9]. Our findings were in agreement with the other studies which also showed that serum AST levels are increased in metabolic syndrome and diabetes [1,3,8-9,12-13].

Associations between elevations in alanine transaminase (ALT) and aspartate transaminase (AST) with Type 2 diabetes mellitus have been reported. Data linking elevated serum aminotransferase levels with metabolic syndrome are also available. Thus, elevated ALT values might be a risk factor for Type 2 diabetes mellitus and metabolic syndrome. Identification of factors associated with the elevated aminotransferases could help in the prevention of metabolic syndrome and Type 2 diabetes mellitus [3].

ALP levels were also significantly increased in metabolic syndrome and diabetics when compared to controls. ALP levels were increased more in diabetics when compared to metabolic syndrome. Alkaline phosphatase levels could be elevated due to obesity, insulin resistance, fatty liver, and hepatosteatosis [14]. Our findings are in accordance with the previous studies [14-17].

In our study it was found that serum total bilirubin levels were significantly increased in diabetics and metabolic syndrome when compared to controls. Serum total bilirubin levels were further increased in diabetics when compared to metabolic syndrome. Our results suggest that in diabetes, bilirubin may not have an antioxidant effect, contrary to the findings in the cardiovascular literature. Bilirubin's exact role in diabetes has not been clearly defined and the currently available data and literature are limited and contradictory. In vitro studies have suggested that bilirubin may act as a pro-oxidant in endothelial cells exposed to glucose [18]. The reasons for this discrepancy are not clear. Bilirubin may be induced by deleterious stressors and therefore may just be a marker for inflammation. Another possibility is that although bilirubin still exerts its antioxidant effect, the oxidative stress induced by diabetes outstrips the effects of bilirubin [18]. Our findings are similar to the findings of previous studies [18-21]. Our results are different from the study published by Libor Vitek [5] and Apoorva Dave et al [22] who found that serum bilirubin levels are significantly decreased in metabolic syndrome and diabetics compared to control.

In our studies serum albumin levels were significantly decreased in patients with metabolic syndrome and type 2 diabetes mellitus when compared to controls. Serum albumin levels were decreased in diabetics when compared to patients with metabolic syndrome. Decreased levels of albumin in cases may be due to insulin deficiency and significant decrease in the fractional synthetic rate of albumin. This is in accordance with the previous studies done [23-25].

It was also found that there is a significant negative correlation of AST and ALP with albumin in patients with metabolic syndrome. But there is no correlation of AST or ALP with albumin in controls and diabetics. Even we did not find any correlation of ALT, AST, ALP with bilirubin in all the three groups. Our studies show that there is a significant deterioration of liver functions in patients with metabolic syndrome and type 2 diabetes mellitus.

Our studies have a few limitations also. First, we have not analysed serum GGT levels in our studies. Further studies in large sample size will help determine cut off risk values of liver enzymes.

Conclusion

In the present study liver functions were assesed in terms of serum ALT, AST, ALT, total bilirubin and albumin. It was found that serum ALT, AST, ALP, total

bilirubin levels were significantly increased in patients with metabolic syndrome and type 2 diabetes mellitus when compared with controls. Serum albumin levels were significantly decreased in patients with metabolic syndrome and diabetes mellitus when compared to controls. Our study concluded that there is significant liver dysfunction in patients with metabolic syndrome and type 2 diabetes mellitus.

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