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Research Article

HEPATIC AMINOTRANSFERASES IN ESSENTIAL HYPERTENSION; AN OBSERVATIONAL STUDY AT A TERTIARY CARE CENTRE OF EASTERN INDIA

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ABSTRACT

Background & Objective: Alanine Aminotransferase (ALT) and Aspartate Aminotransferase (AST) are the principal hepatic enzymes in clinical laboratory setup. ALT and AST are elevated in various types of hepatitis, cirrhosis and hepatic neoplasia. Recently, in some studies, the elevation of ALT has been observed in hypertension and metabolic syndrome. This study was performed to find out the relationship of Aspartate Aminotransferase (AST) and Alanine Aminotransferase (ALT) with essential hypertension (EHTN). **Materials & Methods:** 93 EHTN patients and 99 age and sex matched control individuals in 18-55 years age group were recruited into the study, after obtaining their voluntary informed consent. Hepatic aminotransferase levels and lipid profiles of all the patients were estimated and compared by statistical analysis. **Result:** Serum ALT level appeared significantly higher in HTN group than normotensive group ($p= 0.021$). However, no significant difference was observed in AST levels ($p=0.099$) as well as the lipid profile values among the two groups. **Conclusion:** HTN has possibly contributed towards higher ALT level, which may be considered as a surrogate marker for the same and may also serve as an early marker for its subsequent deleterious consequences like type II diabetes mellitus, metabolic syndrome and carotid atherosclerosis.

Keywords: ALT, AST, Hypertension, metabolic syndrome.

INTRODUCTION

Hypertension (HTN) is defined as Systolic Blood Pressure (SBP) higher than 140 mmHg and/or Diastolic Blood Pressure (DBP) higher than 90 mmHg. The underlying pathology of 80-95%[1] of cases of hypertension is not very clear. This type of hypertension without any well-defined etiopathology is called essential hypertension (EHTN).

Worldwide, the prevalence rate of hypertension in 2000 was 26.4% and the same is projected to be 29.2% in 2025[2]. The estimated total number of adults with hypertension in 2000 was 972 million (957-987 million); 333 million (329-336 million) in economically developed countries and 639 million (625-654 million) in economically developing countries. The number of adults with hypertension in 2025 was predicted to increase by about 60% to a total of 1.56 billion.

In India, the prevalence[3] of hypertension is 8.7 and 13.2 per cent in males and females respectively, as per data provided by a 2005 epidemiological study conducted by Non-communicable Diseases Division of Indian Council of Medical Research (ICMR) and

sponsored by World Health Organisation (WHO).

Essential hypertension is often associated with insulin resistance (IR). 25-50 % of non-obese, non-diabetic patients with EHTN have IR[1].

ALT and AST are the principal aminotransferases of human body. The aminotransferases constitute a group of enzymes that catalyze the interconversion of amino acids to 2-oxo acids by transfer of amino groups.

Transaminases are widely distributed throughout the body. AST is primarily found in the heart, liver, skeletal muscle and kidney. ALT is found primarily in liver and kidney, with lesser amounts in heart and skeletal muscle. AST is found in cytoplasm and mitochondria, but ALT is exclusively cytoplasmic.

Liver disease is the most important cause of increased transaminase activity in serum. In most types of liver disease, ALT activity is higher than that of AST, exceptions being alcoholic hepatitis, hepatic cirrhosis and liver neoplasia.

A number of cross-sectional studies[4,5] have since shown relationships between GGT and ALT and the metabolic syndrome and insulin resistance, suggesting that GGT/ALT may serve as a marker for insulin resistance. Moreover[6,7], studies have suggested that hepatic inflammation may be another possible mechanism by which elevated hepatic enzyme levels are related to diabetes risk. Considering the role of ALT in incident type II Diabetes Mellitus and keeping in mind that the above-mentioned studies have been carried out in people of different ethnicity, there is a perceived need to verify if the association between ALT and hypertension holds for eastern Indian population too.

MATERIALS AND METHODS

The study samples were collected from the OPD Clinical Biochemistry Laboratory at the Department of Biochemistry, Medical College, Kolkata. The study subjects included both male and female essential HTN patients and age and sex matched normotensive individuals in the age group of 18-55 years.

The study period spanned from December 2011 to March 2012.

Patients who were either on any anti-hypertensive drugs or found to have Systolic Blood Pressure (SBP) higher than 140 mmHg and/or Diastolic Blood Pressure (DBP) higher than 90 mmHg on three consecutive days were considered as hypertensives. If all other secondary causes of hypertension were ruled out in them, then their hypertension was considered as essential hypertension. Patients who were neither on any anti-hypertensive drugs nor found to have Systolic Blood Pressure (SBP) higher than 140 mmHg and/or Diastolic Blood Pressure (DBP) higher than 90 mmHg on three consecutive days were considered as normotensives.

Total 192 patients were enrolled into the study. Of them, 93 were hypertensives and 99 were normotensives. The applied selection criteria were as follows

Inclusion Criteria

Essential HTN patients and age and sex matched normotensive patients, who attended the OPDs during the study period and gave their voluntary written informed consent for the study.

Exclusion Criteria

- Pregnant and lactating mothers.
- If the patient is suffering from any of the following conditions:

1. Diabetes Mellitus
2. Renal Disease
3. Liver Disease
4. Cardiac Disease
5. Active Infection
6. Any malignancy

Of the 93 hypertensives, 29 were on Amlodipine (5 mg), 2 were on Atenolol (50 mg), 12 were on Losartan (50 mg), 8 were on Metoprolol (50mg), 6 were on Hydrochlorothiazide (12.5mg), 5 were on Ramipril (5mg), 20 were on Losartan + Hydrochlorothiazide (50mg+12.5mg) and 11 were on Telmisartan + Amlodipine (40mg + 5mg).

Study Protocol: Sample Collection, Analysis

Before collection of data or blood sample, each patient was explained the details of the study including rationale, expected benefits, risk profile, confidentiality safeguards and study protocol. For some patients, help of appropriate interpreter(s) was taken. Only those patients who were willing to follow the study protocol and gave their written consent voluntarily were included in the study. There was neither any financial cost nor any financial incentive for the patient for being part of the study.

1. Appropriate blood samples were collected from HTN patients and age and sex matched normotensive. For estimation of serum ALT, AST, cholesterol, triglyceride, HDL,LDL and VLDL fasting blood sample were drawn into serum (without anticoagulant) gel containing yellow colour capped BD Vacutainer tubes. All samples were

immediately centrifuged and stored at 2-8°C until analysis for the relevant biochemical parameters. All analyses were performed within 3 hours of sample collection.

2. Serum Cholesterol was measured by XL600 autoanalyzer using CHOD-PAP principle.
3. Serum Triglyceride was measured by XL600 autoanalyzer using Glycerol Kinase principle.
4. Serum HDL was measured by ERBA Chem 5 V2 semi-autoanalyzer using PEG Precipitation principle.
5. Serum AST level was measured by XL600 autoanalyzer using Modified IFCC principle.
6. Serum ALT level was measured by XL600 autoanalyzer using Modified IFCC principle.
7. Patients' recent-most blood/plasma/serum values of the afore-mentioned biochemical parameters were noted, if already available, provided they were done on the same day under overnight fasting condition.

Patients' relevant anthropometric data were collected. The serum levels of AST, ALT, total Cholesterol, Triglyceride, HDL and LDL of the two groups were compared.

Statistical Analysis

Statistical analysis was performed with Graph pad Instat 3 version. All values were expressed as mean ± standard deviation and differences in mean values between two groups were analyzed using Student's t-test (Table 1). All tests were two tailed and considered statistically significant if p-value was less than 0.05.

RESULT

The demographic details and the biochemical values of all 192 patients are shown in table 1. Serum ALT level in HTN patients appeared higher than their normotensive counterparts, which was statistically significant (p=0.021) as well. However, no significant difference was observed in terms of serum levels of AST, total cholesterol, triglyceride, HDL and LDL between the two groups.

Table 1: The biochemical parameters of normotensive and hypertensive groups

	Normotensive Group	Hypertensive Group	p-value
Number of patients (n)	99	93	
Male	54(54.5%)	52(55.9%)	0.85
Female	45 (45.5%)	41 (44.9%)	0.93
Age (years)	42.12 ± 18.81	46.63 ± 19.42	0.103
Cholesterol (mg/dL)	190.5 ± 98.3	199.2 ± 103.5	0.55
Triglyceride (mg/dL)	149.4 ± 58.7	162.6 ± 49.4	0.094
LDL (mg/dl)	83.1 ± 19.3	88.3 ± 20.1	0.07
HDL (mg/dL)	43.2 ± 10.1	45.3 ± 9.2	0.134
AST (U/L)	40.7 ± 11.7	43.8 ± 14.2	0.099
ALT (U/L)	36.7 ± 13.2	41.7 ± 16.4	0.021*

* p<0.05 is considered to be statistically significant

DISCUSSION

Our study results reconfirm in Indian population the findings of earlier studies investigating the association of ALT with hypertension[4].

It has been postulated that insulin resistance being one of the principal underlying pathology of essential hypertension as well as elevated hepatic enzymes, insulin resistance and accompanying inflammation may be the shared causal ancestor of both hypertension and elevated hepatic enzyme. Elevated hepatic enzyme has been interpreted as a marker for hepatic steatosis, hepatic insulin resistance[8] and inflammation[6,7]. Several possible mechanisms have been proposed to explain how hepatic enzymes are associated with essential hypertension and increase the risk of the metabolic syndrome and diabetes.

Regarding the inflammatory aspect of the putative link between hypertension and elevated hepatic enzymes, it has been shown that fat accumulation in the liver can stimulate cytokine production and inflammatory cytokines such as tumor necrosis factor-α and interleukin- 6 can influence fatty acid metabolism in the liver and predispose to formation of fatty liver[9]. Thus, another possible mechanism is that elevated liver enzymes may reflect inflammation, which in turn impairs insulin signaling in both the liver and other organs[6].

Evidence for a positive association between ALT[10] and inflammation has come from studies examining subjects with abnormally high levels of ALT, which might reflect nonalcoholic steatohepatitis that can lead to liver inflammation[9]. It has also been suggested that GGT/ALT might be an early marker of oxidative stress[11,12] . Inflammation is one manifestation of oxidative stress, and the pathways that generate the mediators of inflammation such as adhesion molecules and interleukins are all induced by oxidative stress[13].

CONCLUSION

The results of this population-based cross-sectional study suggest that ALT may serve as a surrogate marker for essential hypertension. It should be borne in mind in the clinical practice that elevated levels of ALT may not always indicate increased hepatitis, but may simply suggest the existence of the essential hypertension with its subsequent deleterious consequences viz. type II diabetes mellitus, metabolic syndrome and carotid atherosclerosis.

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