Serum concentration of selected trace elements and Gamma-glutamyltransferase in alcoholic liver disease

Navid N Shah¹, Srinivas Ch², Bhagyalakshmi K³

¹Associate Professor, ²Post Graduate Student, ³Professor & Head, Department of Physiology, Prathima Institute of Medical Sciences, Nagunur, Karimnagar District, Telangana-505417.

Address for correspondence: Dr Navid N Shah, Associate Professor, Department of Physiology, Prathima Institute of Medical Sciences, Nagunur, Karimnagar District, Telangana-505417.

Email: drnavid23@gmail.com

ABSTRACT

Introduction:

In South East Asia, India has turn out to be one of the major producers of alcohol. Hepatic manifestation of alcohol includes fatty liver, alcoholic hepatitis and chronic hepatitis with hepatic fibrosis or cirrhosis.

Objective:

The main aim of our study was to determine the concentrations of some important physiological metal ions and liver enzyme activity in chronic alcoholics.

Materials & Methods:

This was a case control study. The study involved 30 male patients of Alcoholic liver diseases (ALDs) from outpatient and inpatients department of Prathima Institute of Medical Sciences (PIMS) Karimnagar as cases and 30 age-matched healthy male relatives of patients with no chronic illness as control group. AST, ALT, bilirubin, gamma glutamyl transferase (GGT) and serum zinc, magnesium and copper of cases and controls were estimated compared.

Results:

In the current study we found that serum bilirubin levels, serum AST, ALT, GGT rose significantly in cases (P<0.001) when compared to controls. The cases have significantly lower level of serum Zinc and Magnesium when compared to healthy normal controls (P<0.0001). There is a significant elevation of serum copper levels in cases when compared to the healthy controls (P<0.001).

Conclusion:

Except copper both serum zinc and magnesium levels significantly reduced in ALD patients. The liver enzymes elevated in the chronic alcoholics denoting hepatic impairment in the cases. The estimation of the enzymes and cations helps in early diagnosis and also as prognostic marker for treatment in ALD patients.

Keywords: Fibrosis, cirrhosis, gamma glutamyl tranferase, ALD

INTRODUCTION

In South East Asia, India has turn out to be one of the major producers of alcohol constituting 65% of the total alcohol beverage production in this region. Most urban areas have witnessed a rise in the number of bars and nightclubs that have opened in recent years. However, Alcohol is prohibited in some parts of India such as Manipur and Gujarat, but it is lawfully consumed in many states. India is a huge sub-continent and the drinking habits differ greatly between the different states. So, it is impossible to describe a single drinking culture for the whole of India. People who live in the south western state of Kerala are the heaviest drinkers. The Lancet noted that more than half of those who drink alcohol in India would be in the category of hazardous drinking.

Hepatic manifestation of alcohol includes fatty liver, alcoholic hepatitis and chronic hepatitis with hepatic fibrosis or cirrhosis.¹ Hepatic steatosis develops in about 90% of persons who drink more than 60 g/day of alcohol,² however may also take place in individuals who drink less.³ Simple, fatty liver is usually asymptomatic and self limited, and may be completely reversible with abstinence after about 4-6 weeks.⁴ Although, several progression to fibrosis and cirrhosis occurs in 5%-15% of patients despite abstinence.⁵,⁶ Also, continued alcohol use (40 g/day) increased the risk of progression to cirrhosis to 30%, and fibrosis or cirrhosis to 37%.⁷

Serum GGT was noted as a sensitive marker of hepatobiliary disorders.⁸,⁹ Furthermore, this proposal lead to the discovery that GGT was increased in a high proportion of alcoholics not currently showing the symptoms of hepatic disease.¹⁰,¹¹ Also, metals are an important cofactor in many enzymatic reaction so it is important to study the activity role of these metals in other cases of acute hepatic injury due not to viral but to toxic agents and compare it with serum γ-glutamyltranspeptidase activity.

Zinc activates hundreds of metalloenzymes and metal-activated enzyme in vivo and is regarded as important for the metabolism of proteins and nucleic acids.¹²,¹³ It has been determined that humans need nearly 72 trace elements, with
very low concentration of heavy metals, such Cu, Sn, V, Cr, Mo, Mn and Co. Magnesium is an essential co-factor of more than 200 enzymes of our body. It is also one of the most abundant cation in our body along with sodium, potassium, calcium. Magnesium mainly forms the hydroxyapatites which constitute most of the bone and teeth matrix and also enamel. Alcoholic liver disease patients mainly suffers the decreased bile salt secretion and hence thereby decreases the absorption of magnesium as the fatty acids elevated due to decreased bile salts forms insoluble salts with the cation leading to its excretion.

Copper also plays an important role in enzymatic activities by forming co-factor. Copper excretion mainly occurs through biliary route. Thus the homeostasis of copper is mainly the function of liver and biliary tree. Any damage to the hepatobiliary system impairs the copper excretion leading to elevation of copper levels in blood.

The aim of our study was to determine the concentrations of some important physiological metal ions and GGT enzyme activity in fatty liver.

MATERIALS AND METHODS

The sample size was estimated by using open epi software from the previous studies and the minimum sample size with 95% CI is 60 i.e., 30 cases and 30 controls. This was a case control study. The study involved 30 male patients of Alcoholic liver diseases (ALDs) from outpatient and inpatients department of PIMS Karimnagar as cases. The diagnosis of alcoholic liver disease is based on history of chronic significant alcohol abuse, clinical signs of liver disease and supporting laboratory test which are AST, ALT and bilirubin level and gamma glutamyl transferase and ultrasonographic features.

The ALDs patients with chronic HTN, DM, Biliary cirrhosis, renal failure or critically ill were not included in this study. The control group included equal number of age-matched healthy relatives of patients with no chronic illness.

All participants were informed about the nature of the study and the informed consent was obtained. 10 ml of blood was drawn from each individual including both cases and controls into two separate test tubes 5 ml each. One test tube was analyzed for liver enzymes and other sample was analyzed for the metals. Ethical clearance for the current study has been obtained from institutional ethical committee, Prathima Institute of Medical Sciences.

Statistical Analysis: Statistical analyses were performed using Statistical Package for Social Sciences version 20.0 (SPSS Inc., Chicago, IL, USA). Student t test for normally distributed and Mann-Whitney U test for non-normally distributed data were used for comparison between cases and controls. P value of <0.05 was considered to be statistically significant. The data was presented as median, range and mean± SD.

RESULTS

The average ages (Mean±SD) of cases and controls were 35.1 ± 12.6 and 34.5 ± 11.4 years respectively, p=0.16. The median durations of alcohol intake and of alcoholic liver diseases in cases were 13 years (range: 8 – 23) and 6 years (range: 3 – 11) respectively.

Table 1: Comparison of Liver Enzymes in cases and controls

<table>
<thead>
<tr>
<th>Liver Enzymes</th>
<th>Cases (n=30) (Mean±SD)</th>
<th>Controls (n=30) (Mean±SD)</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bilirubin</td>
<td>1.7±0.6</td>
<td>0.5±0.2</td>
<td>&lt;0.001**</td>
</tr>
<tr>
<td>SGOT (AST)</td>
<td>81.2±54.7</td>
<td>24.6±4.4</td>
<td>&lt;0.001**</td>
</tr>
<tr>
<td>SGPT (ALT)</td>
<td>39.3±22.5</td>
<td>21.2±5.2</td>
<td>&lt;0.001**</td>
</tr>
<tr>
<td>GGT</td>
<td>84.2±34.1</td>
<td>28.6±11.3</td>
<td>&lt;0.001**</td>
</tr>
</tbody>
</table>

* Student t test (assuming unequal variances)
** Highly significant

Table 2: Comparison of trace elements in cases and controls

<table>
<thead>
<tr>
<th>Trace Elements</th>
<th>Cases (n=30) (Mean±SD)</th>
<th>Controls (n=30) (Mean±SD)</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zinc (µg/dl)</td>
<td>63.2±22.4</td>
<td>109.6±14.7</td>
<td>&lt;0.001**</td>
</tr>
<tr>
<td>Magnesium (mg/dl)</td>
<td>1.3±0.34</td>
<td>1.9±0.18</td>
<td>&lt;0.001**</td>
</tr>
<tr>
<td>Copper (µg/dl)</td>
<td>147.4±28.9</td>
<td>103.2±18.5</td>
<td>&lt;0.001**</td>
</tr>
</tbody>
</table>

* Mann-Whitney U test
** Highly significant

DISCUSSION

In our study we found that serum bilirubin levels raised significantly in cases (1.7±0.6 mg/dl) when compared to controls (0.5±0.2 mg/dl) (P<0.001). when compared to controls (24.6±4.4) there is a significant raise in serum AST levels in cases (81.2±54.7) P<0.001. In our current study the serum SGPT levels are also raised significantly P<0.001 in cases (39.3±22.5) when compared to the controls (21.2±5.2). [Table 1]

In a study conducted by Anil batta et al when compared to normal individuals there is a significant increase in SGOT and SGPT levels of chronic alcoholics which correlates with our study. Similar elevation of liver enzymes AST and ALT was observed in the study of Ghana population by Quaye IK et al. The serum GGT levels of cases (84.2±34.1) is significantly higher than that of controls (28.6±11.3) P<0.001. Studies conducted by gupta S et al, das sk et al and reyes e at al shows that there is a significant increase in plasma GGT levels of chronic alcoholics when compared to the healthy individuals.
In our study, we found that cases had significantly lower level of serum Zinc (63.2±22.4) compared to healthy normal controls, (109.6±14.7), P<0.0001. When compared to apparently healthy controls (1.9±0.18) there is significant reduction in the serum magnesium levels of cases (1.3±0.34), P<0.001. There is a significant elevation of serum copper levels in cases (147.4±28.9) when compared to the healthy controls (103.2±18.5), P<0.001. [Table 2]

Similar results were seen in the studies conducted by Rodríguez-Moreno F et al, Quaye IK et al and Conde-Martel A et al. The chronic alcoholics mainly suffers from the protein intestinal malabsorption leading to the decreased absorption of zinc and also they suffer mainly with increased urinary losses of these free zinc cations on daily basis showing the reduced serum zinc levels.

Both the cations, zinc and copper compete for the binding sites in intestine as the zinc absorption decreases the binding sites available for copper ions increases leading to increased dietary absorption of copper. In addition to this increased absorption from the gastro intestinal tract the damage to the hepatobiliary system in chronic alcoholic causes decreased excretion of copper finally leading to the elevated serum copper levels which has been observed in this current study.

In the present study the serum magnesium levels in chronic alcoholics reduced significantly when compared to normal people. Bile salts are known for their emulsification and absorption of fats and fatty acids, absence of the bile acids increases the undigested fats in the gastro intestinal tract. In chronic alcoholic as the bile acids production decreases there will be elevation of undigested fats in the intestine, these fats forms insoluble salts with magnesium leading to reduction in its intestinal absorption. This could be the underlying reason for hypomagnesemia as seen in our current study.

The serum level of gamma glutamyl transferase enzyme is widely accepted biomarker for alcoholic liver disease. It is a better index when compared with other liver enzyme estimation for hepatic dysfunction and increased alcohol intake. High alcohol intake is one of the important reasons for increased plasma GGT levels. GGT is mainly produced in the smooth endoplasmic reticulum of hepatocytes. In the current study the plasma GGT levels of cases are significantly higher than the controls. The consumption of high amounts of alcohol for longer periods increases the proliferation of smooth endoplasmic reticulum leading to increased GGT along with other hepatic enzymes in the serum. GGT is also an important indicator of body antioxidant levels and oxidative stress levels.

In the current study the serum bilirubin levels and other hepatic markers levels increased suggesting increased hepatic dysfunction in the chronic alcoholics. The hepatic dysfunction and destruction increases with increases in quantity and duration of alcohol intake proving the harmful effects of alcohol on individuals liver function and overall health.

The main limitation of this current study is the number of cases of high alcohol intake is small and this should be conducted extensively in different population of various cultures and also different duration and type of alcohol intake should be taken into account. Radiological evidence suggesting the hepatic impairment would also add a valuable support for the current study.

CONCLUSION

Alcohol liver disease is an important non congenital liver disease which is increasing both mortality and morbidity in the population. The current study showed the hepatic impairment in the chronic alcoholics when compared to apparently healthy individuals. Except copper both serum zinc and magnesium levels significantly reduced in ALD patients. The liver enzymes elevated in the chronic alcoholics, out of all and most importantly the GGT enzyme which is considered to be significant hepatic and oxidative stress marker increased denoting hepatic impairment in the cases. The estimation of the enzymes and cations helps in early diagnosis of hepatic impairment and can be used for assessing the prognosis of patients under abstinence and treatment.

REFERENCES


