ISSN 0975-6299 Vol 3/Issue 2/April – June 2012

International Journal of Pharma and Bio Sciences

RESEARCH ARTICLE BIOCHEMISTRY

ZINC, COPPER, C-REACTIVE PROTEIN AND LIPID PEROXIDATION IN CHRONIC LIVER DISEASES

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ABSTRACT

Lipid peroxidation is an auto catalytic mechanism leading to oxidative destruction of liver. Alters the Zn^{+}, Cu^{++},CRP levels in chronic liver disease. In liver disorders decreased Zn^{+} levels due to poor appetite during the infection with the help of leukocyte endogen mediator and uptake of more Zn to synthesize nucleic acid, protein and enzymes by liver cells, Cu^{++} levels are high in liver disease because of decreased synthesis of cereloplasmin by the liver. CRP is a inflammatory marker it is elevated in liver disease. The study was carried out in 45 subjects with liver disease, Zn^{+} was significantly (p 0.001) decreased. CRP(0.001), Cu(p 0.001) and MDA(0.001) significantly elevated compared with those of healthy individuals. Thus the study supports the association of trace elements such as Zn^{+}, Cu^{++}, CRP and lipid peroxidation in liver diseases.

KEYWORDS

Zn^{+} - Zinc , Cu^{++} - copper, CRP – C-reactive protein , SOD – Super oxide dismutase MDA – Malondialdehyde

INTRODUCTION

The liver is vulnerable to a wide variety of metabolic, toxic, microbial, circulatory, and neoplastic insults

The dominant primary diseases of the liver are viral hepatitis, Alcoholic liver disease, and hepato cellular carcinoma. Recent surveillance studies in the united state document an annual incidence of newly diagnosed chronic liver disease of 72.3% . 100,000 population. Over half (54%) of patients have hepatitis C viral infection, followed by alcohol induced liver disease (24%) non-alcoholic fatty liver disease (9%), and hepatitis B viral infection(4%) liver disease accounts for over 88,000 deaths per year entire world placing it as the eighth leading cause of death ranking[32].

More often, hepatic damage is secondary, to some of the most common diseases in humans, such as cardiac de compensation disseminated cancer, and extra hepatic functions. The enormous functional reserve of the liver marks the clinical impact of early liver damage. Zinc and copper are essential trace elements for the regulation of metabolic activities . Zinc levels are decreased in the chronic liver disorders due to lack of absorption of zinc from intestine[29]. Copper levels are elevated in liver disorder due to the lack of synthesis of ceruloplasmin, so copper levels are elevated[30,31]. C-reactive protein is a liver specific acute phase protein. CRP is a useful marker for the progression of the chronic liver disease[11,12].

CRP expression in hepatocytes is regulated by cytokines such a inter leukin -1, Inter leukin -6 and tumor necrosis factor alpha[12]. Although several alteration in cytokines have been found in patients with chronic liver disease.

Increased CRP levels in patients is consequent upon increased inflammatory response by the liver due to any insult.

Oxygen free radicals play an important role in the pathogenesis of tissue damage in many pathological conditions, including liver diseases. In chronic liver disease is causally associated with the extent of intra hepatic oxidative stress . Increased levels (or) accelerated generation of reactive oxygen species and toxic degradative products of lipid peroxidation have been reported in the serum of individuals with chronic liver disease[13].

Thus the present study aimed at studying the association mineral status & inflammatory markers in chronic liver disorders.

METERIAL AND METHODS

The study was conducted over a period of six months. The study was using zinc, copper, c-reactive protein and lipid peroxidation parameters among the subjects suffering with chronic liver diseases.

The study includes 45 chronic liver disease subjects admitted in “Medicine” and “Gastroenterology” department in Narayana Medical College & Hospital. They were in the age group of 35 to 50 years.

Of these subjects 16 were diagnosed as cirrhosis, 10 were hepatitis B virus induced liver disease subjects. 8 were diagnosed as hepatocellular carcinoma subjects and 11 were chronic alcoholic liver disease subjects.

The same procedure of sample collection and estimation of zinc, copper, c-reactive protein and lipid peroxidation is a adopted fro control subjects

Copper was estimated by end point method Di-Br-PAESA[21].
Zinc was estimated by Nitro-PAPS method[22].
CRP was estimated as a slide test by RHELAX CRP latex reagent [23].
Malandialdehyde was estimated by thiobarbituric acid reacting substances[24].

RESULTS

The results were expressed as Mean (standard deviation). The p value was used to compare the patient mean value with control mean value.

The mean and standard deviation of all the parameters of the study were calculated in patients and control subjects.
Table I shows the mean, standard deviation & p value of all parameters in patients & controls of Bilirubin , ALP, SGOT and SGPT.
Table I shows the mean, standard deviation & p value of all parameters in patients & controls of Zinc, Copper, CRP and MDA.
The values of patients and control groups are also graphically represented for comparison. The graphs were plotted using mean values of all the study parameters.
Figure I,II,III,IV and V shows the mean values of Bilirubin, SGOT, SGPT, Zinc, Copper , CRP and lipid peroxide in chronic liver subjects and controls as bar diagrams.

Table I
Showing the comparative values of patients and control with statistical analysis

S.No	Parameters	Patients		Controls		P value
		Mean	SD	Mean	SD	
1	Bilirubin	4.37	1.87	0.5	0.2	0.019
2	ALP	426.5	180.3	144.6	44.86	0.001
3	SGOT	387.3	91.7	20.05	5.43	0.001
4	SGPT	458.1	107.6	25	5.60	0.001

Figure I
Comparision of patients with controls Bilirubin (Mean)

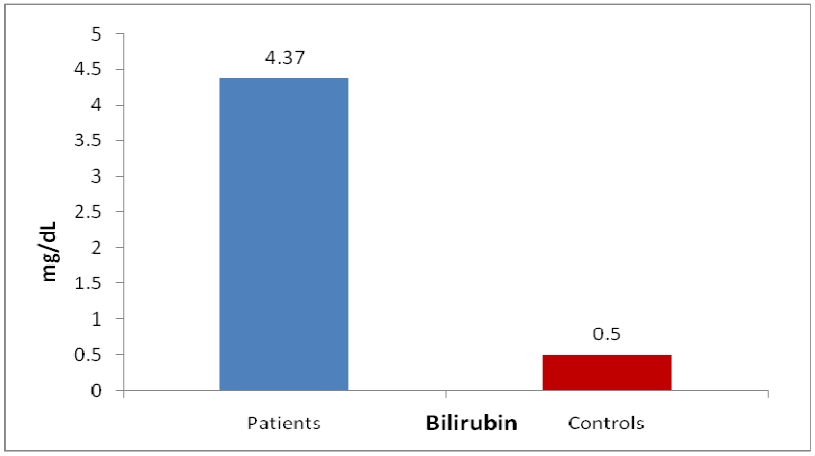


Figure II
Comparision of patients with controls ALP, SGOT, SGPT (Mean)

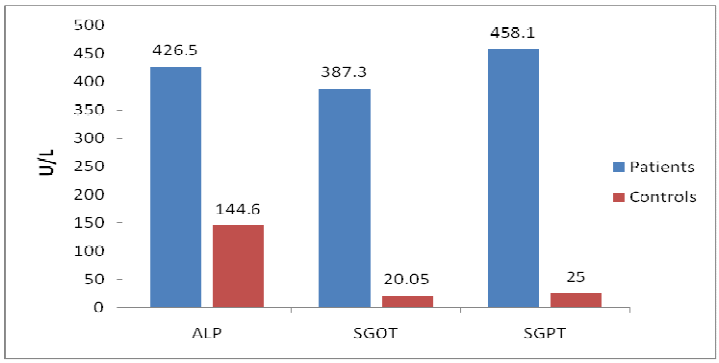


Table II
Showing the comparative values of patients and control with statistical analysis

S.No	Parameters	Patients		Controls		P value
		Mean	SD	Mean	SD	
1	Zinc	40.7	16.04	97.9	18.32	0.001
2	Copper	144.6	41.91	123.2	24.32	0.002
3	CRP	4.05	2.79	0.37	0.07	0.001
4	MDA	9.65	1.20	2.77	2.04	0.001

Figure III
Comparision of patients with controls Zinc and Copper (Mean)

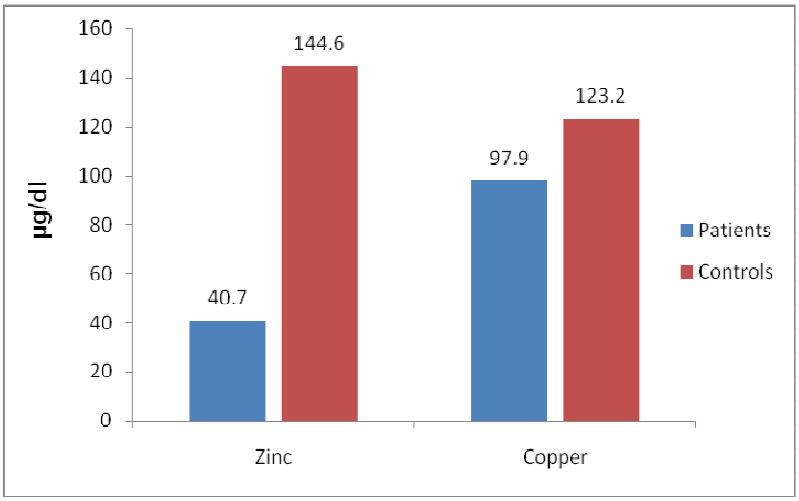


Figure IV
Comparision of patients with controls CRP (Mean)

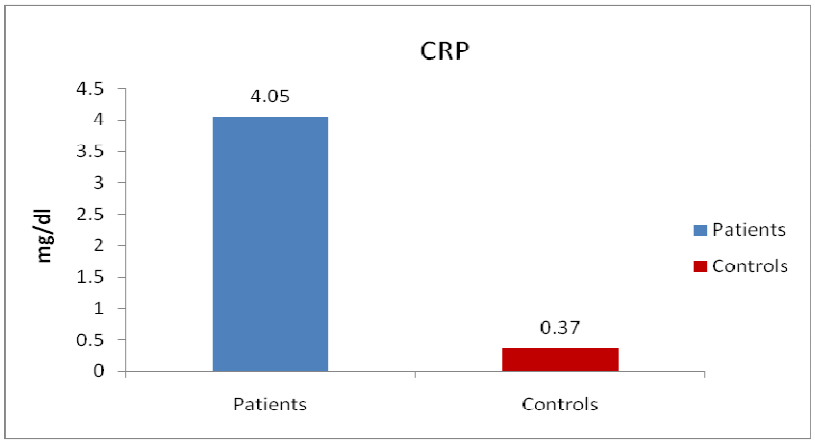
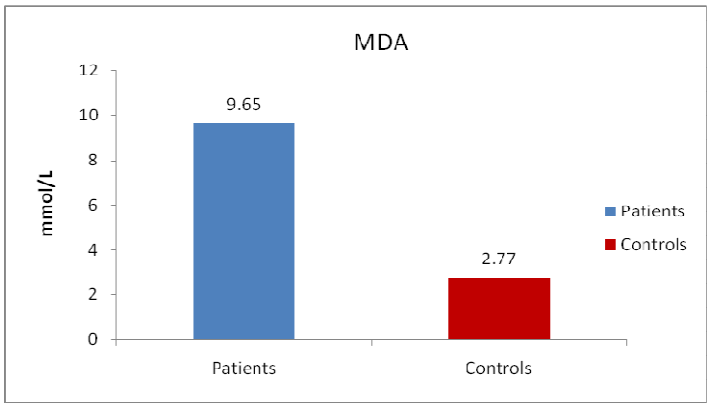


Figure V
Comparision of patients with controls MDA (Mean)



DISCUSSION

In chronic liver diseases Zn levels are low because due to poor appetite, impaired function of intestines and stomach and high pressure of the portal vein, the zinc intake and absorption decreases and also the low content of serum albumin results in less combination with zinc and because of the diffusion characteristic of blood zinc, it is easily lost through urine and sweat[29,30].

In chronic liver diseases decreases the Zn^{++} levels indicates the severity of liver damage[22]. Zn^{++} levels are low due to poor appetite, during the infection with help of leuleocyte endogen mediator and uptake of more Zn^{++} to synthesize nucleic acid, protein and enzymes by liver cells and at the same time poor absorption of Zn^{++} from intestine in liver disorders. Zn^{++} is very essential mineral for the expression of antioxidant enzymes SOD. In chronic liver disorder Zn^{++} levels are low indicating the impairment of antioxidant mechanism leading to free radicals generation. Lipid peroxidation is an auto catalytic mechanism leading to oxidative destruction of hepatic cell membrane that leads to generate lipid peroxidative by products as MDA . CRP is a liver specific acute phase protein CRP levels are increased consequent upon increase in inflammatory response by the liver due to any insult. The above results shows that serum

Cu^{++} concentration is higher than normal individuals elevated Cu^{++} levels indicate an alteration of Cu^{++} metabolism during the acute phase of uncomplicated liver disorder in chronic liver disorders decreases the synthesis of cerluoplasmin that leads to high copper levels in liver disorders.

The study indicates the altered levels of Zn^{++} ,Cu^{++} , CRP & MDA levels in chronic liver disease. Oxidative stress & inflammation lead to altered levels of the above mentioned parameters.

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