Serum Zinc Levels in Cirrhotic Patients Attending General and Specialty Hospitals, Yangon

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Cirrhosis of liver is one of the common medical problem in daily clinical practice and one of the leading causes of morbidity and mortality. Zinc is an essential trace elements for human and plays in many biological roles in the body. Among them, zinc deficiency is thought to be involved in metabolism of ammonia and causes hyperammonia that worsen hepatic encephalopathy. This study aimed to find out the severity of cirrhosis of liver was by Child Turcotte Pugh score and to investigate the associations between serum zinc level and severity of cirrhosis. A hospital-based cross-sectional descriptive study was performed on 78 patients with different underlying causes of cirrhosis of liver at the Medical Units of Yangon General Hospital and Yangon Specialty Hospital. Among the study population, Child grade A was found to be 28.21%, Child grade B was 30.77% and Child grade C was 41.03%. Regarding result of serum zinc level, 62.8% were low level, 28.2% were within normal level and 8.9% were high level. Mean value of serum zinc level in grade A was 0.68 mg/l, grade B was 0.54 mg/l and grade C was 0.48 mg/l (p=0.00). It was found out that there was a high prevalence of zinc deficiency in severe cirrhotic patients. The zinc level was significantly lowest among patients with Child-Pugh C as compare to those with Child-Pugh B and C. Severity of zinc deficiency should be requested for supplementation therapy in cirrhotic patients as to prevent complications such as hepatic encephalopathy, hepatocellular carcinoma and liver failure. Screening for zinc deficiency may need in these patients with more advanced cirrhosis because it seems to be a marker of advanced liver disease and it can be deducted that awareness of serum zinc level among cirrhotic patients is very important in clinical practice.

Keywords: Serum zinc, Cirrhosis

INTRODUCTION

Cirrhosis is the end result of a variety of liver diseases and characterized by fibrosis and architectural distortion of liver with the formation of regenerating parenchymal nodules surrounded by dense bands of scar which has varied clinical manifestation and complications.[1] According to the global burden of disease 2010 study, liver cirrhosis caused 31 million disability adjusted life years (DALYs) or 2% of all deaths worldwide in that year.[2] According to Yangon General Hospital data, mortality rate were 14% and 8% among admitted 877 and 1198 cirrhotic patients in 2011 and 2012, respectively. Child Turcotte Pugh (CTP) prognostic index has been used extensively to cirrhosis patients and to evaluate efficacy of therapeutic procedures.[3] Trace elements play essential role in maintaining vital functions. Excess or deficiency leads to metabolic disorders such as hormonal activites including thyroid hormone, glucacon, insulin, growth hormone, as well as

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the sex hormones.[4] The metabolism of various nutrients in liver diseases indicates the presence and severity of liver disease.[5]

Zinc is the second most prevalent trace element in human body and zinc controls the function of hepatic stellate cells that play a central role in collagen metabolism.[6] Zinc affects fibrotic process in liver by influencing the activity of proteins and enzymes that participate in collagen synthesis and degradation (eg. collagenase, MMPs, prolylhydroxylase). Zinc is also an important cofactor in activation of ornithine transcarbamylase, key enzyme in urea metabolism.[7]

This study was aimed to determine the serum zinc level in different stages of cirrhosis based on Child Turcotte Pugh score and to find out the association of serum zinc level and severity of cirrhosis. If they were associated in clinical practice, screening of serum zinc level was a valuable marker for detection of advanced liver disease and zinc supplementation can be considered to reduce further liver damage and prevent advancement of cirrhosis of liver.

MATERIAL AND METHODS

The study was a cross-sectional descriptive study and 78 cases of cirrhotic patients participated in the study. For selection of participants, inclusion criteria in this study were already diagnosed of cirrhosis of liver patients and any etiology of cirrhosis. Exclusion criteria were patients who have taken zinc supplement, chronic diarrhea disease, history of steatorrhoea, diabetes mellitus and renal disease.

After selection of the participants, they or next of kin were explained about the study and procedure in detail. The written informed consent was taken from selected patients or from their next of kin. Patient particulars (name, age, sex, etc.) were recorded. Severity of cirrhosis was determined according to Child Turcotte Pugh score (Table 1). Under aseptic condition, 5 ml of venous blood were taken with sterile disposable syringe and collected in plain tube.

Table 1. Child Turcotte Pugh Score

Clinical and lab criteria	Points		
	1	2	3
Encephalopathy	None	Mild to moderate (grade 1 or 2)	Severe (grade 3 or 4)
Ascites	None	Mild to moderate (diuretic responsive)	Severe (diuretic refractory)
Bilirubin (mg/dl)	<2	2-3	>3
Albumin (g/dl)	>3.5	2.8-3.5	<2.8
Prothrombin time			
Seconds prolonged	<4	4-6	>6
International normalized ratio	<1.7	1.7-2.3	>2.3

Child Turcotte Pugh Class obtained by adding score for each parameter (total points)

Class A =5 to 6 point (least severe liver disease)
Class B =7 to 9 point (moderately severe liver disease)
Class C =10 to 15 point (most severe liver disease)

There was no need for fasting and no special preparation was required. Blood samples were labeled and sent to Chemical Pathology Section, National Health Laboratory with cold chain as soon as possible. At National Health Laboratory, blood was kept in the room temperature until clotted and it was centrifuged to obtain a serum sample (within 2 hours from blood collection). The serum sample was stored in deep freezer (-20°C) till analysis. All hemolyzed samples were discarded because hemolyzed red cell can introduce relatively high amount of cellular zinc into the plasma.

Serum zinc levels were determined by Atomic Absorption Spectophotometry techniqueused by Shimadzu, AA 6650. The cut-offs points of serum zinc levels were determined as follow: <0.5 mg/l as deficiency, 0.5-1.2 mg/l as normal and >1.2 mg/l as high level. The statistical analyses were performed using stastistical package for social sciences SPSS 16.0. Descriptive analysis of age, sex and serum zinc level of cirrhotic patients are conducted. Kruskal-Wallis rank test was used for statistical analysis of mean serum zinc level among Child Turcotte Pugh Grading A, B and C.

Ethical consideration

This study was carried out according to the guideline of Research and Ethical Committee, University of Medicine (1),

Yangon. Voluntary written informed consent form was taken from the patient or next of kin prior to research. Patients who were refused to participate or give consent were excluded from the study. Appropriate management given by the clinician concerned was not disturbed, interrupted or altered by refusing to participate in the research. Five milliliters of blood were withdrawn from the patients without doing any harm to them with no complication apart from trivial pain at the phlebotomy site. Specimens were used only for this research. At the end of the research, the leftover blood sample was discarded according to Universal Safety Precaution. There was no incentive and no extra charges for participation of this research. Confidentiality of the information collected was strictly maintained. It is researcher's responsibility for scientific misconduct. Result of the study was used only for health care, research purpose.

RESULTS

Figure 1 reveals age distribution among cirrhotic patients. Total 78 patients were included in this study. The mean age was found to be 46 years with the range between 25 to 72 years. The majority of patients 34.6% (27/78) were between 41-50 years of age while the small proportion 7.7% (6/78) and 11.5% (9/78) were between 20-30 years and more than 60 years, respectively.

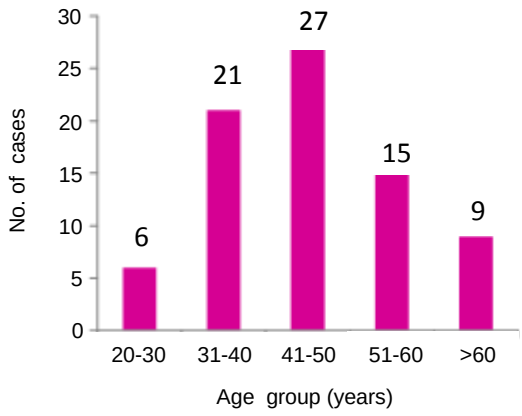

Fig. 1. Age distribution among cirrhotic patients

Between 31-40 years and 51-60 years were 26.9% (21/78) and 19.2% (15/78), respectively. Sex distribution of cirrhotic patients showed male 82% (64/78) and female 18% (14/78). Male and female ratio was 4.5:1. Regarding Child Turcotte Pugh score, 28.21% (22/78) were classified as Class A, 30.77%, (24/78) as Class B, and 41.03% (32/78) as Class C.

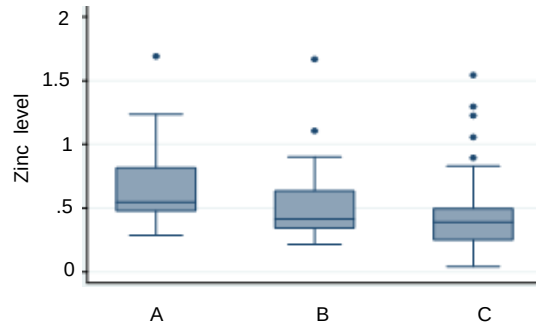

Fig. 2. Association between Child Turcotte Pugh score A, B, C and serum zinc level (mg/l)

Among the study population, 62.8% (49/78) had low zinc level (<0.5 mg/l), 28.2% (22/78) had normal level (0.5-1.2 mg/l) and 8.9% (7/78) had high level (>1.2mg/) (Figure 2).

The number of Child Turcotte Pugh Class A patient was 22/78 with mean zinc level (0.68 mg/l). Zinc level of most of cirrhotic individuals with Child Turcotte Pugh A was within the normal range 0.5-1.2 mg/l. The number of Child Turcotte Pugh Class B was 24/78 with mean zinc value of 0.54 mg/l. Zinc level of most of the cirrhotic individuals with Child Turcotte Pugh B was below normal or lower limit of normal zinc level range of 0.5-1.2 mg/l. The number of Child Turcotte Pugh Class C was 32/78 with mean zinc level 0.48 mg/l. It was found that the mean zinc value was the lowest among cirrhotic individuals with Child Turcotte Pugh C (p=0.00).

Figure 3 reveals distribution of etiology of study cases. Regarding the etiology of cirrhosis of liver, 27% (21/78) were found to be alcoholic, 18% (14/78) were due to viral

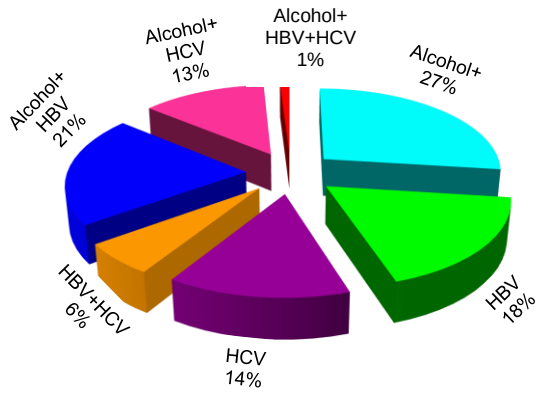

Fig. 3. Distribution of etiology of study cases

hepatitis B infection, 14% (11/78) were found in viral hepatitis C infection, 21% (16/78) were found to be combined alcoholic with HBV infection, 13% (10/78) were due to be combined alcoholic with HCV infection, mixed infection with HBV and HCV were 6% (5/78) and only 1% (1/78) was found to be all combination of alcoholic, viral hepatitis B and C infection.

DISCUSSION

Cirrhosis of liver is one of the common diseases prevalent in Myanmar and a common clinical problem in hospital. It is one of the leading causes of mortality and morbidity. This study investigated correlation between zinc level and cirrhosis of liver patients. Cirrhotic risk factors such as alcohol, hepatitis B and hepatitis C were also studied. In this study, age distribution of patients was between 25 and 72 years. The majority of patients 34.6% (27/78) were between 41-50 years of age. This finding was similar to those of Hein Yar Zar Aung, Hnin Yu Wai and Soomro, *et al.* in which cirrhosis of liver is more prevalent in working age group.[9, 10, 11]

In this study, most of the patients were male 82% (64/78) and 18% (14/78) were female. It is consistent with that of other studies which showed most of the cirrhosis of liver occurred in male patients.[7, 9, 10] This may be due to more exposure of alcohol among male patients. This may be due to increased alcohol consumption among male population in Myanmar and it consequently leads to increased number of male cirrhotic patients. Most of the cirrhotic patients in this study were due to alcohol (27%) followed by HBV, HCV infection and combination of alcoholic with chronic hepatitis infection. Many studies revealed that the most common cause of cirrhosis in Asia and worldwide were alcohol.[12] It is also found out that there is a relationship among decreased serum albumin and zinc deficiency and worsening liver damage that leads to advanced cirrhosis of liver. In alcoholic cirrhotic patients, decreased serum albumin level is due to decreased intake and decreased liver synthesis. Decrease in serum albumin in turn reduces serum zinc level among cirrhotic patients. This condition may be worsen by reduced zinc intake due to significant malnutrition and malabsorption among chronic alcoholic patients.

In this study, infection with HBV and/or HCV was the second most common cause of cirrhosis of liver. In those cases, low serum zinc concentration contributes to oxidative stress and secondary cellular damage. It has been thought that zinc deficiency could directly affect hepatitis C viral replication by supporting structural and functional stability of certain HCV proteins.[11] Hepatitis B viral infection was similar to pathogenesis of HCV. Importantly, marginal zinc deficiency appears to impair the efficacy of hepatitis B vaccination.[13]

Therefore, it can be observed that cirrhosis of liver can also be exaggerated by zinc deficiency among not only alcoholic cirrhotic patients but also those co-infected with HBV and/or HCV infection. This study found out that 63% (49/78) of cirrhotic patients had low serum zinc level, 28% (22/78) had normal serum zinc level and 9% (7/78) had high serum zinc level. In this study, it was demonstrated that there was a high prevalence of zinc deficiency in severe cirrhotic patients. The deficiency was significantly higher in patients with Child Pugh C (mean value=0.48 mg/l) or B (mean=0.54 mg/l) cirrhosis than in those with Child Pugh A (mean=0.68 mg/l) (p=0.00).

A similar study found that serum zinc level was lowered in those with severe cirrhosis than in those with mild cirrhosis in 163 patients.[7] Further, the concentration of serum zinc level decreased with severity of liver disease and found a significant negative correlation between serum zinc and Child score ($p<0.001$).[5] Therefore, screening for zinc deficiency in these patients with more advanced cirrhosis seems to be warranted as a marker of advanced liver disease. On the other side, it is also documented that zinc supplementation corrected the reduced serum zinc level and decreased ammonia concentrations resulting in the prevention of hepatic encephalopathy in 10 patients of decompensated cirrhosis of liver.[14] However, their study sample size was very small and it should be considered for further studies on role of zinc as a therapeutic and prognostic maker. Another study found that the serum zinc concentrations gradually reduced without zinc supplementation in cirrhosis of liver patients and chronic hepatitis C infection. Their prospective study suggested that the serum zinc concentrations increased in approximately half of the patients and lowered cumulative incidence of hepatocellular carcinoma than non-zinc supplementation patients.[15] Further, a study documented that zinc supplementation decreased ethanol-induced hepatic zinc depletion which suppressed the elevated cytochrome P450 enzymes activity and enhanced the activity of alcohol dehydrogenase for suppression of oxidative stress. Zinc administration also enhanced hepatic glutathione and zinc-related antioxidant capacity.[11]

Therefore, screening of zinc deficiency may find its way into the standard management and prognosis of cirrhosis of liver patients. It is also recommended that more clinical trials of zinc supplementation among cirrhotic patients should be conducted and based on their findings, zinc supplementation for cirrhotic patients should be recommended in Myanmar for therapeutic purposes. In conclusion, cirrhosis is a common medical disease not only in Myanmar but also in worldwide. Cirrhosis also has many complications and can reduce life span rate. If complications of cirrhosis can be detected early and prompt treatment is given, there may have more prolong life span and will have a good quality of life. In this study, mean serum zinc level was decreased among Child grade C patients more than those with Child grade B and A. Therefore, it showed there is a marked decrease in serum zinc level among those with more severe or late stage cirrhosis and detection of serum zinc level can predict severity of cirrhosis and vise visa. Therefore, it can be deducted that awareness of serum zinc level among cirrhotic patients is very important in clinical practice. Moreover, cirrhosis of liver is more commonly found in alcoholic patients with or without underlying hepatitis infection. According to this study, alcoholism was the main cause of cirrhosis. Therefore, health education programs on alcoholism and age restriction on sale of alcoholic beverages should be proposed. Legislation of restriction of alcohol consumption or availability in the community by the government is mandatory to prevent health hazard of alcoholic-dependent major and minor health problems and in order to improve the quality of life of Myanmar people.

Competing interests

The authors declare that they have no competing interests.

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