Elevated Vitamin B_{12}: An Indicator of Severity among Cirrhotics

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Original Research Article

ABSTRACT

Concentrations of cyanocobalamin (vitaminB12) in serum have been found to be elevated in acute and chronic liver disease associated with hepatocellular damage.In severe liver disease, liver tissue B12 binding is disrupted and causes B12 to leak out of the liver into the circulation. The cross sectional study was conducted on 50 cirrhotic patients presenting to OPD or admitted in the Department of Medicine, People's Hospital, Bhopal, from November 2017 to April 2018 with objective to estimate serum vitamin B12 levels in patients with chronic liver disease and to find out the relationship between severity of cirrhosis (Child Pugh) with levels of serum Vitamin B12. The inclusion criteria was age>18 years and known and established cases of cirrhosis by ultrasound abdomen. Patients with the history of chronic alcoholic liver disease and patients taking vitamin B12 supplements. Details regarding socio-demographic variables and history was obtained followed by physical, biochemical and histological examination of liver. Majority of the patients belonged to the age group 41-60 years (48%) and 74.0% were males. Mean Vitamin B 12 level in present study was estimated to be 518.2±245.4 pg/ml. The association of mean Vitamin B12 in relation to Child Pugh Class was found to be statistically significant ($p<0.05$). Vitamin B 12 levels in present study were found to be elevated amongst the patients of cirrhosis. Also the association of mean Vitamin B12 in relation to Child Pugh Class was found to be statistically significant ($p<0.05$).

KEY WORDS: vitamin B_{12}, child pugh score, cirrhosis

INTRODUCTION:

Cirrhosis is defined as the histological development of regenerative nodules surrounded by fibrous bands in response to chronic liver injury, that leads to portal hypertension and end stage liver disease. This is accompanied by distortion of the hepatic vasculature. It leads to shunting of the portal and arterial blood supply directly into the hepatic outflow (central veins), compromising exchange between hepatic sinusoids and the adjacent liver parenchyma.[1]

Vitamin B12 is stored primarily in the liver. It acts as a cofactor for two enzymatic reactions, namely, methionine synthesis from homocysteine and succinyl-CoA synthesis from methylmalonyl-CoA, in mammalian systems.[2] Concentrations of cyanocobalamin (vitaminB12) in serum have been found to be elevated in acute and chronic liver disease associated with hepatocellular damage.[3] In severe liver disease, liver tissue B12 binding is disrupted and causes B12 to leak out of the liver into the circulation. Eventually liver disease could produce enough severe tissue B12 deficits to cause metabolic dysfunction despite elevated plasma total B12.[4]Moreover, increased blood vitamin B12 concentration has recently been identified as a prognostic indicator for patients with hepatocellular carcinoma.

In acute viral hepatitis the rise in serum cyanocobalamin seemed to pronounced in the first two weeks of the disease, when bilirubinemia is marked and the liver-function tests indicative of hepatocellular damage are positive.[5] In cirrhosis of the liver elevated cyanocobalamin values were found when clinical and laboratory signs of active hepatitis were present. However normal levels are observed in extrahepatic obstructive jaundice.[3]Depletion of cyanocobalamin stores of the liver has been demonstrated in cirrhosis. This depletion may well be responsible for the development of macrocytic anemia in some cases of cirrhosis.[3]

Since the prevalence of cirrhosis in our country is high, the present study was undertaken to determine the levels of Vitamin B12 in patients with cirrhosis and find out if any correlations exists between the severity of cirrhosis and Vitamin B12.

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MATERIAL AND METHODS:

The present study was conducted as a cross sectional study on cirrhotic patients presenting to OPD or getting admitted in the Department of General Medicine, People's College of Medical Sciences, Hospital and Research Centre, Bhanpur Bhopal,for a period of 6 months from November 2017 to April 2018.

A total of 50 patients were selected using convenient sampling. The study population consists of known and established patients of Liver cirrhosis. The inclusion criteria was age>18 years and known and established cases of cirrhosis by ultrasound abdomen. Patients with the history ofchronic alcoholic liver disease, chronic kidney disease, diabetic patients, patient not willing for study and patients taking vitamin B12 supplements.

The study was approved by Institutional Ethics Committee. After obtaining the informed consent, socio-demographic details were obtained from the patient and entered in preformed pretested questionnaire. A detailed history was elicited, with particular attention to alcohol intake or intake of supplements, to assess the various risk factors for liver cirrhosis. Each patient was examined physically to assess the general condition and the vital data was recorded. Per abdominal examination was done according to the standard protocol and the findings were documented. The physical stigmata of cirrhosis and ultrasonographic findings (like nodular liver surface, coarse echotexture of liver parenchyma, splenomegaly, portal and splenic vein diameters, ascites etc.) was used for including cirrhotic patients in study and child pugh score was used to assess severity of cirrhosis.Based on the severity of the signs and symptoms and the USG reports, the treatment modality was decided. Biochemical analysis including Vitamin B12 level estimation and histopathology was also done.

Data was compiled using MS excel and analysed using Epi Info 7.2 software. Appropriate statistical tests were applied.

RESULTS:

A total of 50 patients were enrolled in present study. Majority of the patients belonged to the age group 41-60 years (48%) followed by 21-40 years (34%). There were 13 (26.0%) females, while 37 (74.0%) were males, showing a male preponderance in the study.

Majority of the patients were having coarse and altered liver echotexture (50%) followed by altered echotexture (38%). Majority of the patients were in the Child Pugh Class B (56%), followed by Class C (32%) whereas only 16% patients belonged to Child Pugh class A.

Table 1: Distribution of patients according to socio-demographic variables.

Socio-demographic variables		Frequency	Percentage
Age Group (years)	15-20	2	4.0
	21-40	17	34.0
	41-60	24	48.0
	61-80	6	12.0
	>80	1	2.0
Gender	Female	13	26.0
	Male	37	74.0

Table 2: Distribution of patients according to liver echotexture.

Liver Echotexture	Frequency (n=50)	Percentage
Altered	19	38.0
Altered with fatty infiltration	1	2.0
Coarse	1	2.0
Coarse and altered	25	50.0
Mild hepatomegaly	1	2.0
Raised echogenicity	1	2.0
Slight altered	1	2.0
Subtle altered	1	2.0

Table 3: Distribution of patients according to Child Pugh Class.

Child Pugh Class	Frequency	Percentage
Class A	8	16.0
Class B	26	56.0
Class C	16	32.0

Table 4: Comparison of mean Vitamin B12 in relation to Child Pugh Class.

Child Pugh Class	Frequency	Vitamin B 12 Mean	SD	f- value	p-value
Class A	8	320.85	177.07		
Class B	26	462.63	193.98	11.385	0.001*
Class C	16	707.18	234.96		

One-way ANOVA applied. P value = 0.001, Significant

Mean Vitamin B 12 level in present study was estimated to be 518.2±245.4 pg/ml.

In Class A, the mean vitamin B12 level was 320.85 ± 177.07 ng/ml, in Class B it was 462.63 ± 193.98 ng/ml and in Class C it was 707.18 ± 234.96 ng/ml. The mean Vitamin B12 was highest in the Child Pugh Class C and lowest in the Child Pugh Class A. The comparison of mean Vitamin B12 in relation to Child Pugh Class was found to be statistically significant ($p<0.05$). To find out the pairwise comparison, post hoc Tukey test was applied.

The pairwise comparisons were done between the pairs – Class A – Class B; Class A – Class C and

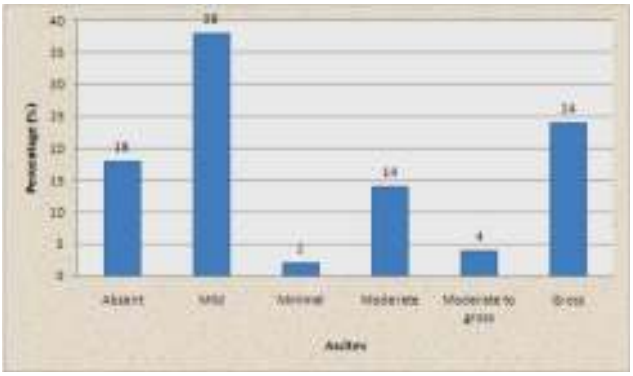

Figure 1: Distribution According to Ascites.

Post-hoc Tukey

Pair	p value	Interpretation
Class A – Class B	0.214	NS
Class A – Class C	0.000 *	S
Class B – Class C	0.001 *	S

* Significant

Class B – Class C. There was no statistically significant difference seen in the pair Class A – Class B ($p>0.05$), showing a comparable vitamin B12 level between the Class A and Class B.

The mean Vitamin B12 level was higher in the Child Pugh Class C in comparison to the Child Pugh Class A ($p<0.05$). The mean Vitamin B12 level was higher in the Child Pugh Class C in comparison to the Child Pugh Class B ($p<0.05$).

DISCUSSION:

Mean age of patients in present study was 46.1± 15.6 years and majority of patients (48%) belonged to 41-60 years of age followed by 21-40 years of age (34%). Majority of patients were male (74%) and only 26% were females. The mean age of patients with liver cirrhosis in a study by Port GZ et al (2014) was 60.7±10.8 years and majority of patients were males (56.3%).[6]

In present study, majority of the patients were having coarse and altered liver echotexture (50%) followed by altered echotexture (38%). Mild ascites was present in 38% patients and gross ascites in 24% patients. Cirrhotic ascitic fluid accumulation represents a very common manifestation of decompensated cirrhosis and results from a number of factors broadly defined in terms of hormonal and cytokine dysregulation and related volume overloading the setting of portal hypertension.[7]

Majority of patients in present study were in Child Pugh Class B (56%) followed by Child Pugh Class C (32%). In a study by Haq MI et al (2016), 17 (17%) patients were in Child Pugh class A and 35 (35%) were in Child Pugh class B and 48 (48%) were in Child Pugh class C.[8]

Amongst patients with Child Pugh Class A in present study, the mean vitamin B12 level was 320.85 ± 177.07 ng/ml, where as in patients with class B and Class C it was 462.63 ± 193.98 ng/ml and 707.18 ± 234.96 ng/ml respectively. The mean Vitamin B12 was highest in the Child Pugh Class C and lowest in the Child Pugh Class A. The comparison of mean Vitamin B12 in relation to Child Pugh Class was found to be statistically significant ($p<0.05$) in present study. These findings were similar to study by Sugihara T et al (2017) in which Serum vitamin B12 levels were significantly higher in patients with cirrhosis than chronic hepatitis [647 (160–2956) vs. 461 (189–2956) pg/mL ($p = 0.029$)]. In patients with Child-Pugh C, Child-Pugh A and Child-Pugh B, the mean B12 level - was 1308 ± 599 pg/mL, 784 ± 559 pg/mL, and 660 ± 464 pg/mL respectively. They also found statistically significant association between Vitamin B12 and Child Pugh Class ($p = 0.036$).[2] Bosy-WestphalA et al (2003) in their study observed that mean plasma folate was normal in patients with liver disease, but vitamin B-12 was elevated in cirrhosis.[9] In patients with Child-Pugh A, Child-Pugh B and Child-Pugh C class, the mean B12 level was 534 ± 384 pg/mL, 724 ± 506 pg/mL, and 1538 ± 918 pg/mL respectively.[9]

In present study, the association between Vitamin B 12 level was also observed between Child Pugh classes using post hoc Tukey test. No statistically significant difference was observed between patients of Child Pugh Class A – Class B ($p>0.05$) whereas the mean Vitamin B12 level was higher in the Child Pugh Class C as compared to the Child Pugh Class A ($p<0.05$). Also the mean Vitamin B12 level was higher in the Child Pugh Class C in comparison to the Child Pugh Class B ($p<0.05$). It was observed that, plasma concentrations of vitamin B-12 was elevated and increased with the severity of liver disease. A cellular leakage of vitamin B-12 with a subsequent intracellular vitamin B-12 deficiency has been proposed for liver cirrhosis.[10]

CONCLUSION:

Vitamin B 12 levels in present study were found to be elevated amongst the patients of cirrhosis. Also the association of mean Vitamin B12 in relation to Child Pugh Class was found to be statistically significant ($p<0.05$). Since elevated Vitamin B 12 level in patients of cirrhosis was associated with Child Pugh Score, it must be assessed in each patient of acute

or chronic liver disease.

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