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RESEARCH ARTICLE

VITMAIN B12 AS SEVERITY AND PROGNOSTIC MARKER IN CHRONIC LIVER DISEASE

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Abstract

Chronic liver disease is an immunocompromised state is well known established fact but there are falsely elevated vitamin b12 levels in patients with chronic liver disease, which can be used as severity and prognostic marker. This study was designed to investigate the association between vitamin B12 levels and liver disease severity and long term prognosis in patients with chronic liver disease.

Methods: An observational longitudinal study was carried over a period of 6 months among indoor patients admitted in department of medicine of a tertiary care hospital in North-Eastern India. The study was conducted on 50 patients diagnosed with chronic liver disease and 50 age and sex matched healthy persons taken as controls. Serum vitamin B12 concentration and other blood parameters were determined. The data were analyzed accordingly by descriptive statistics for the result.

Result: The study populations were predominantly male with mean age 50.80±10.35. Mean total serum vitamin B12 concentration was significantly higher in patients with chronic liver disease (1639 ± 504 pg/ml) when compared to control group (650 ± 300pg/ml). Also among patients with chronic liver disease Child-Pugh C (1858 ± 359 pg/mL) had higher B12 levels when compared to those with Child-Pugh B (1076 ± 370 pg/mL). Out of 50 people, 4 were died and their mean B12 was (2113 ± 112 pg/ml).

Conclusion: Falsely increased B12 levels are due to increased excretion of vitaminB12 into serum from the liver and these serumB12 levels correlates with the severity and prognosis of the patient.

Introduction:-

In 1926, a team of physicians from Harvard University discovered that eating half a pound of liver everyday would prevent pernicious anemia in most patients. From this point, researchers worldwide sought to isolate the anemia-preventing substance from liver[1] .In1947, Folkers and his team isolated vitaminB12(cobalamin), producing tiny, bright red crystals of the vitamin.The following year,this new compound was tested on a patient who suffered from pernicious anemia, curing them. Vitamin B12 is stored primarily in the liver; this vitamin is essential for one-carbon metabolism and cell division. It acts as a cofactor for two enzymatic reactions, namely, methionine synthesis from

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homocysteine and succinyl-CoA synthes is from methylmalonyl-CoA[2], in mammalian systems. Some studies have indicated that elevated serum levels of vitamin B12 might be a sign of a serious and life-threatening disease as damage to liver releases this stored vitaminB12 which is responsible for these falsely high vitamin B12 levels.

Liver diseases are fast being recognized as public health priorities in India. The burden of liver disease in India is significant because it alone contributed to 18.3% of the two million global liver disease–related deaths in 2015[3]. Contribution of cirrhosis and its complications, collectively chronic liver diseases (CLDs), as causes of mortality in India have been increasing progressively since 1980, compared with China, the other country in Asia with a large population, where it remains stationary and is even showing downward trends. The cultural lifestyle transition that India is passing through currently with progressive adoption of a western diet, sedentary habits, along with an aura of freedom from long held taboos around alcohol in the society create grounds for a spectrum of liver diseases in India that shows signs of a rapid switch[4]. This change includes increasing overall importance of alcoholic liver disease (ALD) and non alcoholic fatty liver disease (NAFLD) as causes of liver disease over and above viral causative factors. Liver disease epidemiology in India is in a transition. Better screening strategies, more effective linkage to care for early stage liver disease, and improved awareness on preventive steps in an integrated way could be useful interventions[5].
As described above intervening early can prevent the morbidity and mortality in patients with chronic liver disease, this study was designed to investigate the association between vitamin B12 levels and liver disease severity and long term prognosis in patients with chronic liver disease.

Material And Methods:-

An observational longitudinal study was carried over a period of 6months among indoor patients admitted in department of medicine of a tertiary care hospital in North-Eastern India. .The study was conducted on 50 cases diagnosed with chronic liver disease and 50 age and sex matched healthy people taken as controls. Serum vitamin B12 concentration and other blood parameters were determined. Diagnosed patients were differentiated into compensated CLD and decompensated CLD and were compared with the b12levels and other blood parameters accordingly.

Statistical Analysis:-

Descriptive statistics like mean and percentages were used for the analysis and interpretation of the results and represents in the form of tables and charts. Comparison of the groups was done by t tests. Statistical analysis was performed using SPSS version 21.

Results:-

This study was conducted to investigate the association between serum vitaminB12 levels and liver disease severity and long term prognosis in patients with chronic liver disease who were admitted in the department of general medicine of Agartala government medical college. All patients who were diagnosed with chronic liver disease were included in the study among them 45% were new rest were old, people those who received vitamin B12 in injectable or tablet form are excluded. Among the study population most of them where male (69%) with mean age 50.80±10.35, most of the patients where in fourth to fifth decade as shown in figure 1. In males most of them were daily laborers (24%) followed by drivers (20%) in females most of them where housewives8% (figure2). Most common etiology in males was alcohol 49% followed by non alcoholic steato hepatitis (NASH) 12% and hepatitis B 3% where as in females it was NASH 16% followed by alcohol and hepatitis B10% and 4% respectively (figure3). In the study population 74% of the people had decompensated chronic liver disease and 26% of them were compensated (table 1 & figure 4). Among them 28% of the people belong to CTP (child turcottee pughs score) class B and 72% belong to class C. Mean total serum vitamin B12 concentration was significantly higher in patients with chronic liver disease (1639±504pg/ml) when compared to normal people (650±300pg/ml), also among patients with chronic liver disease Child-Pugh C (1858±359pg/ml) had higher B12 levels when compared to those with Child-PughB (1076±370pg/ml). Out of 50 people, 4 were died and their mean B12 was (2113±112pg/ml).

Figure1:-

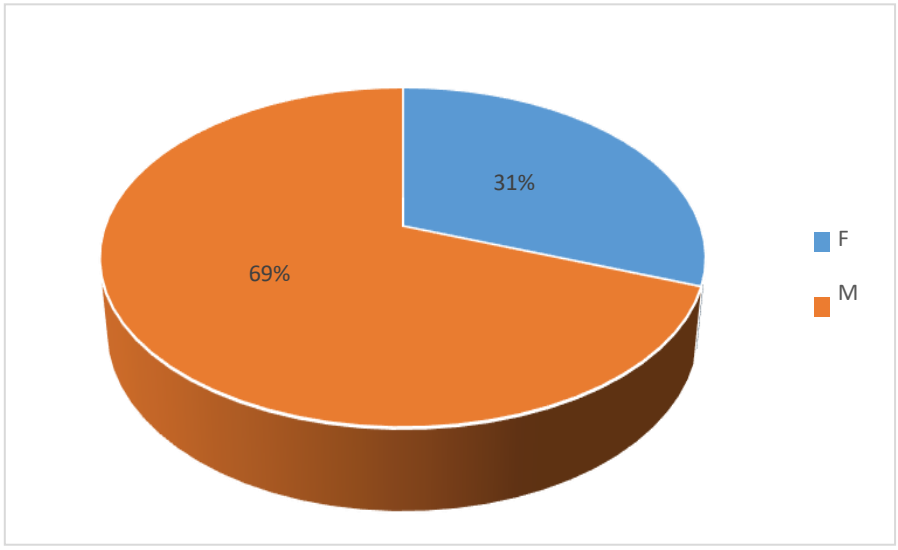


Figure-1.1:-

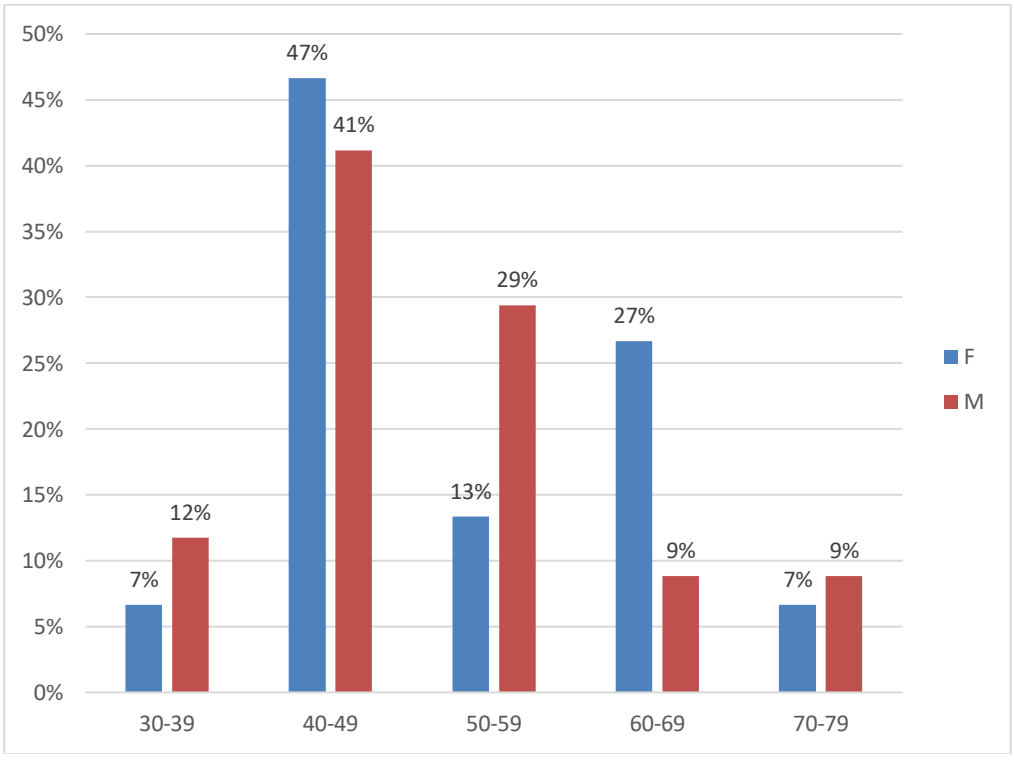


FIGURE2 :-

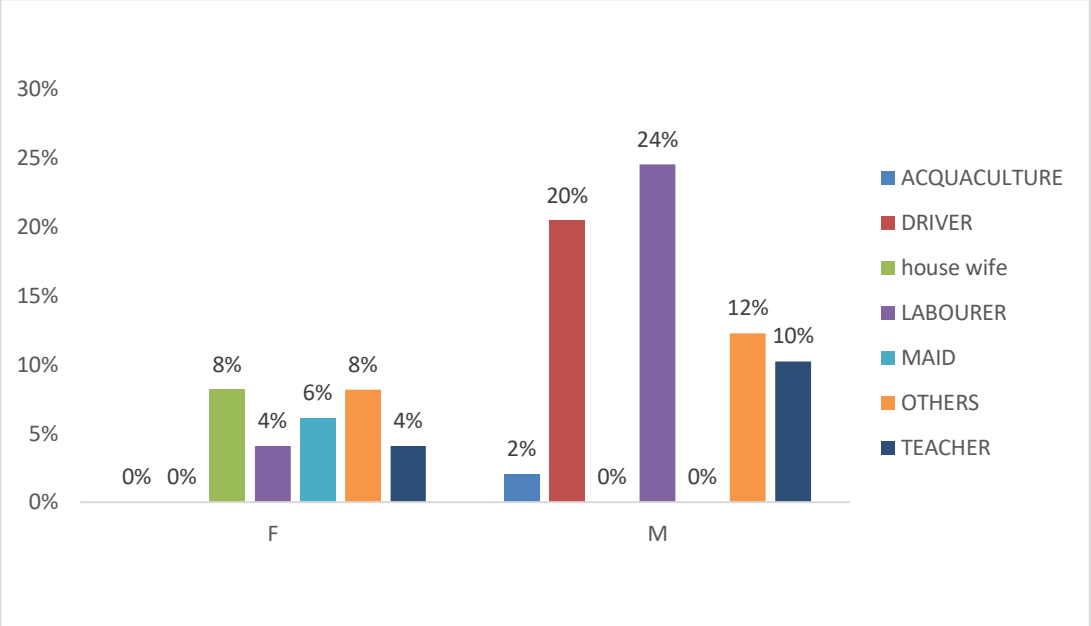


FIGURE 3:-

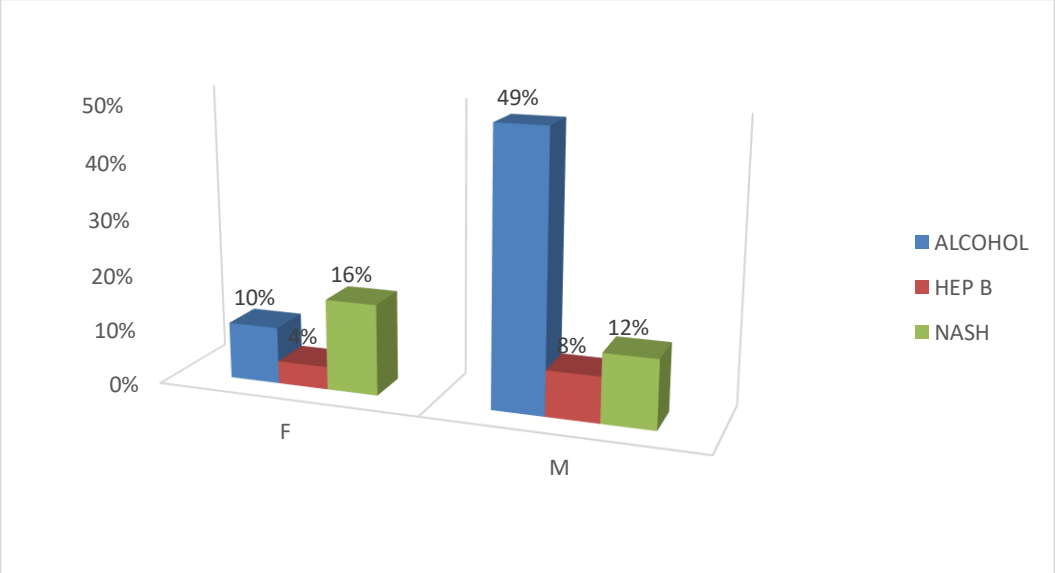
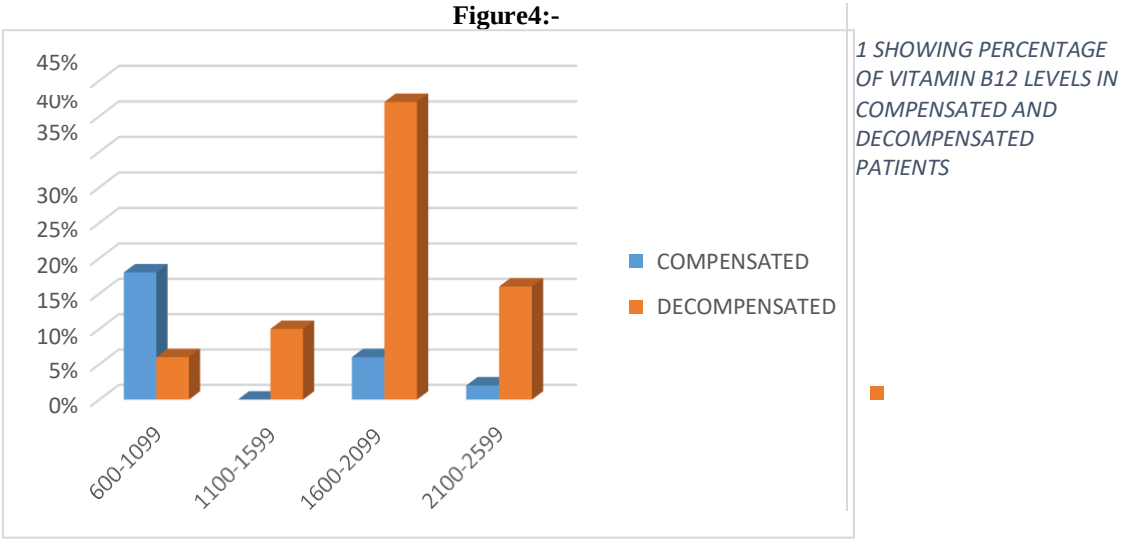


Table 1:- Showing percentage of people with compensated and decompensated CLD with their vitamin B12 levels.

Countof B12	**ColumnLabels**		
Row Labels	**COMPENSATED**	**DECOMPENSATED**	**Grand Total**
600-1099	18%	6%	24%
1100-1599	0%	10%	10%
1600-2099	6%	42%	48%
2100-2599	2%	16%	18%
Grand Total	**26%**	**74%**	**100%**

Figure4:-



1 SHOWING PERCENTAGE OF VITAMIN B12 LEVELS IN COMPENSATED AND DECOMPENSATED PATIENTS

Figure 5:-

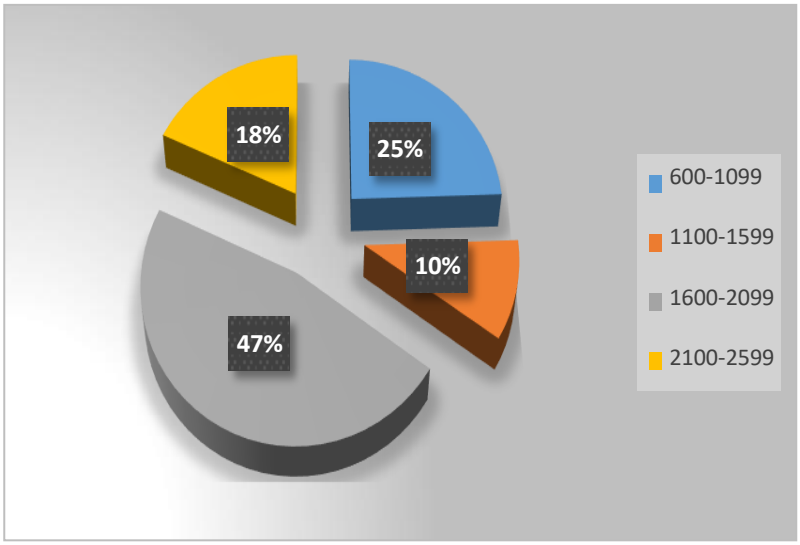
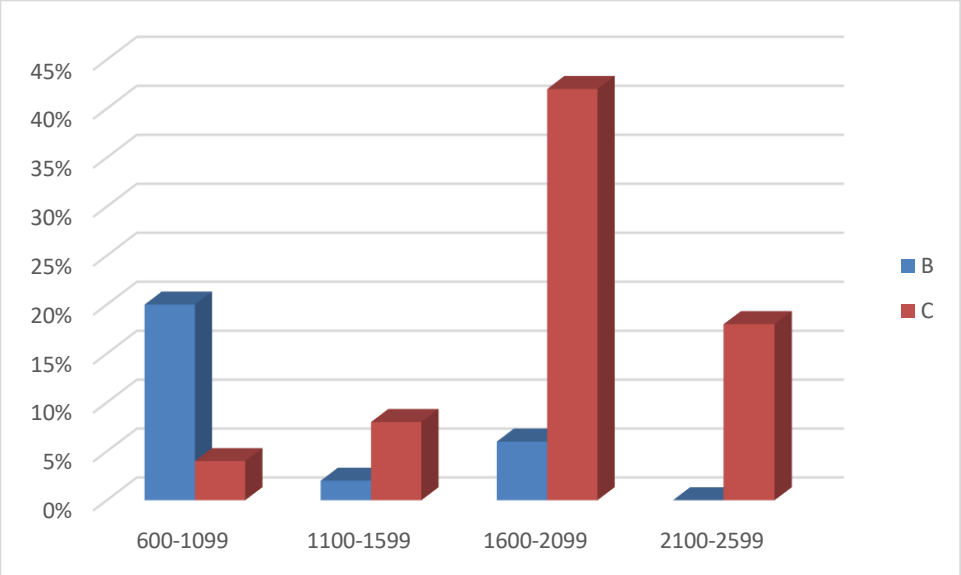


Figure6:-



VITAMIN B12 LEVELS ACCORDING TO CTP CLASS B & C

SumofB12	ColumnLabels				
RowLabels	**LOWER**	**LOWER MIDDLE**	**UPPER**	**UPPER MIDDLE**	**GrandTotal**
600-1099	3%	3%	3%	3%	13%
1100-1599	5%	3%	0%	0%	8%
1600-2099	25%	9%	14%	7%	55%
2100-2599	16%	8%	0%	0%	24%
GrandTotal	**50%**	**23%**	**17%**	**10%**	**100%**

VitaminB12 Levels According Their Socio-Economic Class.

Discussion:-

In this study we observed a male predominant population, vitamin b12 levels were found to be higher in the study group with mean vitamin B12 1639 ± 504 pg/ml when compared with controls (650 ± 300 pg/ml) which is highly significant (p value <0.05). Also it is observed that vitamin b12 levels are higher in decompensated chronic liver disease patients as 58% of the people have vitamin b12 levels >1600 when compared to compensated chronic liver disease. It is observed that patients with CTP class C had higher vitamin b12 levels when compared with CTP class A and B, Out of 50 people, 4 were died and their mean B12 was (2113 ± 112 pg/ml) which is highly significant. In the study vitamin b12 levels were found to be increased in the patients due to the fact that the storage functioning of the liver is disrupted in liver damage which causes leakage of vitamin b12 from the hepatic cells and causing increased vitamin b12 in the circulation. A limitation of our study is the small number of patients. Also studies should be conducted to establish correlation of vitamin B12 with acute liver failure, viral hepatitis and hepatocellular carcinoma.

A prospective observational study done by Muro N et al observed that cirrhotic patients presented plasma levels of vitamin B12 higher 1151 ± 568pg/ml in patients and 440 ±133pg/ml in controls (p <0.05)[6]. Kanazawa S et al observed that alcoholics had low levels of vitamin B12 in the liver and high in plasma. These findings suggest how retention of cobalamin occurs in peripheral tissues, followed by an accumulation of this vitamin in plasma[7]. Harsharan kaur et al also observed increased vitamin b12 levels in cirrhotic patients when compared to control group[8].

Conclusion:-

Even though cirrhosis is an immunocompromised state falsely elevated B12 levels are due to increased excretion of stored vitamin B12 in to serum from the damaged liver cells. These serum B12 levels correlates with the severity and

prognosis of the patient and also it helps in early intervention and treatment with which morbidity and mortality burden can be reduced.

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