ORIGINAL RESEARCH PAPER

Gastroenterology

BIOCHEMICAL AND CLINICAL PROFILE OF CIRRHOTIC PATIENTS BY- ULTRA SONOGRAPHICAL PARAMETERS,TYPE OF ANEMIA PICTURE AND SPLEEN DIAMETER RATIO

KEY WORDS:

Dr Ajay Kumar Nandmer Asst. Professor Medicine

Dr Vijay Kumar Nandmer* Professor Medicine *Corresponding Author

ABSTRACT

Cause of cirrhosis, the pathologic features consist of the development of fibrosis to the point that there is architectural distortion with the formation of regenerative nodules. This results in a decrease in hepatocellular mass, and thus function, and an alteration of blood flow. The induction of fibrosis occurs with activation of hepatic stellate cells, resulting in the formation of increased amounts of collagen and other components of the extracellular matrix.[1]

Portal hypertension is a significant complicating feature of decompensated cirrhosis and is responsible for the development of ascites and bleeding from esophagogastric varices, two complications that signify decompensated cirrhosis. Portal hypertension is defined as the elevation of the hepatic venous pressure gradient (HVPG) to >5 mmHg. Portal hypertension is caused by a combination of two simultaneously occurring hemodynamic processes: (1) increased intrahepatic resistance to the passage of blood flow through the liver due to cirrhosis and regenerative nodules, and (2) increased splanchnic blood flow secondary to vasodilatation within the splanchnic vascular bed. Portal hypertension is directly responsible for the two major complications of cirrhosis, variceal hemorrhage and ascites. Variceal hemorrhage is an immediate life-threatening problem with a 20–30% mortality associated with each episode of bleeding.[1]

Cirrhosis is the most common cause of portal hypertension and clinically significant portal hypertension is present in >60% of patients with cirrhosis. Approximately 5–15% of cirrhotic per year develop varices, and it is estimated that the majority of patients with cirrhosis will develop varices over their lifetime. In patients with cirrhosis who are being followed chronically, the development of portal hypertension is usually revealed by the presence of thrombocytopenia; the appearance of an enlarged spleen; or the development of ascites, encephalopathy and/or esophageal varices with or without bleeding.[1]

Congestive splenomegaly is common in patients with portal hypertension. Clinical features include the presence of an enlarged spleen on physical examination and the development of thrombocytopenia and leucopenia in patients who have cirrhosis. Some patients will have fairly significant left-sided and left upper quadrant abdominal pain related to an enlarged and engorged spleen. Splenomegaly itself usually requires no specific treatment, although splenectomy can be successfully performed under very special circumstances. Hypersplenism with the development of thrombocytopenia is a common feature of patients with cirrhosis and is usually the first indication of portal hypertension.[1]

In our study, we are analyzed the simple biochemical and ultrasonographical parameters which can predict the esophageal varices which may be cost effective. And we are used contrast CD echo to identify the intrapulmonary vascular dilation hence, making the diagnosis of hepatopulmonary syndrome.

AIM & OBJECTIVES

- To study the clinical, biochemical and ultra sonographical parameters which would non –invasively predict the presence of esophageal varices in patients with liver cirrhosis.
- To correlate the platelet count / spleen diameter ratio with grade of esophageal varices
- To study the various type of anemia picture in cirrhotic patients
- To compare the serum Testosterone level and testicular volume in Cirrhotic patient with the normal controls.
- Prevalence of hepatopulmonary syndrome-by evaluation through contrast echo cardiography.

MATERIALS AND METHODS

50 diagnosed case of cirrhotic (25 female, 25 male) patients, aged between 20yrs to 60 yrs, confirmed by Ultra sonography and other Biochemical parameters are selected from the Medical OPD and Medical ward in the period of July 2009 – December 2009 and they undergone the following investigations. The patients were selected according to inclusion and exclusion criteria.

Inclusion Criteria:

- Age more than 20 years and bellow 60 yrs.
- All patients with cirrhosis of the liver detected by USG.

Exclusion Criteria:

- Age bellow 20 years and above 60yrs
- Hepatocellular carcinoma detected by USG.
- Primary Hematological disorder.
- Active UGI bleed on admission.
- Taking B-Blocker for primary prophylaxis of esophageal varices.
- All diagnosed diabetes mellitus.
- Taking alcohol in the past 6 months.
- History of pyrexia in the past 4 weeks.

All patients were undergone the following investigations and the patients were classified according to CHILD-PUGH'S CLASSIFICATION.

- Peripheral smear picture for comment with platelet count.
- Liver profile (including liver enzymes, serum Bilirubin & Prothrombin time).
- Serum albumin.
- Ultra sonography for Liver architecture, spleen diameter, portal vein diameter and free fluid.
- Upper GI endoscopy.

CD Echo followed by contrast CD echo (agitated saline used as a contrast)

Echocardiogram was performed in conventional views as per recommendations of American society of echocardiography. 10ml of agitated normal saline was injected as a contrast through the antecubital vein in less than 2 sec and echocardiography was performed continuously for 2mts. Two separate echocardio graphers analyzed recordings independently. No untoward complications were seen during the procedure.

Out of 50 patients, 25 male patients were selected and 25 male healthy volunteers were selected from the medical OPD and consent was taken. All the male patients and controls were undergone the following investigations.

- Total Serum Testosterone level
- Testicular volume by ultra sonography gray scale.

The following parameters were defined

- **Cirrhosis:** Detected by USG (Altered Coarse Echo texture of

the liver parenchyma with surface micronodularity in the setting CLD).
- **Splenomegaly:** Spleen bipolar diameter more than 100 mm BY USG.
- **Normal platelet count:** 150-450×10^3/cu.mm .
- **Normal total serum testosterone level** 300-1000 ng/dL.

Size of Esophageal varices :
1. **Large:** Varices in the lower 3rd of the esophagus that occupied at least a third of the lumen or protrudes into the esophageal lumen and touch each other (presence of confluence) and did not flatten with air insufflations.
2. **Small:** Varices in the lower 3rd of the esophagus and occupied less than a third of the esophageal lumen or minimally protrude into the lumen but did not flatten with air insufflations.

- **CD Echocardiography** for RV function and LV function & pulmonary artery pressure.
- **Contrast CD Echo with agitated saline:** To measure the shunt fraction (intra-pulmonary shunt).Presence of air bubbles in the left Atrium within 8 seconds to be considered Positive.
- **Platelet count / spleen diameter ratio:** PLT.COUNT × 100^3/ spleen diameter in mm.

All the data were analyzed in the SPSS 14 version for windows and Mean, Standard deviation, pearsan's correlation efficient and independent T-test were used to identify the significance of study.

DISCUSSION AND SUMMARY

1.NON-INVASIVE PARAMETERS TO PREDICT THE ESOPHA GEAL VARICES

In our study, Out of 50 patients, 13 patients (26%) were in the class A, 23 patients (46%) were in the class B and 14 patients (28%) were in the class C.

On correlation of platelet count alone with esophageal varices, cirrhotic patients with no esophageal varices showed the mean platelet count of 153.64 with SD ± 28.02, patients with small esophageal varices showed the mean platelet count of 132.94 with SD ± 16.49 and patients with large esophageal varices showed the mean platelet count of 90.27 with SD ± 19.32. The correlation was significant with a Pearson correlation coefficient r= - 0.801 with a 2-tailed significance of sig. (2-tailed) of 0.000. (Correlation is significant at the 0.01 level (2-tailed)).

On correlation of portal vein diameter alone with esophageal varices, cirrhotic patients with no esophageal varices showed the mean portal vein diameter of 12.9 with SD ± 1.93, patients with small esophageal varices showed the mean portal vein diameter of 14.24 with SD ± 2.20 and patients with large esophageal varices showed the mean portal vein diameter of 15.80 with SD ± 2.05. The correlation was significant with a Pearson correlation coefficient r= - 0.570 with a 2-tailed significance of sig. (2-tailed) of 0.000. (Correlation is significant at the 0.01 level (2-tailed)).

On correlation of spleen diameter alone with esophageal varices, cirrhotic patients with no esophageal varices showed the mean spleen diameter of 141.82 with SD ± 19.52, patients with small esophageal varices showed the mean spleen diameter of 143.70 with SD ± 15.64 and patients with large esophageal varices showed the mean spleen diameter of 178.18 with SD ± 22.12. The correlation was significant with a Pearson correlation coefficient r= 0.679 with a 2-tailed significance of sig. (2-tailed) of .000. (Correlation is significant at the 0.01 level (2-tailed)).

On correlation of platelet count and spleen diameter ratio with esophageal varices, patients with no esophageal varices showed the mean platelet count /spleen diameter ratio of 1.09 with SD ± 0.20 patients with small esophageal varices showed the mean platelet count /spleen diameter ratio of 0.94 with SD ± 0.16 and patients with large esophageal varices showed the mean platelet count /spleen diameter ratio of 0.52 with SD ± 0.15. The correlation was significant with a Pearson correlation coefficient r= - 0.900 with a 2-tailed significance of sig. (2-tailed) of 0.000. (Correlation is significant at the 0.01 level (2-tailed)).

Platelet count alone with a mean value of 132.9 (×10^3/cu.mm) can predict the esophageal varices with a sensitivity of 74.36%, specificity of 72.73%, positive predictive value of 90.62% and negative predictive value of 44%.

Portal vein diameter alone with a mean of 14.23mm can predict the esophageal varices with a sensitivity of 69.23%, specificity of 81.8% and positive predictive value of 93.11% and negative predictive value of 42.8%.

Spleen diameter alone with a mean of 143.7 mm can predict the esophageal varices with a sensitivity of 74.35%, specificity of 63.63%, positive predictive value of 87.87%, and negative predictive value of 41.17%.

Platelet count and spleen diameter ratio with a mean value of 0.93 (×10^3) can predict the esophageal varices with a sensitivity of 79.5%, specificity of 72.73%, positive predictive value of 91.18% and negative predictive value of 50%.

These findings are comparable with the other studies like given bellow.

Edoardo G Giannini et.al [11] showed in their study the prevalence of EV was 54.1%. The platelet count/spleen diameter ratio had 86.0% (95% CI, 80.7–90.4%) diagnostic accuracy for EV, which was significantly greater as compared with either accuracy of platelet count alone (83.6%, 95% CI 78 0–88.3%, P = 0.038) or spleen diameter alone (80.2%, 95% CI 74.3–85.3%, P = 0.018). The 909 cutoff had 91.5% sensitivity (95% CI 85.0– 95.9%), 67.0% specificity (95% CI 56.9–76.1%), 76.6% positive predictive value, 87.0% negative predictive value, 2.77 positive likelihood ratio, and 0.13 negative likelihood ratio for the diagnosis of EV.

Schwarzenberge et.al[21]analysed over 137 patients with 87 (63.5%) men and a mean age of 56 years. Seventy-six (55%) patients had esophageal varices. The mean age, sex, and etiology of cirrhosis were similar between those with and without varices. Using a platelet count/spleen diameter ratio with a cut-off value of 909, yielded a negative predictive value of only 73% and a positive predictive value of 74%.and he concluded the platelet count/spleen diameter ratio with a cut-off value of 909 may not be sufficiently accurate in predicting the presence of esophageal varices. Upper endoscopy remains the method of choice to screen for the presence of varices.

2. CORERELATION OF SERUM TESTOSTERONE AND TESTICULAR VOLUME IN CIRRHOSIS.

In age matched groups, in the age group 20-30yrs, the mean testosterone level were 237.73ng/dl in cases and 604.64ng/dl in controls. In the age group of 31-40yrs, the mean testosterone levels were 179.5ng/dl in cases and 609.5ng/dl in controls. In the age group of 41-50yrs, the mean testosterone levels were 168.68ng/dl in cases and 524.67ng/dl in controls. In the age group of 51-60yrs, the mean testosterone levels were 170.69ng/dl in cases and 372.52ng/dl in controls.

The mean testosterone level was 183.78ng/dl with SD ± 99.73 in cases and 522.46ng/dl with SD ± 120.90. The difference was statistically significant in independent T-test with a Sig. (2-tailed) 0.000.

In age matched groups, in the age group 20-30yrs, the mean testicular volume was 8.52ml in cases and 19.07ml in controls. In the age group of 31-40yrs, the mean testicular volume was 7.86ml in cases and 18.42ml in controls. In the age group of 41-50yrs, the mean testicular volume was 8.44ml in cases and 17.74ml in controls. In the age group of 51-60yrs, the mean testicular volume was 6.8ml in cases and 14.59ml in controls.

The mean testicular volume was 7.80 with SD ± 2.73 in cases and

17.43 with SD ± 2.32. The difference was statistically significant in independent T-test with a Sig. (2-tailed) 0.000.

And the serum testosterone level and testicular volume were not correlated with Child-Pugh's classification.

3. HEPATOPULMONARY SYNDROME-EVALUATION BY CONTRAST ECHOCARDIOGRAPHY

Out of 50 patients, 14(28%) showed intra pulmonary vascular dilatation as evidenced by the appearance of contrast in the left atrium within 8 sec (positive contrast echo). Remaining 36(72%) patients did not show any positive result.

The etiological factors in the positive cases were 5 cases of HBV related cirrhosis (36%), 5 cases of Alcoholic cirrhosis (36%), 1case of HCV related cirrhosis (7%) and 3 cases of Unidentified etiology (21%).

There was no significant correlation between the HPS and the CHILD-PUGH'S classification as shown above 7 cases were in class B (50%),and 7 cases were in class C (50%)).

CONCLUSION

NONINVASIVE PARAMETERS FOR PREDICTION OF ESOPHA GEAL VARICES

Even though noninvasive parameters can predict the presence of Esophageal varices, the negative predict value of all parameters are very low. The cut off value of all the noninvasive parameters can't rule out the esophageal varices. So the noninvasive parameters can not be an alternative of upper GI endoscopy.

The platelet count / spleen diameter mean value of 0.52 can predict the large esophageal varices with 100 % specificity with a positive predict value of 100%.

SERUM TESTOSTERONE LEVEL AND TESTICULAR VOLUME

In cirrhotic patients, the serum testosterone level was significantly lower side compared to the controls and the testicular volume also was in the lower side. This can explain the pathophysiology of feminization in male cirrhotics. Some of these patients had the significant testicular atrophy.

And the testosterone level and testicular volume were not correlated with the severity of the disease as defined by child-Pugh's classification.

HEPATOPULMONARY SYNDROME

Our study prevalence rate of HPS is 28% as evidenced by presence of contrast in the left atrium in contrast echocardiography.

HPS is a dreaded complication of cirrhosis with mean survival of 11 months. Screening with contrast echo can identify patients having intra pulmonary shunt. This could be an alternative to pulmonary angiography and other invasive tests prior to consideration for Liver Transplantation.

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