PLATELET COUNT- A NON INVASIVE PREDICTOR OF PORTAL HYPERTENSION IN PATIENTS WITH ASCITES

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ABSTRACT

BACKGROUND

Ascites is the accumulation of fluid in the peritoneal cavity and the most common cause of ascites is portal hypertension. The main causes of portal hypertension are cirrhosis (75%), malignancies (10%), cardiac failure (5%) and infections (10%). So, the evaluation of cause of ascites is needed for treatment. It will be more economical to screen the patients who are at high risk of having varices and also lower the burden on endoscopic units.[5] Identification of noninvasive predictors of OV and PHG will allow upper gastrointestinal tract (GIT) endoscopy to be carried out only in selected group of patients thus avoid unnecessary intervention and at the same time not to miss patients at risk of bleeding.[6] Majority of the studies show thrombocytopenia as the most useful predictor for cirrhosis in the background of viral aetiology. Hypersplenism and decreased thrombopoietin are the reasons for thrombocytopenia in cirrhosis.

MATERIALS AND METHODS

Study was conducted in the inpatients who were admitted to the Department of General Medicine, R.L. Jalappa Hospital attached to Sri Devaraj Urs Medical College, Kolar In total, 50 patients with liver cirrhosis were selected. Patients were recruited based on history such as exposure to alcohol and chronic hepatitis B and C infections), past medical records, previous admissions due to ascites, hepatic encephalopathy, biochemical abnormalities in the presence of ultrasonography findings, or liver biopsy where available.

RESULTS

Platelet count was lower in patients with haematemesis and oesophageal varices which was statistically significant ($P<0.05$). Hence platelet count can be one of the non-invasive investigations for the prediction of portal hypertension with ascites.

CONCLUSION

Platelet count was significantly low in the patients with signs of portal hypertension and oesophageal varices. Hence Platelet count can be used at bedside to choose the best therapeutic options and avoid useless expensive procedures in patients with an expected poor survival outcome.

KEYWORDS

Platelet Count, Oesophageal Varices, Portal Hypertension, Ascites.

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BACKGROUND

Ascites is the accumulation of fluid in the peritoneal cavity and most common cause of ascites is portal hypertension. The main causes of Portal Hypertension are cirrhosis (75%) and other causes like malignancies (10%), cardiac failure (5%) and infections (10%). So, the evaluation of cause of ascites is needed for treatment.[1] Portal hypertension is directly responsible for the two major complication of chronic liver disease such as variceal bleed and ascites.[2] Variceal haemorrhage is an immediate life-threatening problem in patients with portal hypertension with 20-30% mortality rate associated with each bleeding. Early detection of portal hypertension before development of its dreadful complication such as oesophageal varices can reduce morbidity and mortality.[3] Current guidelines recommend screening for oesophageal varices with upper GI endoscopy in all patients with cirrhosis and starting prophylactic treatment in those with medium to large varices, and in patients without varices upper GI endoscopy is repeated in 2-3 years whereas in patients with small oesophageal varices endoscopy is repeated at 1-2 years.[4] It will be more economical to screen the patients who are at high risk of having varices and also lower the burden on endoscopic units.[5] Identification of minimally/non-invasive methods to detect oesophageal varices and portal hypertension will make us to perform upper GI endoscopy in a very selected group of patients who are most suspicious of having the

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varices and also not to miss the patient who are at the most risk of bleeding.[6] Early detection of the portal hypertension by non- invasive methods such as platelet count will allow us to detect the patient with portal hypertension and those who really need upper GI endoscopy to prevent dreadful complication of portal hypertension such as the oesophageal varices bleed and also by selecting the patients who really need upper GI endoscopy, we can also reduce the health care burden and cost.[7] Cirrhosis is usually diagnosed in patients who are having a massive ascites, variceal bleeding, hepatic encephalopathy, splenomegaly. But new diagnosis of cirrhosis in patients with abnormal liver enzymes and previously unsuspected cirrhosis is challenging. There won't be any clinical manifestation in patients with early cirrhosis. Liver biopsy is the gold standard for the diagnosis, but it is a invasive procedure and associated with the most serious complications such as the bleeding. Ultrasonography have variable sensitivity and specificity in identifying the cirrhosis and is not available in every scenario such as the rural setting where the ultrasound is very rarely available. In various studies low platelet count was identified as the single most useful predictor for cirrhosis with viral aetiology.[8] Impaired thrombopoiesis due to reduced thrombopoietin from the hepatic cells and destruction of platelets due to hypersplenism secondary to the portal hypertension are the causes of thrombocytopenia in patients with cirrhosis. But in patients with cirrhosis in whom alcohol is the etiological factor the role of platelet count to differentiate between cirrhotic and non-cirrhotic liver disease is unclear because alcohol itself causes thrombocytopenia by bone marrow depression and direct toxicity to the platelets.[9,10] Isolated thrombocytopenia occur if alcohol is administered regularly for 3-5 weeks.[10] And this effects lasts for 5-6 days after abstinence from alcohol and platelet count reach normal after that.[10]

There is dearth of data on the role of Platelet Count in predicting portal hypertension with ascites in this part of the world and hence this study was planned to establish a relationship between platelet count and portal hypertension with ascites.

Objectives

To predict the presence of portal hypertension in patients with ascites by measuring platelet count.

MATERIALS AND METHODS

This analytical cross-sectional study was conducted in the Inpatients who were admitted to the Department of General Medicine, R.L. Jalappa Hospital attached to Sri Devaraj Urs Medical College, Kolar from June 2018 to September 2018.

A total sample size of 48 was calculated prior to data collection by using 98% power to detect a change in sensitivity from 0.5 to 0.1 using a two-sided binomial test and 94% power to detect a change in specificity from 0.5 to 0.878 using a two-sided binomial test. The target significance level is 0.01. The actual significance level achieved by the sensitivity test is 0.1250 and achieved by the specificity test is 0.0066. The prevalence of the disease is 0.1.

In total, 50 patients with liver cirrhosis were selected. patients were recruited based on history like such as exposure to alcohol and chronic hepatitis B and C infections), past medical records, previous admissions due to ascites, hepatic encephalopathy, biochemical abnormalities in the presence of ultrasonography findings, or liver biopsy where available.

Inclusion Criteria

All stable patients with liver cirrhosis irrespective of the aetiology.

Exclusion Criteria

1. History of recent bleeding
2. History of haematological diseases
3. DIC
4. Infections
5. Patients on drugs causing thrombocytopenia

Patients attending R. L. Jalappa hospital who fulfil the inclusion criteria were enrolled in to study after obtaining a written informed consent from inpatients. And relevant information such as the demographic data clinical profile and laboratory values are entered in to the proforma. And a clinical history will be elicited from the participants especially regarding the jaundice, drug abuse, alcohol history, previous blood transfusions, and high-risk behaviour. And a detailed general physical examination and relevant systemic examination is done to look for the presence of ascites, splenomegaly and other signs of liver cell failure such as jaundice, pallor, parotid enlargement, palmar erythema, Dupuytren contracture, loss of axillary hair, gynecomastia, spider nave, testicular atrophy etc,

Under aseptic condition 10 ml of blood was drawn from the brachial vein and subjected to the investigations like CBC, RFT, LFT and serum electrolytes. Patients underwent ultrasound abdomen to confirm the ascites and to look for other signs of portal hypertension such as the splenomegaly, portal vein diameter. For platelet count, 2 mL blood was drawn, collected in ethylene- diamine-tetra-acetic acid (EDTA)-containing tubes, and analysed using an automated haematology analyser. And are subjected for upper GI endoscopy to look for oesophageal varices.

Statistical Analyses

Data was entered in EpiData version 3.1 (The EpiData Association, Odense, Denmark) and analysis was done using SPSS version 22. Mean, standard deviation (SD), and ranges were used to scrutinise the quantitative data.

Ethical Considerations

Prior to the onset of the study, ethical approval was obtained from Institutional Ethics Committee (IEC), Kolar. A written informed consent was obtained from all the study participants. All the collected information was kept confidential, and it is being used for research purpose only.

RESULTS

The Present study included 50 patients who presented to us with clinical features of Portal Hypertension with Ascites. 48 (96%) were males, 14 had presented with Hematemesis and 15 presented with Hepatic Encephalopathy. 33 had grade II ascites, 16 had grade III ascites and only 1 had grade I ascites. 7 had Hepatitis B and 3 were positive for Hepatitis C. 43 out 50 people had history of alcohol consumption. Oesophageal Varices which is an important complication of Portal Hypertension was seen in 38(76%) in Endoscopy. (Table 1)

Variable			Total
Gender	Male	48	50
	Female	2	
Hematemesis	Present	14	50
	Absent	36	
Hepatic Encephalopathy	Present	15	50
	Absent	35	
Ascites	Grade I	1	50
	Grade II	33	
	Grade III	16	
HBsAg	Positive	7	50
	Negative	43	
HCV	Positive	3	50
	Negative	47	
Cause	Alcoholic	40	50
	Alcoholic + HBsAg	3	
	HBsAg	4	
	HCV	3	
Oesophageal Varices	Absent	12	50
	Grade I	9	
	Grade II	14	
	Grade III	15	

Table 1. Distribution of Various Disease Specific Variables among Study Population

	Mean ± Std. Deviation	Minimum	Maximum
Age	50.26 ± 14.41	27	80
Platelet	144260.0 ± 69482.580	15000	376000
Serum Albumin	2.198 ± 0.423	1.40	3.80
AST	142.66 ± 156.994	18	1090
ALT	91.78 ± 159.571	7	1100
INR	1.630 ± 0.9307	0.9000	5.6000
Ascitic Albumin	0.340 ± 0.2499	0.1	1.0
SAAG	1.868 ± 0.5211	1.1000	3.7000

Table 2. Descriptive Statistics of the Various Investigations done among Study Population

The mean age of the patients was 50.26 ± 14.41. Table II shows the Mean ± SD, Minimum and Maximum for all the Investigations which were performed which included Platelet Count, Serum Albumin, AST, ALT, INR, Ascitic Albumin and SAAG.

		Mean ± Standard Deviation	Minimum	Maximum	P value
Hematemesis	Absent	152194 ± 74579	39000	376000	<0.05*
	Present	123857 ± 50990	15000	198000	
Hepatic Encephalopathy	Absent	141514 ± 72016	39000	376000	0.69
	Present	150667 ± 65108	15000	272000	
Oesophageal Varices	Absent	179250 ± 64350	39000	272000	<0.05*
	Present	133211 ± 68118	15000	376000	

Table 3. Comparison of Platelet Count with Portal Hypertension Signs

*Chi-square test was used.

Table 3 shows the Mean and Standard deviation of the platelet count in the patients with the presence and absence of Portal Hypertension signs. The platelet count was lower in patients with Hematemesis and Oesophageal Varices which was Statistically Significant (P<0.05). Hence platelet count can be one of the non-invasive investigation for the prediction of portal hypertension with ascites.

DISCUSSION

Liver Cirrhosis is a result of advanced liver disease, in which normal liver tissue is replaced by fibrotic tissue. These changes lead to loss of liver function which will manifest as Portal Hypertension Signs which includes Ascites. The most common causes for Chronic Liver disease are alcoholism, infection with hepatitis B and hepatitis C viruses, and fatty liver.

Severe upper gastrointestinal (UGI) bleeding as a complication of portal hypertension develops in about 30%-40% of cirrhotics. Despite significant improvements in the early diagnosis and treatment of esophago-gastric variceal haemorrhage, the mortality rate of first variceal haemorrhage remains high (20%-35%). Numerous non-invasive serologic markers have been proposed for diagnosing alcoholic cirrhosis. The AST platelet count index (APRI index) that was developed was shown to have good sensitivity and specificity for predicting cirrhosis in patients with hepatitis C, but in patients with alcoholic cirrhosis it was found to have low sensitivity and specificity.[11] The FibroIndex uses the platelet count, AST level, and gamma globulin level to detect significant fibrosis in chronic hepatitis C, but its accuracy has yet to be validated.[12] The major problem with these models is that the components of the tests are not readily available in most clinical laboratories; some of the tests are expensive, and others are too cumbersome to be of use to the physician in a clinical setting. Thus there is a need to develop a simple, objective model to help identify cirrhosis in alcoholics. Many studies have shown that a positive relationship of thrombocytopenia with presence as well as grades of oesophageal varices.[13,14] In patients with cirrhosis, low platelet count is usually considered a surrogate marker of portal hypertension (PHT), though patients with documented PHT may have a normal platelet count.[15] Actually, 40% of our patients had a normal platelet count, in spite of overtly decompensated PHT. It is difficult to know the prevalence of thrombocytopenia in this group of patients. Platelet count showed a highly significant statistical inverse correlation with oesophageal varices and Hematemesis which is in agreement with Thomopulos et al., who reported that platelet count was the only common factor found to be significant predictor of both small and large varices.[16]

CONCLUSION

Considering the disease burden and economic cost of end stage liver disease diagnosis which will in turn aid in its management, it is essential to screen patients with non-invasive techniques over conventional endoscopy.

These non-invasive variables can be reliable predictors of oesophageal varices and help us to screen the cirrhotic patients who are at increased risk for oesophageal varices and who will benefit by undergoing the endoscopic examination. Platelet count was significantly low in the patients with signs of portal hypertension and oesophageal varices. Hence platelet count can be used as a bedside investigation to choose the best therapeutic options and avoid useless expensive procedures in patients with an expected poor survival outcome. There is no universally accepted platelet function assay in cirrhosis and hence there is a need for one in order to establish evidence based clinical guidelines. However large multicentric studies with larger sample are needed to confirm these findings.

Limitations

We have used imaging modality to make diagnosis of cirrhosis rather than the biopsy studies which is the gold standard investigative modality for cirrhosis. But in current era it is very rarely used as it is an invasive modality and it is associated with lot of serious complications such as bleeding.

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