RELATION BETWEEN PLATELET COUNT, OESOPHAGEAL VARICES AND HEMATEMESIS /MELENA SYMPTOMS IN CIRRHOTIC PATIENTS- A COMPARATIVE STUDY

Deep Mehta[1], Santosh Kumar[2], Ruchit Patel[3], Jitendra D. Lakhani[4]

[1]Resident, Department of General Medicine, SBKS MI & RC, Waghodia, Vadodara, Gujrat.
[2]Associate Professor, Department of General Medicine, SBKS MI & RC, Waghodia, Vadodara, Gujrat.
[3]Resident, Department of General Medicine, SBKS MI & RC, Waghodia, Vadodara, Gujrat.
[4]Professor, Department of General Medicine, SBKS MI & RC, Waghodia, Vadodara, Gujrat.

ABSTRACT

BACKGROUND

Cirrhosis of liver is an end stage of chronic liver disease. This is emerging as an important cause of mortality and morbidity worldwide. Different causes of cirrhosis present with similar clinicopathological features, but their clinical course may be different. Alcohol is a leading cause of cirrhosis followed by viral hepatitis, diabetes and other causes. Complication of cirrhosis occurs either due to development of portal hypertension or impaired hepatic synthetic function or both. Complications include gastro-oesophageal varices, ascites, hepatic encephalopathy (HE), hepato-pulmonary hypertension, hepatocellular carcinoma, hepatorenal syndrome, spontaneous bacterial peritonitis, and coagulation disorders. This study was undertaken to determine the prevalence of thrombocytopenia and oesophageal varices among alcoholic liver cirrhosis patients having hematemesis/melena, and to compare it with non-alcoholic cirrhotic patients.

METHODS

Study was done in the Department of General Medicine, Dhiraj Hospital, Piparia, Vadodara. 90 patients detected with cirrhosis of liver were enrolled in this study. A detailed history, physical examination and necessary investigations were done.

RESULTS

35 out of 60 (58.33%) alcoholic patients and 6 out of 30 (20%) non-alcoholic patients had thrombocytopenia. Out of 90 selected patients of cirrhosis of liver, 32 (35.55%) had small while 58 (64.45%) had large oesophageal varices. 40% of those presented with small oesophageal varices had alcoholic liver cirrhosis as underlying cause while 26.67% had non-alcoholic cirrhosis, the difference being statistically significant.

CONCLUSION

Prevalence of thrombocytopenia in cirrhosis of liver is very common. Significantly more severe thrombocytopenia is found in alcoholic liver cirrhosis patients. Most of the alcoholic patients developed small varices when compared with non-alcoholic patients. Haemorrhagic episodes were less in alcoholic patients.

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BACKGROUND

Cirrhosis of liver is an end stage of chronic liver disease. This is emerging as an important cause of mortality and morbidity worldwide. Different causes of cirrhosis present with similar clinic-pathological features, but their clinical course may be different.[1,2] Alcohol is a leading cause of cirrhosis followed by viral hepatitis, diabetes and other causes.[3] Complication of cirrhosis occurs either due to development of portal hypertension or impaired hepatic synthetic function or both. Complications include gastro-oesophageal varices, ascites, hepatic encephalopathy (HE), hepato-pulmonary hypertension, hepatocellular carcinoma, hepatorenal syndrome, spontaneous bacterial peritonitis, and coagulation disorders.

Blood clotting mechanism in human body is maintained due to integrity of the vascular system, platelets, as well as several proteins present in plasma. In chronic liver disease, thrombocytopenia is the most common haematological abnormality,[4] with prevalence of 64% to 84% in cirrhotic patients.[5] In cirrhosis, factors contributing to thrombocytopenia include sequestration of platelets in spleen secondary to portal hypertension, impaired thrombopoiesis due to decrease production of hepatic thrombopoietin[6,7] and others. Alcohol leads to ineffective thrombopoiesis and decreased life span of platlets[8] by its effect on bone marrow. Thrombocytopenia is an indicator of advance liver disease and is associated with poor prognosis, it may be difficult for clinician to prescribe some medications as well as carry out invasive diagnostic and or therapeutic procedures in such type of patients.[9,10] Other Gastrointestinal manifestations in patients of cirrhosis includes the development of esophageal varices, gastric varices, and intestinal vasculopathy. Upper GI endoscopy

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Corresponding Author:
Dr. Santosh Kumar,
Staff Qr – E3, Dhiraj Hospital,
SVU, Waghodiya, Vadodara- 391760, Gujrat.
E-mail: santimd52@gmail.com
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remains the gold standard method for screening of gastroesophageal varices. In cirrhotic patients with previously having no varices, 5-15% develops esophageal varices annually and overall incidence of varices in cirrhotic patients is 50-60%.[11] The one-year rate of first variceal hemorrhage is 5% for small varices and15% for large varices while life threatening variceal bleeding can occurs in 30-40% of patients with varices.[12] Progression of small varices to large varices is around 5-10% per year.[13]

This study was carried out to know the relation between platelets count, grade of esophageal varices and presenting symptoms in alcoholic and non-alcoholic cirrhotic patients.

METHODS

Present study was undertaken to study the prevalence of thrombocytopenia and oesophageal varices in alcoholic liver cirrhosis patients. This was an observational pilot study. It was conducted from July 2018 to December 2018 in the Department of Medicine of SBKS MI & RC and Dhiraj hospital, Sumandeep Vidyapeeth, Piparia. All patients admitted with liver cirrhosis who presented with hematemesis or melena or bleeding diathesis, were included in the study. All included patients were evaluated for risk factors. Data was collected using a pretested proforma, meeting the objectives of the study. Detailed history was taken regarding duration of illness, symptoms, comorbid conditions. Patients were asked about melena, hematemesis or both and episode of such attacks in last 6 months. CBC, renal function test, urine routine microscopy, ultrasonography of abdomen and pelvis, liver function test, serum electrolytes, stool for occult blood was done in all patients. An Upper gastro intestinal endoscopy was performed on all patients. The data so collected was then analysed.

Statistical Analysis

Mean and standard deviation are reported as relevant. Significant differences between groups were evaluated using t-test and chi-square test method wherever appropriate. P value of less than 0.05 was considered significant.

RESULTS

Total 90 patients of cirrhosis of liver were included in this study. 60 patients had alcoholic cirrhosis while 30 had non-alcoholic cirrhosis. Alcoholic group patients were younger and had male predominance, Male to female ratio was 7.57:1. Non-alcoholic group patients were older age group with male to female ratio was 2.75:1. Maximum alcoholic liver cirrhosis patients were found in age group of 41-50 years. (Table-1)

	Alcoholic				Non Alcoholic				Total
	Male	%	Female	%	Male	%	Female	%	
< 30 Years	3	2.50%	0	0.00%	0	0.00%	1	3.33%	4.00
31 to 40 Yrs.	9	7.50%	1	0.83%	3	10.00%	2	6.67%	15
41 to 50 Yrs.	31	25.83%	4	3.33%	2	6.67%	1	3.33%	38
51 to 60 Yrs.	2	1.67%	2	1.67%	12	40.00%	3	10.00%	19
61 to 70 Yrs.	7	5.83%	0	0.00%	5	16.67%	1	3.33%	13
> 70 Yrs.	1	0.83%	0	0.00%	0	0.00%	0	0.00%	1
Total	53	44.17%	7	5.83%	22	73.33%	8	26.67%	90

Table 1. Age-Wise Distribution

35 out of 60 (58.33%) alcoholic patients had thrombocytopenia, whereas it was 20% (6 out of 30) in non alcoholic group. (Table-2)

Platelets	Non Alcoholic		Alcoholic		Total	Chi Square	p value
	N	%	N	%			
< 0.50 (Severe)	1	33.33%	2	66.67%	3	0.33	0.563
0.50 to 0.750 (Moderate)	1	10.00%	9	90.00%	10	6.4	**0.011**
0.751 to 1.50 (Mild)	4	14.29%	24	85.71%	28	14.286	**0.001**
1.51 to 2.00	8	30.77%	18	69.23%	26	3.846	**0.049**
2.01 to 2.50	15	71.43%	6	28.57%	21	3.875	0.05
> 2.50	1	50.00%	1	50.00%	2	NA	NA
Total	30	33.33%	60	66.67%	90	NA	NA

Table 2. Prevalence of Thrombocytopenia

In analysis of symptoms like melena and hematemesis, it is found that these symptoms occurred in 76.66% (23 out of 30) of patients in non-alcoholic group, and only in 80% (48out of 60) of patients in alcoholic group. (Table 3A)

Symptoms	Non Alcoholic		Alcoholic		Total
	N	%	N	%	
Melena Alone	5	35.71%	9	64.26%	14
Hematemesis Alone	18	31.57%	39	68.42%	57
Both Melena & Hematemesis	7	36.84%	12	63.15%	19
Total	**30**	**33.33%**	**60**	**66.67%**	**90**

Table 3A. Presentation of Patients

The frequency of haemorrhagic episode in last 6 months in non-alcoholic group (n=30) was 5.2 and in the alcoholic group (n=60) was 3.3. Overall frequency of haemorrhagic episode in studied patients (n=90) was 3.93. (Table 3B(1))

Variables	Frequency
Non-Alcoholic Group (n=30)	5.2
Alcoholic Group (n=60)	3.3
Overall (n=90)	3.9

Table 3b (1). Frequency of Haemorrhagic Episodes in Last 6 Months in Non-Alcoholic and Alcoholic Group

First attack of life-threatening variceal bleed in non-alcoholic group was seen in 4 (13.33%) patients and in alcoholic group was seen in 2 patients (3.33%). (Table-3B(2))

Variable	Non Alcoholic		Alcoholic	
	N	%	N	%
First Attack of Life-Threatening Variceal Bleed	4	13.33%	2	3.33%

Table 3b (2). First Attack of Life Threatening Variceal Bleed in Non-Alcoholic and Alcoholic Group Patients

In analysis of oesophageal varices, 32 of 90 patients (35.55%) had small oesophageal varices and 58 patients (64.45%) had large oesophageal varices. 40% of those presented with small oesophageal varices had alcoholic liver cirrhosis as underlying cause, with statistically significant difference (p value <0.05). Grading of varices was done according to criteria given by north Italian endoscopic club for study and treatment of oesophageal varices.[14] (Table-4)

Esophageal Varices (Grade)	Non Alcoholic		Alcoholic		Total	p Value
	N	%	N	%		
Small	8	26.67%	24	40.00%	32	**0.001**
Large	22	73.33%	36	60.00%	58	0.066
Total	**30**	**100.00%**	**60**	**100.00%**	**90**	

Table 4. Prevalence of Oesophageal Varices

DISCUSSION

Cirrhosis of liver patient can have thrombocytopenia because of various reasons. It may be because of splenic sequestration, reduced activity of thrombopoietin, bone marrow suppression, chronic hepatitis C virus infection, and may be effect of alcohol consumption.

In our study prevalence of thrombocytopenia was 45.55%, which is reported in literature in as many as 76% of cirrhotic patients.[15] Moderate thrombocytopenia (which is defined as platelet count if 50000-75000 per µL) is reported in 11.1% of our patients (10 out of 90 patients). In this study we wanted to find out whether magnitude of thrombocytopenia is different among alcoholic and non-alcoholic cirrhosis patients or not. 20% of non-alcoholic patients had thrombocytopenia, while it was 58.33% in alcoholic patients.

In the present study, we observed that history of chronic alcoholism has a significant effect on platelet count. Platelet counts in alcoholic liver cirrhosis patients were significantly lower than those in non-alcoholics. Alcohol consumption causes hypocellularity leading to pancytopenia. Chronic alcoholism has also been linked to insufficient availability of iron and other micronutrients such as vitamin B12 and folate for erythropoiesis. This is probably due to ethanol related mal-absorption, which leads to the impaired haematopoiesis. Decrease in number of platelets and abnormal platelet function is related to the chronic alcoholism. Moreover, alcohol-related thrombocytopenia may be present as an acute alcohol effect which returns to normal within one week of abstinence. Alcohol affects not only platelet production but also cause platelet dysfunction. Patients who consume excessive amounts of alcohol can exhibit a wide spectrum of platelet abnormalities. These abnormalities include impaired platelet aggregation, decreased secretion or activity of platelet-derived proteins involved in blood clotting. Prolongation of bleeding in the absence of thrombocytopenia[11] may be result of above mentioned factors.

Alcohol consumption predisposes to cerebral haemorrhage, this effect of alcohol is considered similar to that of aspirin. The platelet rebound effect of alcohol drinking as described in various researches, may lead to more haemorrhagic episodes. To find out whether alcoholic liver cirrhosis patients had more melena or / and hematemesis, we compared these haemorrhagic symptoms in alcoholic and non-alcoholic patient. Though we found

more severe thrombocytopenia in alcoholic group, the haemorrhagic episodes were less in them, may be because that bleeding episodes were more related to platelet dysfunction than platelet number.[16]

Acute transient platelet rebound effect is maintained in patients taking alcohol. Our patients were having chronic alcohol liver disease and we presume that they might not be consuming alcohol anymore and the occurrence of haemorrhagic episodes may be less. Small oesophageal varices were noted significantly higher in alcoholic patients, whereas large oesophageal varices were more common in non-alcoholics. This may also be the reason why in our study alcoholic liver cirrhosis patients had less severe haemorrhagic episodes in comparison with non-alcoholic patients. It is an interesting area of research whether alcoholic liver cirrhosis patients were different from non-alcoholic patients. In the present study we tried to differentiate some of the aspects like platelet counts, haemorrhagic symptoms and type of oesophageal varices because both the groups were different. Our data may have limitations, but our study showed that the portal hypertension developed in alcoholic liver cirrhosis may be different from non-alcoholic cirrhosis. This is a pilot work and further research as well as cohort studies having similar number, duration and age, sex groups will find out these differences which may give further insight in genesis of portal hypertension in alcoholic and non-alcoholic liver cirrhosis patients. Alcohol- related cirrhosis is characterised by some peculiar features of portal- hepatic haemodynamics, compared to cirrhosis of other aetiologies.

CONCLUSION

Prevalence of thrombocytopenia in cirrhosis of liver is very common and found in 45.55% of patients. Significantly, more severe thrombocytopenia was found in alcoholic liver cirrhosis patients. Alcoholic patients developed small varices when compared with non-alcoholic patients. Haemorrhagic episodes were less in alcoholic patients.

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