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Hypersplenism in patients with liver cirrhosis and portal hypertension: Predictors, and correlations

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Abstract

Hypersplenism is a common disorder in the setting of liver cirrhosis and portal hypertension (PHT). The presence of hypersplenism suggests more advanced liver disease and an increased risk of complications. This work tried to assess frequency of hypersplenism, correlations, and its predictors in patients with liver cirrhosis and PHT. Our study included 303 patients with liver cirrhosis and PHT, and 7 patients were excluded later. The study was carried out at AlRajhi Liver hospital, Assiut University, Egypt, from February 2018 to December 2021. All patients were subjected to full clinical evaluation, laboratory investigations, abdominal Ultrasound, and upper endoscopy. Portal hemodynamics were assessed in 100 patients using doppler ultrasound. A total of 182 patients (61.5%) were found to have hypersplenism. Chronic HCV infection was the causative agent of cirrhosis in the majority of patients (70.9%), with no significant difference between both groups. Chronic co-morbid diseases were not found to affect the development of hypersplenism. We have found significant differences between the hypersplenism and non-hypersplenism group regarding all clinical presentation data. As regards to sonographic findings, patients with hypersplenism had significantly higher splenic diameter ($p< 0.001$), portal vein diameter, more frequent portosystemic collaterals, portal vein thrombosis and HCC. Also, frequency of ascites, especially marked ascites, was significantly higher ($p< 0.001$), Regarding portal hemodynamics parameters, portal vein velocity (PVV) and time averaged mean velocity (TAMV), were the doppler parameters which showed significant differences between both groups ($p=0.026$ & 0.033). Predictors of hypersplenism, were in descending order; ascites, haematemesis and or melena, PV diameter, splenic diameter, PVV, and the presence of portosystemic collaterals. Patients with hypersplenism were categorized according to severity using a scoring index, into mild and moderate/severe, but no significant difference was found between both groups, apart from significant high frequency of varices. Hypersplenism is a common disorder in the setting of liver cirrhosis and PHT. The development of hypersplenism is associated with advanced liver disease, and increased risk of disease related complications. Ascites, haematemesis and or melena, PV diameter, splenic diameter, PVV, and portosystemic collateral may predict the development of hypersplenism. Doppler US may be used as a non-invasive marker for PHT and hypersplenism.

Keywords: Hypersplenism, liver cirrhosis, portal hypertension, thrombosis, haematemesis

Full length article *Corresponding Author, e-mail: ramybarody@yahoo.com

1. Introduction

The criteria of hypersplenism include anemia, leukopenia, thrombocytopenia, or a combination of them, hypercellular or normocellular bone marrow, splenomegaly, and improvement after splenectomy Hypersplenism is a common manifestation of PHT in patients with chronic liver diseases, and correlates with the severity of liver cirrhosis, The presence of hypersplenism suggests more advanced liver disease and an increased risk of complications [1, 2]. Splenomegaly is often used radiologically as an indicator of cirrhosis [3].Many studies also investigated the relationship between size of gastroesophageal varices and platelet count/spleen diameter ratio in cirrhotic patients which also suggested that it could be used as a non-invasive indicator of esophageal varices [4]. However, a little is published on the actual frequency of hypersplenism and its correlations with liver disease. To date, no studies have fully assessed these correlations of hypersplenism in cirrhotic patients, which can be useful in diagnostic aspects, assessment, grading of severity, therapeutic interventions or may even lead to the

development of a new scoring system for hypersplenism and more comprehensive scoring system for assessment of liver cirrhosis and PHT. The current study aimed to assess the prevalence and pattern of hypersplenism in patients with liver cirrhosis and portal hypertension. In addition to elucidate the relationship between hypersplenism and severity of liver disease.

2. Patients and Methods

2.1. Study design & setting

A cross sectional study was carried out on patients presented to the outpatient clinic and patients admitted at Al Rajhi Liver Hospital, Assiut University Hospitals, Faculty of Medicine, Assiut University, Assiut, Egypt.

2.2. Patients

A total of 303 patients who presented to the outpatient clinics or admitted to the ward, who fulfilled the inclusion criteria were recruited in the study during the period from February 2018 to December 2021 excluding the period from March 2020 to September 2020, as the hospital was turned into an isolation center for COVID 19.

2.3. Selection criteria

All patients with documented evidence of liver cirrhosis (of any etiology other than alcoholic cirrhosis) and PHT, based on history, clinical examination, abdominal ultrasound examination, or upper gastrointestinal endoscopy were recruited. Any patient with one or more of the following criteria was excluded; splenomegaly of any cause other than liver cirrhosis, lymphoproliferative disorders, extrahepatic malignancy, associated severe cardiovascular disease, age younger than 18 years old or older than 70 years old, and/or failure to obtain consent.

2.4. Baseline evaluation

All included patients were subjected to thorough history taking, complete physical examination, routine laboratory investigations (peripheral hemogram, renal functions, liver functions, prothrombin time, concentration and INR) and abdominal ultrasonography. Liver cirrhosis severity was graded according to Child-Pugh and the Model of End-stage Liver Disease (MELD) scores **[5-7].**

2.5. Assessment of the presence and severity of hypersplenism

The blood picture (hemogram) and blood film were done for all the 296 patients. Haematologically, hypersplenism was defined as leukocyte count of $<4.0\times10^9$/L, an erythrocyte count of $<4.0\times10^{12}$/L, and/or a platelet count of $<150\times10^9$/L [8]. The prevalence and pattern of hypersplenism were assessed. Owing to the finding of only anemia in many patients without other cytopenia, which could be a result of many factors as hematemesis, anaemia of chronic disease in hepatic patients, and as work up to exclude anaemia couldn't be done in all these patients, so anaemia alone was not considered as a cytopenia parameter of hypersplenism unless combined with leucopenia or thrombocytopenia, exclusion of anaemia only as a single parameter of hypersplenism was stated in previous studies [2, 9]. Depending mainly on the severity, cytopenia, was graded as mild, moderate, or severe, and given a total score of <2 points, 2-3 points, and >3 points, respectively. PLTs count of $50\text{-}100\times10^9$/L was scored as 1, $30\text{-}50\times10^9$/L as 2, and $<30\times10^9$/L as 3; a RBCs count of $3\text{-}4\times10^{12}$/L was scored as 0, and $<3\times10^{12}$/L as 1; a WBC count of $2\text{-}4\times10^9$/L was scored as 0, and $<2\times10^9$/L as 1 **[8]**. Presence of hypersplenism in patients with cirrhosis and PHT, was assessed in comparison with those who did not develop hypersplenism, and comparison between different grades of hypersplenism was also done, as regards to Child-Pugh score, MELD score, presence of HCC, PVT, ascites, portosystemic collaterals, portal haemodynamics and other clinical data.

2.6. Bone marrow examination

Due to risks and other limitations to perform bone marrow examination for all the patients recruited in the study, and refusal of other patients, and still no solid guidelines to change the management plans. Only 63 patients with hypersplenism associated with cirrhosis and PHT, were subjected to bone marrow aspirate by a single experienced clinical pathology staff member, as a representative sample.

2.7. Assessment of portal hemodynamics

A total of 100 patients out of the enrolled patients were subjected to Duplex Doppler ultrasonography. The PV diameter was measured, and the portal flow velocity (PVV) in centimeters per second (cm/s) was measured. During the measurement of velocity, the angle between the Doppler beam and the long axis of vessel should be less than 60^o for accuracy. Other measures obtained included portal vein distance, TAMV (time-averaged mean velocity), area, and hepatic arterial resistive index.

2.8. Statistical Analysis

Data were verified, coded by the researcher, and analyzed using IBM-SPSS 24.0 (IBM-SPSS Inc., Chicago, IL, USA)· Descriptive statistics: Means, standard deviations, medians, ranges, frequency, and percentages were calculated. Test of significances: Chi square test was used to compare the difference in distribution of frequencies among different groups. Test of normality, Shapiro-Wilk/ Kolmogorov Smirnoff was used to test the normality of continuous variables. For continuous variables independent sample t-test was calculated to test the mean differences between groups. Multivariable logistic regression analysis was calculated to investigate the independent significant predictors of hypersplenism (Odds Ratio -OR-, 95% confidence interval -95% CI-). Spearman Rank Correlation Analysis was used to test the association between variables. To compare the difference in CHILD and MELD scores in different flow grade and pattern, one-way ANOVA test was used to compare the mean difference; post-hoc test was calculated using Bonferroni corrections for pairwise comparisons. A p-value < 0.05 was considered significant.

3. Results

Our study included 303 patients who fulfilled the inclusion criteria. Out of those patients, seven patients were excluded as following; 2 patients had cholangiocarcinoma, 2 patients had lymphoma, 1 patient had gall bladder carcinoma, 1 patient had hypocellular bone marrow results and another patient had bone marrow biopsy result of hypoplasia suggestive of lymphoproliferative disorder. So, a

total of 296 patients were included in the study results, and 182 patients were found to have hypersplenism**.**

3.1. Baseline data and clinical evaluation based on development of hypersplenism (table 1)

Mean age of those patients with hypersplenism was significantly lower in comparison to those without hypersplenism (56.37 ± 13.1 vs. 60.43 ± 9.4 (years); *p*= 0.004). Also, patients with hypersplenism had significantly lower frequency of smoking (9.9% vs. 19.3%; *p*= 0.021).

3.2. Pattern of Cytopenia (table 2)

Mono-cytopenia was found in 56 patients, bi-cytopenia in 52 patients, while pan-cytopenia was observed in 74. Anemia was present in 174 patients but excluded alone as a single parameter for hypersplenism as explained before. Leucopenia was present in 120 patients, and thrombocytopenia in 163 patients.

3.3. Ultrasound findings among the studied patients based on development of hypersplenism (table 3)

Patients with hypersplenism had significantly higher splenic diameter (160.25 ± 27.1 vs. 148.94 ± 18.3 (mm); *p*< 0.001), portal vein diameter (19.03 ± 13.2 vs. 17.89 ± 16.6 (mm); *p*= 0.015) and more frequent portosystemic collaterals (23.6% vs. 11.4%; *p*= 0.009), portal vein thrombosis (11.5% vs. 6.2%; *p*= 0.043) and HCC (18.6% vs. 10.6%; *p*= 0.030).

3.4. Portal hemodynamics based on development of hypersplenism (table 4)

Patients with hypersplenism had significantly lower portal vein velocity (PVV) (17.55 ± 7.8 vs. 20.38 ± 5.5 (ml/sec); *p*= 0.026) and time averaged mean velocity (TAMV) (6.53 ± 2.8 vs. 7.80 ± 3.1 (ml/sec); *p*= 0.033).

3.5. Disease severity based on development of hypersplenism (table 5)

Patients with hypersplenism had significantly higher Child score (8.32 ± 1.8 vs. 6.91 ± 1.8; *p*< 0.001) and MELD score (14.29 ± 4.9 vs. 11.82 ± 4.6; *p*< 0.001) in comparison to those without hypersplenism. Also, patients with hypersplenism had more advanced Child class.

3.6. Predictors of hypersplenism (table 6)

Predictors of hypersplenism among patients with liver cirrhosis and PHT were as follows; ascites, hematemesis and or melena, portal vein diameter, splenic size, portal vein velocity, and presence of portosystemic collaterals. The best variables that could predict presence of hypersplenism was ascites, with adjusted odds ratio (95% confidence interval) = 3.790 (p =0.001).

3.7. Characteristics of patients with hypersplenism based on its severity (table 7)

Patients with hypersplenism were categorized into two groups based on the severity of hypersplenism. A total of 102 patients were categorized as mild, and 80 patients with moderate and severe hypersplenism were categorized into the 2nd group. Both groups had insignificant differences as regard different characteristics (*p*> 0.05) with exception of significantly higher frequency of varices among those with moderate/severe hypersplenism (87.5% vs. 76.5%; *p*= 0.039).

4. Discussion

Secondary to drawbacks of hypersplenism and cytopenias and fair high prevalence of liver cirrhosis in Egypt where estimated percentage of Egyptians manifested by any liver diseases in the age group from 1 to 59 years old was 2.9% [10], in addition to paucity of studies that discussed such issue and its implications in patients with liver cirrhosis, we conducted this work to assess the prevalence and pattern of hypersplenism and grade the severity of cytopenias in patients with cirrhosis and portal hypertension. In this work a total of 296 patients with liver cirrhosis and PHT were included in the study analysis; out of those patients 182 (61.5%) patients had hypersplenism. This percentage of hypersplenism is relatively high and yet was comparable with many previous studies that reported frequency of hypersplenism among cirrhotic patients ranging between 2% and 80.5% [11-20]. Some of the variation is attributable to different criteria for leukopenia and thrombocytopenia, different criteria used to define hypersplenism, and different study populations. In addition, many studies included active alcoholics in whom alcohol effects on bone marrow production may have been implicated. Also, these variations may be secondary to enrolled different etiologies of liver cirrhosis. Another explanation of wide variations in frequency of hypersplenism among cirrhotic patients may be attributed to the severity of liver disease among the studied patients where *Ashraf et al.* considered up to 68% of their studied patients had hypersplenism secondary to late stage of liver disease in those patients [18]. In the current study, we found patients with hypersplenism had significantly lower mean age (56.37 ± 13.1 vs. 60.43 ± 9.4 (years); *p*= 0.004) in comparison to those without hypersplenism, which was in contrast to that reported by other studies [21]. This can be explained by the high prevalence of HCV in younger age groups in our locality, and that our study did not include patients more than 70 years old, which was not a condition in other studies. Also, those patients without hypersplenism had significantly higher frequency of smoking (19.3% vs. 9.9%; *p*= 0.021). As regards to the clinical history, we found that patients with hypersplenism had higher frequency of haematemesis and or melena (59.8% vs. 31.6%; *p*< 0.001), encephalopathy (36.8% vs. 18.4%; *p*= 0.04), ascites (48.3% vs 23.7%; p= 0.02), and those with suspected SBP (9.9% vs. 4.4%; *p*= 0.021). So, based on these findings, we could assume that patients with hypersplenism are at higher risk to develop different complication of liver cirrhosis as bleeding varices, encephalopathy. ascites and SBP. This was consistent with the study of *Liangpunsakul et al*. that revealed that hypersplenism is an independent predictor of variceal bleeding, SBP, and death. If these findings are confirmed, severe hypersplenism may constitute an indication for instituting prophylactic measures against variceal bleeding and bacterial infections in patients with cirrhosis and PHT [9]. Also, many previous studies have shown that thrombocytopenia is an independent risk factor for developing large esophageal varices, together with the relationship we noted between hypersplenism and variceal bleeding, as clinical presentation, is possibly reflective of that association [9, 22-24].

Table 1: Baseline characteristics and clinical data based on development of hypersplenismtz

Parameter		Hypersplenism (182 = n)	No-Hypersplenism (114 = n)	P-value
Age/years		13.1 ± 56.37	9.4 ± 60.43	0.004
Sex	Female	(%37.9) 69	(%30.7) 35	0.206
	Male	(%62.1) 113	(%69.3.2) 79	
Smoking		(%9.9) 18	(%19.3) 22	0.021
Diabetes mellitus		(%32) 58	(%29.8) 34	0.689
Hypertension		(%23.2) 42	(%22.8) 26	0.937
Other chronic disease		(%6.6) 12	(%7.9) 9	0.671
Hepatitis C virus		(%70.9) 129	(%78.9) 90	0.124
Hepatitis B virus		(%5.5) 10	(%2.6) 3	0.242
Hematemesis/Melena		(%59.8) 109	(%31.6) 36	0.001 >
Encephalopathy		(%36.8) 67	(%18.4) 21	0.04
Ascites		(%48.3) 88	(%23.7) 27	0.02
Suspected SBP		(%9.9) 18	(%4.4) 5	0.021

0.05 > Data expressed as frequency (percentage), mean (SD). P value was significant if

Table 2: Pattern of cytopenia

Cytopenia Pattern of	
Mono-cytopenia	56
Bi-cytopenia	52
Pan-cytopenia	74
Anaemia	174
Leucopenia	120
Thrombocytopenia	163

Table 3: Ultrasound findings in studied patients based on development of hypersplenism

Parameter	(182=n)Hypersplenism	(114 =n) No-hypersplenism	P-value
Splenic diameter (mm)	27.1 ± 160.25	18.3 ± 148.94	0.001 >
Portosystemic collateral	(%23.6) 43	(%11.4) 13	0.009
PV diameter (mm)	13.2 ± 19.03	16.6 ± 17.89	0.015
PV thrombosis	(%11.5) 21	(%6.2) 13	0.043
HCC	(%18.6) 38	(%10.6) 10	0.030
***BCLC**			0.04
Stage 0/A	(%15.8) 6	(%20) 2	
Stage B	(%31.6) 12	(%20) 2	
Stage C/D	(%52.6) 20	(%60) 6	
Ascites	(%68.7) 125	(%43) 49	0.001 >
Ascites grade			
Mild	(%17.6) 32	(%18.4) 21	
Moderate	(%37.9) 69	(%15.8) 18	0.001 >
Marked	(%13.2) 24	(%8.8) 10	

.0.05 > Data expressed as frequency (percentage), mean (SD). P value was significant if
PV: portal vein; HCC: hepatocellular carcinoma; BCLC: Barcelona Clinic of Liver Cancer
here was calculated based on those with HCC Percentage*

Table 4: Portal hemodynamics based on development of hypersplenism

	Hypersplenism (n = 182)	No-Hypersplenism (n = 114)	P-value
Portal vein velocity			
Mean ± SD	7.8 ± 17.55	5.5 ± 20.38	0.026
Median (Range)	(42 - 0) 17	(33 - 0) 20	
TAMV			
Mean ± SD	2.8 ± 6.53	3.1 ± 7.80	0.033
Median (Range)	(14 - 0) 6	(17 - 2) 7	
Volume flow			
Mean ± SD	63.9 ± 459.28	320.4 ± 700.50	0.094
Median (Range)	(1531 - 0) 447	(1255 – 146) 700.5	
Hepatic artery RI			
Mean ± SD	0.1 ± 0.64	0.1 ± 0.63	0.751
Median (Range)	(0.9 – 0.2) 0.63	(0.8 – 0.2) 0.64	

.0.05 > Data expressed as median (range), mean (SD). P value was significant if
TAMV: time averaged mean velocity; RI: resistive index

Table 5: Disease severity based on development of hypersplenism

Parameter	Hypersplenism (n = 182)	No- Hypersplenism (n = 114)	P-value
Child score			
Mean ± SD	1.8 ± 8.32	1.8 ± 6.91	0.001 >
Median (Range)	(13 - 5) 8	(13 - 5) 6.5	
CHILD class			
A	(%17.1) 31	(%50) 57	0.001 >
B	(%52.7) 96	(%39.5) 45	
C	(%30.2) 55	(%10.5) 12	
MELD score			
Mean ± SD	4.9 ± 14.29	4.6 ± 11.82	0.001 >
Median (Range)	(30 - 6.5) 13.5	(30.5 – 6.5) 11	

.0.05 > Data expressed as frequency (percentage), median (range), mean (SD). P value was significant if
MELD: model for end stage liver disease

Table 6: Predictors of hypersplenism based on the current Study

Variable	Adjusted odds ratio (95% CI)	P-value
Ascites	(6.636 – 2.165) 3.790	0.001
Hematemesis/melena	(3.872 – 2.140) 2.191	0.007
Portal vein diameter (mm)	(0.994 – 0.954) 0.974	0.012
Splenic size (mm)	(1.036 – 1.003) 1.020	0.019
Portal vein velocity (ml/sec)	(0.991 – 0.885) 0.938	0.035
Portosystemic collaterals	(3.112 – 1.073) 1.120	0.039
Sex (female)	(2.754 – 0.276) 0.872	0.815

CI: confidence interval .0.05 > P value was significant if

Table 7: Characteristics of patients with hypersplenism based on Severity

Parameter	Mild (n = 102)	Moderate/severe (n = 80)	P-value
Child score	1.9 ± 8.28	1.6 ± 8.37	0.738
Child class			
A	(%19.6) 20	(%13.8) 11	0.214
B	(%47.1) 48	(%60) 48	
C	(%33.3) 34	(%26.3) 21	
MELD score			
Mean ± SD	5.3 ± 14.64	4.3 ± 13.85	0.272
Median (Range)	(28 – 6.5) 13	(30 - 7.5) 13.5	
HCC	(%12.7) 13	(%20) 16	0.131
Ascites	(%33.3) 34	(%28.8) 23	0.309
Grade I	(%16.7) 17	(%18.8) 15	0.513
Grade II	(%38.2) 39	(%37.5) 30	
Grade III	(%11.8) 12	(%15) 12	
Varices	(%76.5) 78	(%87.5) 70	0.039
Grade I	(%18.6) 19	(%12.5) 10	0.005
Grade II	(%21.6) 22	(%17.5) 14	
Grade III	(%36.3) 37	(%57.5) 46	
Portal vein velocity (ml/s)	9.7 ± 18.12	4.2 ± 16.78	0.401
Time averaged mean velocity (ml/s)	3.4 ± 6.29	2.1 ± 6.79	0.200
Volume flow	200.5 ± 311.61	431.2 ± 562.65	0.129
Hepatic artery RI	0.1 ± 0.62	0.1 ± 0.70	0.182
Splenic stiffness	8.9 ± 23.01	7.1 ± 19.18	0.341

.0.05 > Data expressed as frequency (percentage), median (range), mean (SD). P value was significant if

One of the important findings in the current study, that during ultrasound evaluation of enrolled patients is that patients with hypersplenism had significantly higher splenic diameter (160.25 ± 27.1 vs. 148.94 ± 18.3 (mm); $p< 0.001$) in comparison to those without hypersplenism. Moreover, the frequency of PVT, HCC and degree of ascites by ultrasound was significantly higher among those with hypersplenism. In agreement with these findings, ***Berzigotti et al.*** demonstrated a significant inverse correlation between the size of the spleen and the platelets count in patients with liver cirrhosis. They noted also that spleen enlarges over time in cirrhotic patients, and, they also observed that a spleen enlargement on ultrasound follow-up is associated with the appearance and growth of esophageal varices, and with the occurrence of a first decompensation of cirrhosis in patients with compensated disease [25]. To our knowledge, the current study is considered the first study to discuss portal hemodynamics among patients with hypersplenism. Patients with hypersplenism had significantly lower portal vein velocity (17.55 ± 7.8 vs. 20.38 ± 5.5 (ml/sec); p= 0.026) and time averaged mean velocity (TAMV) (6.53 ± 2.8 vs. 7.80 ± 3.1 (ml/sec); p= 0.033) in comparison to those without hypersplenism. This point could be explained by increase in hepatic vascular resistance to portal blood flow, which underlies the development of PHT in cirrhosis. Hepatic vascular resistance occurs partly because of architectural changes, fibrosis, vascular occlusion and capillarization of sinusoids, with affection portal vein velocity. This process increased with advancing of the liver diseases and hence, this may be correlated with hypersplenism [26, 27]. Our study found that patients with hypersplenism had higher frequency of HCC. In line with the current study, *Orlando et al.*, concluded that splenomegaly and hypersplenism seems to be an important prognostic factor in patients with liver cirrhosis, which represents a risk factor for PHT and even HCC [1]. In the current work we found significant association between liver disease severity and hypersplenism where patients with hypersplenism had significantly higher Child score (8.32 ± 1.8 vs. 6.91 ± 1.8; p< 0.001) and MELD score (14.29 ± 4.9 vs. 11.82 ± 4.6; p< 0.001) in comparison to those without hypersplenism. Also, patients with hypersplenism had more advanced Child class. Previous studies recorded the same findings [9]. Also, as pointed before, many studied showed that progressive decrease in platelet count is considered as a noninvasive indicator for the development of PHT due to severe liver fibrosis or cirrhosis. Overall, the degree of thrombocytopenia appears to be proportionally related to the severity of liver disease but is not associated with spontaneous bleeding, unless platelets count decrease to <50,000–60,000/μL [28-32]. Based on the current study, predictors of hypersplenism among patients with liver cirrhosis and PHT were in descending order of frequency as follows; ascites, hematemesis and or melena, portal vein diameter, splenic size, portal vein velocity, and presence of portosystemic collaterals. The best variables that

could predict presence of hypersplenism was ascites, with highest odd's ration that was 3.790. Although there is no previous study that searched about different predictors of hypersplenism among patients with liver cirrhosis and PHT, but a previous study revealed that decompensated liver disease [odds ratio (OR), 2.0; 95% confidence interval (CI), 1.1–3.7] and a history of alcohol consumption (OR 2.3; 95% CI, 1.4–3.8) were independent predictors of severe hypersplenism. In our study, we categorized patients based on severity of hypersplenism into either mild and moderate/severe hypersplenism, and both groups had insignificant differences as regard different characteristics (p> 0.05) with exception of significantly higher frequency of varices among those with moderate/severe hypersplenism (87.5% vs. 76.5%; p= 0.039). Also, the grade of varices was more advanced among those with moderate/severe hypersplenism. Based on these findings, we could assume that frequency of hypersplenism, whatever its severity, increases with more advanced liver disease, and specifically more with higher portal pressure. The current study acknowledges some limitations. These included: bone marrow samples could not be taken for all patients for final confirmation of hypersplenism, due to limitations and hazards associated with bone marrow samples in advanced cirrhotic patients, and still there will be no change of management plans according to current guidelines, yet 61 patients (nearly one third of the patients with hypersplenism), had the final confirmation by bone marrow sampling. Still many studies did not count on bone marrow samples for final confirmation. We could not do long term follow up of those patients to assess effect of hypersplenism on survival analysis of those patients. Also, we didn't offer any therapeutic trials to those patients especially those with severe hypersplenism such as selective splenectomy, microwave and/or splenic angioembolization but none of these methods are well studied. Another limitation of the current study was being conducted in single center, and yet this study had many points of strength; being the first study discussing hypersplenism in liver cirrhosis in our locality, and predictors of hypersplenism, grading hypersplenism by scoring system, and relatively high sample size.

5. Conclusion

Hypersplenism is fairly common in cirrhotic patients with PHT. Ascites, hematemesis and or melena, PV diameter, splenic diameter, PVV, and portosystemic collateral may predict the development of hypersplenism. Also, doppler US may be used as a non-invasive marker for PHT and hypersplenism. Decreased PVV is associated with the development of hypersplenism and more advanced liver disease, and lower values can predict the development of varices. Further studies are needed to elucidate the relationship between hypersplenism and HCC, and the role of hypersplenism in the development of HCC.

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