Correlation Between Thrombocytopenia, Survival, Mortality And Complications In Cirrhotic Patients

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Abstract:
Background: Thrombocytopenia is common in patients with chronic liver disease. Its pathogenesis is multifactorial. The aim of our study is to assess the frequency of thrombocytopenia in cirrhotic patients, as well as to evaluate the prognostic value of thrombocytopenia and its correlation with survival, and the occurrence of cirrhosis-related complications.

Materials and Methods: This is a retrospective analytical study, conducted over a two-year period from January 2020 to December 2022. We included any cirrhosis selected based on a range of clinical, biological, radiological and endoscopic arguments. Thrombocytopenia was defined as a platelet count < 150,000/L. Data were collected on a survey form and analyzed using SPSS software. We used the Chi-square test to analyze our results. The significance threshold was set at a p-value of less than 0.05.

Results: Our study included 98 patients. The incidence of thrombocytopenia was 75%. The mean age of our patients was 50 years, with M/F sex ratio of 1.04. A correlation was demonstrated between the degree of thrombocytopenia and overall survival, as assessed by the ALBI score (p=0.02). There was also a correlation between the degree of thrombocytopenia and mortality (p=0.0002). Of the total number of patients, 55% had ascites. There was a correlation between the degree of thrombocytopenia and the risk of ascites (p=0.03). There was also a correlation between the degree of thrombocytopenia and the risk of spontaneous infection of ascites fluid (p=0.00007). A correlation between the degree of thrombocytopenia and the occurrence of an advanced CHILD score (p=0.0017) was noted. Of 98 cirrhotic patients, 11% presented bleeding unrelated to portal hypertension (metrorrhagia, epistaxis, gingivorrhagia, etc.) correlated with the degree of thrombocytopenia (p=0.008). However, there was no correlation between the degree of thrombocytopenia and the presence or recurrence of esophageal varices (p=0.186). On the other hand, our study showed no correlation between the degree of thrombocytopenia and the occurrence of hepatocellular carcinoma (p=0.055).

Conclusion: Thrombocytopenia is an important prognostic factor correlated with overall survival and portal hypertensive complications in cirrhotic patients.

Key Word: Cirrhosis, thrombocytopenia, complications, prognosis.

I. Introduction

Thrombocytopenia is common in patients with liver cirrhosis. Its prevalence ranges from 64% to 84%. Its pathogenesis is multifactorial, including splenic sequestration of platelets secondary to portal hypertension, reduced thrombopoietin production and myelosuppression[1].

According to several studies, in addition to being an indicator of advanced disease, thrombocytopenia can be a predictive factor in the prognosis of cirrhosis, mortality and complications of portal hypertension. In addition, it often prevents patients from receiving invasive diagnostic or therapeutic procedures [2,3].

The aim of our work is to evaluate the frequency of thrombocytopenia in cirrhotic patients, and to assess the prognostic value of thrombocytopenia. We will study the correlation with survival, mortality, as well as the occurrence of cirrhosis-related complications (presence of esophageal varices, presence of ascites and ascites fluid infection, CHILD score, presence of thrombosis, hepatocellular carcinoma,) and its interference with the performance of invasive procedures.

II. Material And Methods

This is a retrospective analytical study conducted over a two-year period, from January 2020 to December 2022, in the gastroenterology department of CHU Mohammed VI in Tangier.
We included any cirrhosis based on clinical, biological, radiological and endoscopic evidence.

Thrombocytopenia is defined as a platelet count < 150,000/L. Mild thrombocytopenia or grade 1 is defined by a platelet count between 75,000 and 15,000,000/L. Moderate thrombocytopenia or grade 2 is defined

by a platelet count between 50,000 and 75,000/L. Severe thrombocytopenia or grade 3 is defined by a platelet count between 25,000 and 50,000/L. Very severe thrombocytopenia or grade 4 is defined by a platelet count strictly below 25,000/L.
We excluded all unproven cirrhosis as well as files that could not be processed.
        Data were collected on a survey form and analyzed using SPSS (Statistical Package for the (Statistical Package for the Social Sciences) software version 27. We used the Chi-square test to compare our results. We used the univariate linear logistic regression model and a plotted ROC curve for mortality. The significance threshold was set at a p-value of less than 0.05 (p< 0.05).

## III. Result

Descriptive study
        Our study included 98 patients. The mean age of our patients was 50 years, with extremes ranging from 5 to 86 years. There was a slight male predominance, with M/F sex ratio of 1.04. The prevalence of thrombocytopenia was 75% (n=74). For these patients, mild thrombocytopenia was found in 39 % (n=29), moderate in 24%(n=18), severe in 24%(n=19) and very severe in 12%(n=8) (Figure1). A CHILD A score was found in 29 %(n=29) of patients, a CHILD B in 37%(n=36), and a CHILD C in 34%(n=33) (Figure2). Ascites was found in 55% (n=54) of cirrhotic patients, including 10% with spontaneous infection of the ascites fluid (Figure3).Among our patients, 95% (n=93) had esophageal varices, of which 17% (n=16) were grade 1, 25 %(n=23) grade 2 and 58% (n=54) grade 3(Figure4). Portal thrombosis was found in 30% (n=30). HCC was found in 8% (n=8) of patients.
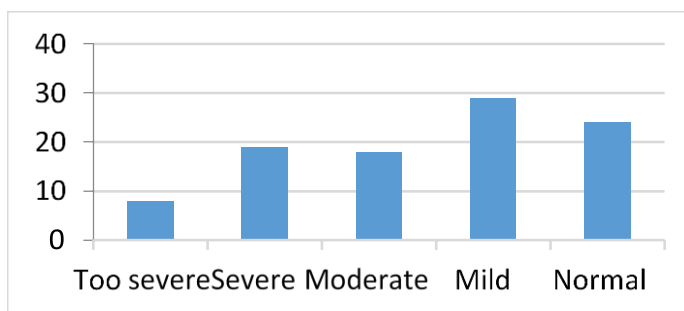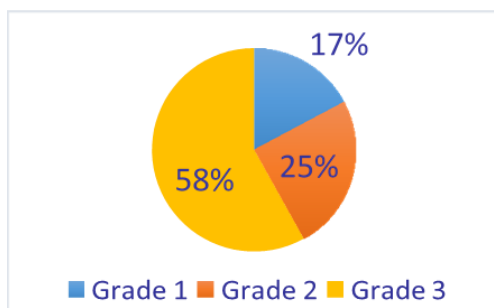

Figure 1: Distribution of patients according to thrombocytopenia severity.
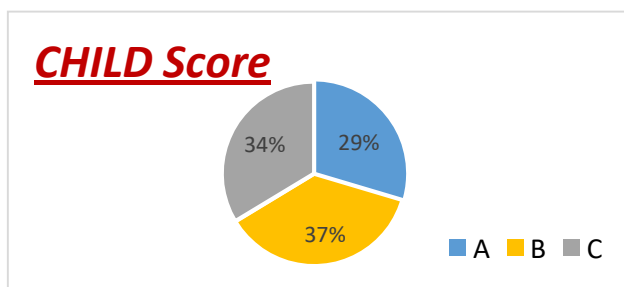
Figure 2: Distribution of patients according to CHILD score.
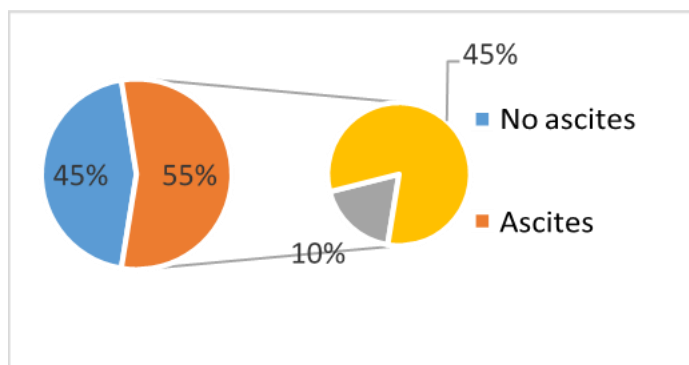
Figure 3: Distribution of patients according to the presence of ascites.

Figure 4: Distribution of patients by grade of esophageal varices.

Analytical study

Once all the data was collected, they were analyzed to determine whether there was a correlation between the degree of thrombocytopenia and survival, mortality and the occurrence of portal hypertension complications. The parameters were correlated with the degree of thrombocytopenia, using the univariate logistic regression model. A correlation was demonstrated between the degree of thrombocytopenia and overall survival, as assessed by the ALBI score (p-value 0.02). There was also a correlation between the degree of thrombocytopenia and mortality (p-value 0.0002). Of the total number of patients, 55% had ascites. There was a correlation between the degree of thrombocytopenia and the risk of spontaneous infection of ascites fluid (p-value 0.00007). There was also a correlation between the degree of thrombocytopenia and the occurrence of an advanced CHILD score (p- value 0.0017). Of 98 cirrhotic patients, 11% presented bleeding unrelated to portal hypertension (metrorrhagia, epistaxis, gingivorrhagia, etc.). In these patients, severe to very severe thrombocytopenia was observed in 64% of cases, and moderate thrombocytopenia in 36%. The risk of bleeding unrelated to portal hypertension was also correlated with the degree of thrombocytopenia (p-value 0.008). In addition, there was a correlation between the degree of thrombocytopenia and the difficulty of performing invasive procedures such as dental care, ascites puncture and liver biopsy (p-value 0.01). However, there was no correlation between the degree of thrombocytopenia and the presence or recurrence of esophageal varices (p-value 0.186). Similarly, our study showed no correlation between the degree of thrombocytopenia and the occurrence of hepatocellular carcinoma (p-value 0.055) (Table 1).

Table 1: Correlation between thrombocytopenia and complications of portal hypertension in cirrhotic patients by regression model, univariate.

CORRELATION BETWEEN THROMBOCYTOPENIA AND :	OR	CONFIDENCE INTERVAL	SIGNIFICANCE(P-VALUE)
MORTALITY	0.999979	(0.999956-0.99999)	**0.002**
PRESENCE OF ASCITES	0.999991	(0.999984-0.999997)	**0.03**
SPONTANEOUS ASCITES INFECTION	0.999971	(0.99995-0.99998)	**<0.01**
OCCURRENCE OF AN ADVANCED CHILD	0.999981	(0.99997-0.99999)	**<0.01**
HEPATOCARCINOMA	0,999981	(0.999962-1,000000)	0,055
RISK OF BLEEDING UNRELATED TO PORTAL HYPERTENSION	0.99996	(0.99994-0.99999)	**0.008**
ESOPHAGEAL VARICES	**0,999995**	**(0,999989-1,000002)**	0,186
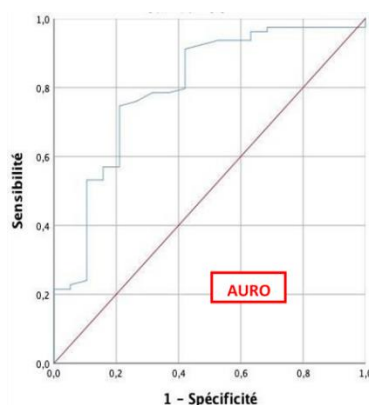
Figure 5: ROC curve for mortality with area under the curve at 79% and a value of P< 0.01
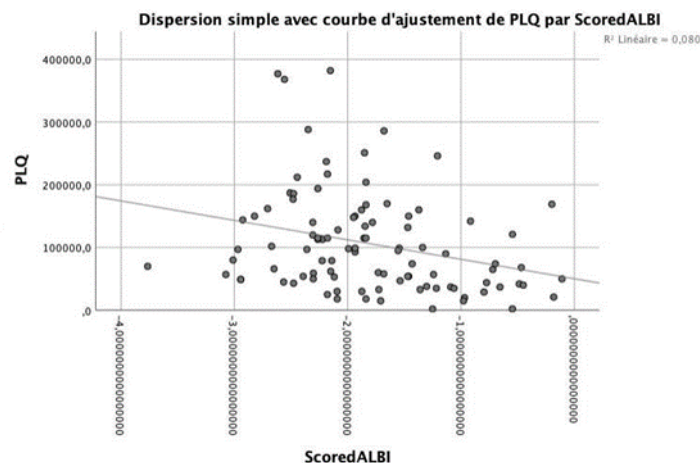
Figure 6: Correlation between ALBI score and platelet count in linear regression

IV. Discussion

Thrombocytopenia is a frequent complication of chronic liver disease. Among patients undergoing bone marrow biopsies for thrombocytopenia of unknown etiology, the prevalence of cirrhosis reaches 35% [4]. The degree of thrombocytopenia is proportional to the severity of liver disease. Consequently, platelet counts are often used in the diagnosis and evaluation of liver disease [3]. For example, the Baveno VI criteria for portal hypertension use platelet count as an indicator of advanced liver disease [1]. In addition, an inverse relationship between thrombocytopenia and liver fibrosis was proven by several simple tests using readily available hematological and biochemical markers. These include the APRI (aspartate aminotransferase to platelet ratio index) score, fibrosis-4 (FIB-4), which are widely validated [5,6].

Our study demonstrated a correlation between the degree of thrombocytopenia, mortality, survival and the occurrence of cirrhosis-related complications. These results have been confirmed by other studies [7] including a Chinese cohort of 3939 patients with acute decompensation of cirrhosis. In this study, the cumulative incidence of adverse events (bleeding, ascites, infection and mortality) within 90 days in patients was inversely associated with platelet count. Based on univariate and multivariate analyses in this study, the group with platelet counts below 20,000/uL had the highest risk of an adverse event. The risk of a 90-day adverse event in patients increased by 5% for each 10,000/uL decrease in platelet count below 210,000/L[7].

Overall survival was assessed in our study using the ALBI score, and linear regression showed that the lower the platelet count, the lower the median survival. The PALBI score, which integrates the platelet count with the albumin-bilirubin ratio (ALBI), predicts survival in patients with decompensated cirrhosis. This score outperformed the Child Pugh score in patients awaiting liver transplantation [8].

Of our total number of patients, 55% had ascites. There was a correlation between the degree of thrombocytopenia and the risk of ascites. There was also a correlation between the degree of thrombocytopenia and the risk of spontaneous infection of ascites fluid. Similar results were demonstrated by a Scandinavian study including 392 cirrhotic patients with ascitic decompensation, who underwent systematic paracentesis. Thrombocytopenia≤100,000 /µL was found to be an independent predictor of spontaneous ascites fluid infection [9].

Several series have investigated the relationship between thrombocytopenia and hepatocellular carcinoma (HCC). Two Japanese studies have shown that the presence of thrombocytopenia is an independent risk factor for the development of HCC in patients with viral hepatitis B and non-alcoholic fatty liver disease [10,11]. On the other hand, a cohort of 430 patients with tumors of small diameters ≤ 3 cm, alpha-fetoprotein (AFP) values, thrombocytopenia and elevated bilirubin levels were associated with smaller tumors [12]. However, our series showed no correlation between the degree of thrombocytopenia and the occurrence of hepatocellular carcinoma. This difference is probably explained by the low sample size in our series.

Portal hypertension can be identified by non-invasive tests such as liver elasticity measurement, alone or combined with platelet count and spleen size[13]. Sarangapani et al have confirmed that thrombocytopenia, splenomegaly and portal vein size strongly predict the presence of esophageal varices [14]. Unlike our study, which found no correlation between the degree of thrombocytopenia and the presence or recurrence of esophageal varices.

Some limitations of the study deserve to be recalled.The first was the retrospective nature of the study, with certain data missing, notably prior platelet transfusion or the administration of certain drugs that could influence the count. The second is the absence of histological evidence of cirrhosis. Finally, the small number of patients may influence the statistical strength of the data.

V. Conclusion

Platelet count is an often available and inexpensive test with high prognostic value. Our study has shown that thrombocytopenia is an important prognostic element correlated with overall survival and portal hypertensive complications in cirrhotic patients. Furthermore, the combination of different clinical, haematological and biochemical markers may be more useful for a better prediction of cirrhosis-related complications.

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