



# PLATELET COUNT/SPLEEN DIAMETER RATIO TO PREDICT ESOPHAGEAL VARICES AND BLEEDING RISK IN PATIENTS WITH LIVER FAILURE

COCIENTE PLAQUETAS/BAZO PARA EL DIAGNÓSTICO DE VÁRICES ESOFÁGICAS Y RIESGO DE SANGRADO EN PACIENTES CON INSUFICIENCIA HEPÁTICA

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## ABSTRACT

Upper gastrointestinal bleeding of variceal origin has a high mortality. The sensitivity and specificity of the ratio number of platelets / largest diameter of the spleen was determined for the diagnosis of esophageal varices with risk of bleeding in patients with liver failure; A process study, carried out in a second level medical care hospital, was performed ultrasound, hematic cytometry, liver function tests and endoscopy.

There were 70 patients with liver failure, 28 women (20 with hepatitis C virus) and 42 men (31 with alcoholism). The spleen / platelet ratio has a sensitivity of 90%, specificity 83%, false positives 16%, false negatives 9%, positive predictive value 94%, negative predictive value 75%, prevalence of 74% and diagnostic certainty of 88% to diagnose esophageal varices with risk of bleeding.

The platelet / spleen ratio is useful and non-invasive to diagnose esophageal varices with risk of bleeding, in hospitals where endoscopy is not available.

**Key words:** Esophageal and Gastric Varices; Gastrointestinal Hemorrhage; Hepatic failure; Hepatic Insufficiency; Diagnosis (source: MeSH NLM).

## RESUMEN

El sangrado de tubo digestivo alto de origen variceal tiene una mortalidad alta. Se determinó la sensibilidad y especificidad del cociente número de plaquetas/diámetro mayor del bazo para diagnóstico de várices esofágicas con riesgo de sangrado en pacientes con insuficiencia hepática; estudio de proceso, realizado en un hospital de segundo nivel de atención médica, se realizó ultrasonido, citometría hemática, pruebas de función hepática y endoscopia.

Fueron 70 pacientes con insuficiencia hepática, 28 mujeres (20 con virus de hepatitis C) y 42 hombres (31 con etilismo).

El cociente bazo/plaquetas tiene una sensibilidad de 90%, especificidad 83%, falsos positivos 16%, falsos negativos 9%, valor predictivo positivo 94%, valor predictivo negativo 75%, prevalencia del 74% y certeza diagnóstica del 88% para diagnosticar várices esofágicas con riesgo de sangrado.

El cociente plaquetas/bazo es útil y no invasivo para diagnosticar várices esofágicas con riesgo de sangrado, en hospitales donde no se cuenta con endoscopia.

**Palabras clave:** Várices esofágicas y gástricas; Hemorragia gastrointestinal; Fallo hepático; Insuficiencia hepática; Diagnóstico (fuente: DeCS BIREME).

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## INTRODUCTION

Portal hypertension is the increase of portosystemic pressure in any segment of the portal venous system, caused by pre-hepatic or post-hepatic alterations or by other causes<sup>(1)</sup>. It occurs when the portocaval gradient is higher than 5 mmHg and is the most frequent and studied cause of hepatic cirrhosis. From 5 to 33% of these patients have varices, which may appear at any part of the gastrointestinal tract, the most frequent site being the distal centimeters of the esophagus. The presence of varices is correlated with the severity of liver disease<sup>(1,2)</sup>. The hepatic venous pressure gradient is the ratio between portal pressure and vena cava pressure and predicts the appearance of varices. Clinically significant portal hypertension is 10 mmHg, and is a prognosis factor in patients suffering from portal hypertension<sup>(1)</sup>.

When the gradient reaches 12 mmHg, variceal hemorrhage occurs. The main risk factors are: international normalized ratio (INR) greater than 1.5, portal vein diameter greater than 13 mm, and thrombocytopenia. When the patient has one or more of these conditions, it is necessary to perform upper gastrointestinal endoscopy to look for varices and to perform primary prophylaxis against bleeding in cirrhotic patients<sup>(1-3)</sup>.

In upper gastrointestinal bleeding (UGH), endoscopy has a high sensitivity and specificity in locating and identifying lesions that cause bleeding. In addition, it offers the possibility of a therapeutic approach and primary prophylactic treatment<sup>(2,4,5)</sup>.

Certain noninvasive tests are useful in detecting patients at risk of esophageal varices. These include platelet count, splenomegaly, portal vein diameter greater than 13 mm by abdominal ultrasound and lately elastography. However, none of these tests has diagnostic accuracy for large esophageal varices<sup>(1,6,7)</sup>.

The platelet count/spleen bipolar diameter (P/B) ratio of less than 909 is a non-invasive parameter that predicts the presence of esophageal varices in cirrhotic patients<sup>(8)</sup>. It can be a diagnostic and follow-up alternative to endoscopy, which is expensive and difficult to access, and may be contraindicated in some patients<sup>(8,9)</sup>.

The objective was to determine the sensitivity and specificity of the platelet count/spleen major diameter (P/B) ratio for the diagnosis of esophageal varices with risk of bleeding in patients with liver failure.

## THE STUDY

A cross-sectional study was carried out in which a test of a test was performed in a secondary-level hospital of Instituto Mexicano del Seguro Social (IMSS) (IMSS) in Puebla, Mexico. Patients with liver failure of any degree of severity, of both sexes, over 18 years of age and who agreed to participate in the study by filling out and signing an informed consent form were included; patients with acute liver failure and those who died during the study were excluded.

Liver failure was defined by the presence of an INR >1.5, increased aminotransferases, anemia, leukopenia, hypoalbuminemia, and liver disease manifested by anorexia, weight loss, weakness, fatigue, osteoporosis, ascites, jaundice, asterixis, hepatic stench, gynecomastia, hepatomegaly, palmar erythema, testicular atrophy, gynecoid hair or encephalopathy<sup>(13-15)</sup>.

Acute liver failure was considered when the duration of the disease was less than 26 weeks of evolution and without previously known liver disease<sup>(10,11)</sup>.

Patients were recruited from the gastroenterology department and evaluated for severity according to the Child-Pugh classification<sup>(12)</sup>.

Platelet/spleen indices lower than or equal to 909 were found to be normal<sup>(1,6)</sup>.

Hematic cytometry, liver function tests (in those older than one month from the previous control), upper gastrointestinal endoscopy with Fujinon endoscope model Eve EG 450WR5 and splenic ultrasound with Siemens Acuson X300 ultrasound were performed to determine the largest diameter of the spleen. For the statistical analysis, 2 x 2 tables were used for sensitivity, specificity, predictive values and test efficacy. Correlation of severity scales was performed with Spearman's rank correlation coefficient and a value of  $p \leq 0.05$  was considered statistically significant. The study was approved by the Comité Local de Investigación y Ética en Investigación en Salud 2102 with registration number: R-2016-2102-12, and the anonymity of the participating patients was preserved at all times.

## FINDINGS

Seventy patients were recruited. The sample was predominantly male and geriatric patients. The characteristics in terms of sex and etiology of liver disease are shown in Table 1.



The average age was 59.6, minimum 35, maximum 85, SD=10.92 years. Regarding age groups, 3 (4.3%) patients were in the 18 to 40 years old group, 28 (40%) in the 41 to 60 years old group and 39 (55.7%) patients in the group older than or equal to 61 years old.

Regarding Child-Pugh classification, stage B was the most frequent with 32 (45.7%) patients. Details are shown in Graphic 1.

According to the Dagradi classification for esophageal varices<sup>(3)</sup>, there were 21 (30%) Grade III patients. The rest of the details can be seen in Graphic 2.

The correlation between P/B and Child-Pugh was

0.72,  $p < 0.05$ , and between P/B and Dagradi was 0.59 ( $p < 0.05$ ), (a value of  $p < 0.05$  Spearman was considered statistically significant).

Of the 70 patients included in the sample, 47 (67%) patients presented esophageal varices at endoscopy and positive P/B index, 5 (7%) presented positive endoscopy for esophageal varices and 1.4% of patients presented negative P/B, with the following results: sensitivity 90%, specificity 83%, false positives 16%, false negatives 9%, positive predictive value of 94%, a negative predictive value of 75%, prevalence of 74% and a diagnostic certainty of 88% for P/B as a predictor of esophageal varices with risk of bleeding (Table 2).

**Table 1.** Population characteristics.

Sex	Men	Women
Virus hepatitis C		
Virus hepatitis B	0	20
Etilism	0	1
Unidentified	31	0
No identificada	11	7
Total	42	28
Total of patients=70		

**Table 2.** Comparison of the P/B index with endoscopy results.

		Endoscopic result		Total
		+	-	
Index P/B <909	+	47	3	50
	-	5	15	20
Total		52	18	70

SENSIBILITY =  $a/(a+c) = 0,90$  (90%).

FALSE POSITIVES =  $b/(b+d)=0,16$  (16%).

POSITIVE PREDICTIVE VALUE =  $a/(a+b)=0,94$  (94%).

PREVALENCE =  $(a+c)/(a+b+c+d) = 0,74$  (74%).

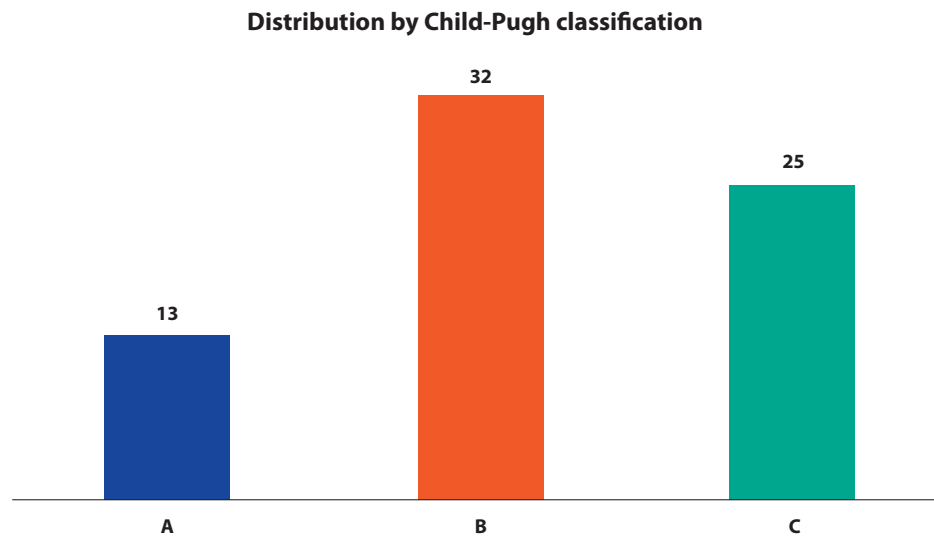
SPECIFICITY =  $d/(b+d) = 0,83$  (83%).

FALSE NEGATIVES =  $c/(a+c) = 0,09$  (9%).

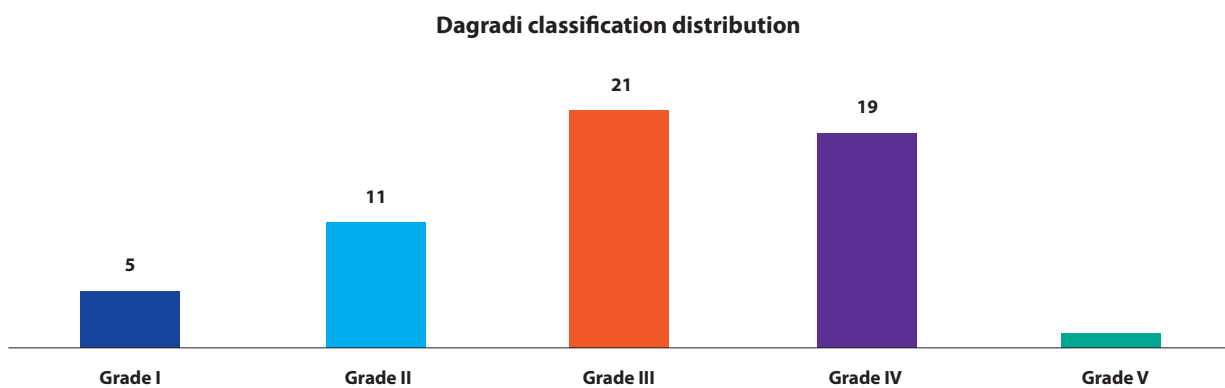
NEGATIVE PREDICTIVE VALUE =  $d/(c+d) = 0,75$  (75%).

DIAGNÓSTICA CERTAINTY =  $(a+d)/(a+b+c+d) = 0,88$  (88%).

Abreviations: + = positive, - = negative, P/B = platelets/spleen.



**Graphic 1.** Distribution of patients according to Child-Pugh classification.



**Graphic 2.** Distribution according to Dagradi classification.

## DISCUSSION

Portal hypertension is the main complication of chronic liver diseases that develop cirrhosis. It can cause esophageal varices in up to 30% of patients<sup>(1, 6-9,12)</sup>. The most frequent causes are viral, alcoholic and of unidentified cause<sup>(1)</sup>.

Endoscopy is the diagnostic method of choice in HDA, it has high sensitivity and specificity since it records and identifies the location of the lesions that cause bleeding in the esophagus, stomach and duodenum. Nowadays, it is still the most accurate technique for diagnosing and staging esophageal varices, especially those of grade I, and for visualizing signs of risk for hemorrhage. This method provides the diagnosis and offers the possibility of a

therapeutic approach<sup>(4,5,13)</sup>.

The frequency of bleeding esophageal varices is 100 in every 100,000 persons per year; it is a medical emergency associated with high mortality, especially in older adults<sup>(1-3,5-9)</sup>.

Esophageal varices, which occur in 100 out of every 100,000 persons per year, are a medical emergency associated with high mortality, especially in older adults<sup>(1-3,5-9,13,14)</sup>.

However, since endoscopy is an invasive diagnostic method, it has both relative and absolute contraindications. In developing countries, the availability of an endoscopic study is limited, therefore, different less invasive methods such as the P/B index have been implemented<sup>(4,6-9,13,14)</sup>.



The P/B index is inexpensive, is run quickly and requires no major skills for its performance. It is seen as a safe alternative in countries with limited economic resources that do not have endoscopy services, and another advantage is that it can be calculated rapidly<sup>(6,8,13-15)</sup>.

Since 2003, the high value of P/B has been demonstrated, even in the subgroup of patients with compensated liver disease<sup>(6)</sup>.

The value of P/B 909 or lower has been considered an indicator of esophageal varices<sup>(6,8,14,15)</sup>. Reports in the Latin American population range from acceptable to very good for sensitivity, specificity and positive and negative predictive values<sup>(8,14,15)</sup>. In this study the results of the test in comparison with endoscopy were very high in sensitivity (90%), specificity (83%) and positive predictive value (94%), but low in negative predictive value (75%).

Some studies carried out in the Mexican population report a moderate correlation between P/B and esophageal varices: a P/B value greater than 0.7 correlated with Baveno grade I varices (<5 mm), and less than 0.7 with grade II varices (>5 mm) and with a low predominance in the advanced stages of Child-Pugh (of liver function) and Dagradi (of esophageal varices)<sup>(14)</sup>, for which reason we consider it necessary to analyze the patient selection criteria.

In this study, in which 70 patients were included, there was a higher correlation between P/B and Dagradi, with a higher percentage of patients in Child-Pugh stages B and C, compared to other studies.

As mentioned above, performing endoscopy for esophageal varices screening every one to two years in high-risk patients can be difficult and impractical<sup>(9)</sup>. Non-invasive parameters associated with high-risk esophageal varices help to reduce the need for endoscopic studies to be performed at this

frequency and can be used to distinguish between high- and low-risk patients. This could be used to follow up only high- or very high-risk patients with endoscopic studies<sup>(6,9,10,12)</sup>.

It is also necessary to mention that a diagnostic endoscopy for esophageal varices should be performed in patients with risk factors, such as a Child-Pugh A<sup>(12,13,15)</sup>.

However, the P/B index is useful for stratification of cirrhosis patients into risk categories where portal hypertension data exist. This is especially relevant for those patients whose health status and conditions do not allow an invasive study, but who are at high risk of developing esophageal varices<sup>(6,9,10-12)</sup>.

In this study, most of the patients had Child-Pugh B and C classification. These stages are those with the highest risk to be associated with esophageal varices and bleeding according to international literature<sup>(9, 12-15)</sup>.

The results of the test performed on the P/B index are consistent with other studies, although some show wide ranges of variability among them<sup>(6,8,13-15)</sup>.

The P/B is strongly associated with the presence of esophageal varices<sup>(1,6,13,14)</sup>, and its negative predictive value is reproducible, in this study with 75% and with a diagnostic certainty of 88%.

## CONCLUSION

The P/B index presents false negatives of 9%, with a positive predictive value of 94%, a negative predictive value of 75%, with a prevalence of 74% and a diagnostic certainty of 88%, so it can be considered a useful and non-invasive study to diagnose esophageal varices especially in patients and/or places such as the first and second level of care, without availability of endoscopy.

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