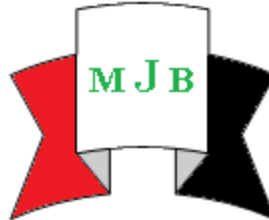


Platelets Count As A Predictor For Portal Hypertension in Patients With Ascites

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Abstract

Background: Serum Ascetic Albumin Gradient is a good biochemical marker and a better discriminator of portal hypertension. Patients with gradients of >1.1 g/dL have portal hypertension, while those with gradients of <1.1 g/dL do not, with accuracy rate 97% and sensitivity of 100%. Thrombocytopenia is a frequent and challenging clinical disorder in patients with portal hypertension. The most sensitive and specific laboratory finding suggestive of cirrhosis in the setting of chronic liver disease is a low platelet count ($<150 \times 10^9/L$), which occurs as a result of portal hypertension and hypersplenism.

Aim of Study: To predict the presence of portal hypertension in patient with ascites by measuring the platelets count.

Patients and Methods: Fifty patients with ascites were sent for complete blood picture, serum albumin, echo study, abdominal ultrasound and albumin in ascites fluid along with thorough medical history and examination. we calculate the SAAG for all patients and classified into two groups , the first has SAAG > 1.1 g/dl and considered to have portal hypertension, the second has SAAG <1.1 g/dl.

Results: In this study, 50 patients with ascites their ages ranges from (34-60) years ,25 of them had SAAG more than 1.1g/dl , 20 of them had platelet count $<150 \times 10^9/L$. while 25 patients with SAAG less than 1.1g/dl, 7 of them had platelet count $<150 \times 10^9/L$. this indicate significant correlation between low platelet count and portal hypertension (p value 0.0002) (the measured sensitivity=84%, specificity=76%, P.P.V=77%, N.P.V=82%) . Another significant correlation was seen between splenomegaly detected by U/S and portal hypertension, 25 patient had SAAG more than 1.1g/dl, of them 12 had splenomegaly (p value 0.00039) (the measured sensitivity=48%, specificity=96%, P.P.V=92%, N.P.V=64%)

Conclusion: Thrombocytopenia in patient with ascites may predict portal hypertension.

Keywords : AFTP (Ascetic fluid total protein), CLD(Chronic Liver Disease), EV(Esophageal varices) HI (Hematological Indices) , HVP (Hepatic venous pressure gradient) , N.P.V (negative predictive value), PHT (Portal Hypertension), P.P.V(positive predictive value), PLT(Platelets), SAAG (Serum Acetic- Albumin Gradient) SD (Standard Deviation)

تعداد الصفائح الدموية كمؤشر لارتفاع الضغط البوابي عند المرضى المصابين باستسقاء البطن

الخلاصة

خلفية الدراسة: ان ميل الالبومين بين مصل الدم والسائل البطني هو مؤشر كيميائي حيوي جيد وفضل محدد لارتفاع الضغط البوابي . المرضى ذوي ميل الالبومين بين مصل الدم والسائل البطني اعلى من ١,١ غرام/لتر لديهم ارتفاع في الضغط البوابي, بنما المرضى ذوي ميل الالبومين بين مصل الدم والسائل البطني ادنى من ١,١ غرام/لتر ليس لديهم ارتفاع في الضغط البوابي, بمعدل دقة ٩٧% وحساسية ١٠٠%. ان انخفاض تعداد الصفائح الدموية هو خلل متكرر وتحدي سريري عند المرضى المصابين بارتفاع الضغط البوابي. ان اكثر النتائج المخبرية حساسية وتحديدًا التي تقترح تشمع الكبد على خلفية مراضة الكبد المزمنة هو انخفاض تعداد الصفائح الدموية لأقل من $150 \times 10^9/L$, والذي يحدث نتيجة لارتفاع الضغط البوابي وتضخم الطحال.

الهدف من الدراسة: للتحري عن وجود ارتفاع الضغط البوابي عند المرضى المصابين باستسقاء البطن من خلال قياس تعداد الصفائح الدموية.

المرضى والطرائق: لخمسين مريض مصابين باستسقاء البطن تم اجراء تحليل صورة الدم الكاملة بقياس الالبومين في مصل الدم وفي السائل البطني, وعمل فحص الايكو للقلب وفحص السونار للبطن مع اخذ تاريخ طبي و فحص سريري مفصل, تم قياس ميل الالبومين بين مصل الدم والسائل البطني لكل المرضى وتم تصنيفهم الى مجموعتين , الاولى ذات ميل اعلى من ١,١ غرام/لتر والاخرى ذات ميل اقل من ١,١ غرام/لتر.

النتائج: في هذه الدراسة خمسين مريض مصاب باستسقاء البطن اعمارهم تتراوح بين (٣٤-٦٠) سنة, منهم ٢٥ مريض ميل الالبومين بين مصل الدم والسائل البطني اعلى من ١,١ غرام/لتر, منهم ٢٠ مريض لديهم تعداد صفائح اقل من $10^9 \times 150$ /لتر. بينما ٢٥ مريض ميل الالبومين بين مصل الدم والسائل البطني اقل من ١,١ غرام/لتر, منهم ٧ مريض لديه تعداد صفائح اقل من $10^9 \times 150$ /لتر, وهذا يدل على علاقة معتبرة بين انخفاض تعداد الصفائح مع ارتفاع الضغط البوابي. وتم ملاحظة علاقة معتبرة اخرى بين تضخم الطحال المكتشف بالسونار مع ارتفاع الضغط البوابي فمن ٢٥ مريض بميل اعلى من ١,١ غرام/لتر منهم ١٢ مريض لديه تضخم في الطحال.

الاستنتاج: انخفاض تعداد الصفائح عند المرضى المصابين باستسقاء البطن يؤشر على ارتفاع الضغط البوابي.

Introduction:

Portal hypertension is defined as the elevation of the hepatic venous pressure gradient to $>5\text{mmHg}$ ¹ but clinical complication start when the portal pressure reaches 12mmHg ^{1,2}. Portal hypertension is caused by a combination of two simultaneously occurring hemodynamic processes².

1- increased intrahepatic resistance to the passage of blood flow through the liver which is due to (first) deposition of fibrous tissue and subsequent compression by regenerative nodules (fixed component) and (second) active vasoconstriction (functional component), Early in the portal hypertensive process, the spleen grows and sequesters platelets and other formed blood cells, thereby leading to hypersplenism^{3,4}.

2- Increased splanchnic blood flow secondary to vasodilation within the splanchnic vascular bed. Portal hypertension is the major complication of Chronic Liver Disease⁵ and it is directly responsible for the two major complications of cirrhosis: variceal hemorrhage and ascites⁶. Variceal hemorrhage is an immediate life-threatening problem with a 20–30% mortality rate associated with each episode of bleeding^{7,8}.

The causes of portal hypertension are usually categorized as pre hepatic, intrahepatic, and post hepatic. Intrahepatic causes account for over 95% of cases of portal

hypertension and are represented by the major forms of cirrhosis⁸.

Ascites is the accumulation of fluid within the peritoneal cavity. Overwhelmingly, the most common cause of ascites is portal hypertension related to cirrhosis⁹. However, clinicians should remember that malignant or infectious causes of ascites can be present as well, and careful differentiation of these other causes is obviously important for patient care¹⁰.

Ascites is caused by cirrhosis in 75% of cases, malignancy in 10%, and cardiac failure in 5%; other causes account for the remaining 10%^{9,10}.

The initial, most cost-effective and least invasive method to confirm the presence of ascites is abdominal ultrasonography.¹⁻⁸

The traditional classification of ascites is based on estimation of ascetic fluid total protein (AFTP), which is high ($\geq 25\text{ g/l}$) in exudate and low ($< 25\text{ g/l}$) in transudate¹¹.

This classification however has a limitation to correctly identify the etiological and pathophysiological factors involved in development of ascites¹²; these drawbacks led to development of a new approach to classify ascites, based on serum ascites albumin gradient (SAAG)¹³.

Serum ascites albumin gradient (SAAG) which is being used to differentiate ascetic fluid into two categories: first with gradient $> 1.1\text{ g/dl}$ in cases with portal hypertension and second with gradient $< 1.1\text{ g/dl}$ in ascites

unrelated to portal hypertension. The superiority of SAAG to differentiate the ascites and to assess presence and degree of esophageal varices is well established^(1,2,8-10), SAAG had accuracy of 97% for portal hypertension¹⁴.

Thrombocytopenia:- (platelet counts $<150 \times 10^9/L$) is a common complication in patients with chronic liver disease (CLD)¹⁵, reported in as many as 76% of cirrhotic patients¹⁶, and it is one of the most frequent hematological disorders in cirrhotic and non-cirrhotic portal hypertension¹⁷. The mechanism of thrombocytopenia classically is thought to be caused by splenic sequestration and destruction of platelets. Portal hypertension resulting in hypersplenism is considered to play a role in splenic platelet sequestration¹⁸. In clinical experience some cirrhotic patients have normal platelet counts or some of them are thrombocytopenic without splenomegaly¹⁹.

Aim of Study

To predict the presence of portal hypertension in patient with ascites simply by measuring the platelets count.

Patients and Methods

Fifty patients with ascites who attending Al- Sader medical city were enrolled in this study during the period from January 2011 to January 2013 those patients were admitted in the medical ward or gastroenterology unit for various purposes , (24) were males and (26) were females , their age ranging from (34 - 60) years the mean was (49.84 ± 7.56) .

Detailed history and physical examination were taken and blood samples were drawn (four milliliter) from all patients and sent for complete blood picture by using (SYSMEX KX-21), serum albumin (two milliliter), ascetic fluid were aspirated (ten milliliter) and sent for albumin level using (ABBOT ARCHITECT plus device) .

Patients underwent echocardiography study by using (SONEX machine) and

abdominal ultrasound by using (Medison machine) .

We calculated the SAAG by the following formula : (SA – AA) and categorize the patients into two groups, the first group , patients with SAAG $> 1.1g/dl$ and second group SAAG $< 1.1g/dl$ for purpose of analysis .

In this study, we excluded:-

1. Congestive Cardiac failure (Ejection Fraction <45).
2. History of recent bleeding.
3. History, clinical and laboratory evidence of Hematological diseases (biochemical evidence of Diffuse intravascular coagulation) .

Statistical analysis

This study is a cross sectional; statistics was performed using chi square test, and p value of less than 0.05 was considered statistically significant. Sensitivity calculated as the following (true positive/true positive + true negative), specificity calculated as the following (true negative/ true negative + false positive), positive predictive value calculated as (true positive / true positive + false positive), negative predictive value is calculated as (true negative / true negative + false negative).

Results

Fifty patients with ascites with their ages ranging from (34-60) years with a mean age (49.84 ± 7.56) were enrolled In this study the mean for platelets count for all patients was (193.4 ± 118.558) , the main characteristics of patients were demonstrated in table (1).

Out of 25 patients (14 were males and 11 were females) with SAAG more than $1.1g/dl$ and considered to be portal hypertension, 20 (80%) of them had platelets count less than $150 \times 10^9/L$ while 5 (20%) of them had normal platelets count with (p value 0.0002, the measured sensitivity of thrombocytopenia as test for high SAAG (PHT) =(84%, specificity=76%, P.P.V=77%, N.P.V=82%),

which is statistically significant as shown in table (2) .

Out of 25 patients whom SAAG < 1.1g/dl (15 females and 10 males) , only 7 of them (28%) had platelets count <150×10⁹/L and 18 (72%) of them had normal platelet which is statistically significant(p value 0.0002) as in table (2) .

Out of 25 patients having SAAG more than 1.1g/dl, 12(48%) of them had splenomegaly by ultrasound (8 males and ,4 females) (p value 0.00039,the measured sensitivity of splenomegaly as test for high SAAG (PHT)=48%, specificity=96%, P.P.V=92%, N.P.V=64%) and 13(52%) had

no splenomegaly by ultrasound (7 females and 6 males) (p value 0.00039) which is statistically significant as shown in table (3) .

Out of 25 patients with ascites whom had SAAG <1.1g/dl, one patient (4%) had splenomegaly while 24 patients (96%) had no splenomegaly as in table (3) (p value 0.00039).

There was significant relation between the presence of splenomegaly and thrombocytopenia. Of total 13 patients with splenomegaly 12(92.3%) had platelets count <150×10⁹/L, 1(7.69%) had platelets count>150×10⁹/L (P value=0.0012) table (4).

Table (1) : The characteristics and demography of fifty patients with ascites.(SAAG= serum ascetic albumin gradient , PLT=platelet, M= Male, F= Female ,N= Numbers).

Patients characteristic s	SAAG< 1.1 g/dl N=25	SAAG> 1.1 g/dl N=25	PLT< 150×10 ⁹ /L N=27	PLT> 150×10 ⁹ /L N=23	+VE SPLEEN N=13	-VE SPLEEN N=37	TOTAL N=50
SEX M/F	10/15	14/11	14/13	10/13	9/4	15/22	23/27
MEAN AGE (years)± SD	49.16±8.7	50.52±6.34	50.4±6.9	49.13±8.35	49.92±5.9	49.8±8.14	49.84±7.56

Table (2) :The relation of thrombocytopenia to patients with portal hypertension and control group.

Patient group	Platelets <150×10 ⁹ /L	Platelets >150×10 ⁹ /L	Total
SAAG >1.1 g/dl	20	5	25
SAAG <1.1 g/dl	7	18	25
Total	27	23	50

(P values = 0.0002).

Table (3): The relationship between splenic size among patients with portal hypertension and the patients in the control group.

Patient group	Splenomegaly	No Splenomegaly	Total
SAAG >1.1 g/dl	12	13	25
SAAG <1.1 g/dl	1	24	25
Total	13	37	50

(P-value = 0.00039).

Table (4) : The relation between the presence of splenomegaly and the platelet count.

Patient group	Plt <150×10 ⁹ /L	Plt >150×10 ⁹ /L	Total
Splenomegaly	12	1	13
No splenomegaly	15	22	37
Total	27	23	50

(P value=0.0012).

Discussion

This study shows that high percentage (80%) of patients with portal hypertension based on SAAG > 1.1g/dl had thrombocytopenia which is statistically significant, which was correlated to many studies^{20,21}.

Gill⁴ *et al*, found that 83.3% of patient with Portal hypertension and Esophageal Varices had thrombocytopenia, and the level of less than 100×10⁹/L associated with large EV⁴. Tafarel JR *et al*²² showed that Platelet count lower than 92,000×10⁹/L had sensitivity of 65.7%, specificity of 57.9% as predictor of portal hypertension.

Burton *et al*²³ that study the non- invasive predictor of portal hypertension in liver cirrhosis who consider low platelet count as independent factor for esophageal varices (the consequence of portal hypertension) along with other parameters like splenic diameter, ALT/AST and child pugh score.

In 2007, Burton *et al*²³ published the validation of a model for predicting size and presence of varices based upon platelet count and Child- Pugh class. The first model aimed to detect large varices in Child-Pugh A patients with a platelet count <80×10⁹/L and had a sensitivity of 58%, specificity 79%, PPV 30%, and NPV 92%. The second model aimed to identifying any varices in Child B/C patients with a platelet count <90 and had a sensitivity of 60%, specificity of 59%, PPV 80%, and NPV 34%.

The discrepancy between the results here may be due to the difference in the number of sample patients and the cutoff level of the platelet count in various studies.

Barrera *et al*²⁴ calculate that splenomegaly had sensitivity of 75% and specificity of 68.7%. Ehab H. Nashaat *et al*²⁵, calculate that splenomegaly had sensitivity of 82% and specificity of 60% for maximum spleen diameter ratio of >145 mm (the normal diameter 140 mm length, 40mm width)²⁶, the

deference between these studies and this study may be operator dependent sonographer results or due to small sample of patients in this study.

Conclusion

Thrombocytopenia in patient with ascites may predict portal hypertension.

Recommendation

Any patient with ascites should be sent for platelet count in which thrombocytopenia may predict underlying portal hypertension. Further studies to detect correlation of platelet count with esophageal varices and to define the relation with multiple and lower platelet count.

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