


ORIGINAL ARTICLE

# Accuracy of noninvasive tests in the prediction of portal hypertensive gastropathy in Egyptian patients with cirrhosis

Ibrahim F Amer,\* Eslam M El Shennawy,\* Hassan El Batea,\* Mohammed Hussien Ahmed,\* Shimaa El Sharawy<sup>†</sup> and Aya M Mahros\* 

\*Gastroenterology, Hepatology and Infectious Diseases, Faculty of Medicine, Kafrelsheikh University, Kafr el-Sheikh and <sup>†</sup>Tropical Medicine Department, Faculty of Medicine, Tanta University, Tanta, Egypt

## Key words

cirrhosis, noninvasive, portal hypertensive gastropathy, predictors.

Accepted for publication 19 December 2020.

## Correspondence

Aya M Mahros, Gastroenterology, Hepatology and Infectious Diseases, Faculty of Medicine, Kafrelsheikh University, ELGeish street, Kafrelsheikh 3115, Egypt.  
Email: yoye\_85@hotmail.com

**Declaration of conflict of interest:** None.

## Abstract

**Background and Aim:** Liver cirrhosis (LC) is commonly associated with portal hypertensive gastropathy (PHG), and it causes gastrointestinal (GI) bleeding. Esophagogastroduodenoscopy (EGD) is the gold standard in diagnosing PHG. Besides its invasiveness, the disadvantages of EGD include psychological and financial problems. We aimed to evaluate the diagnostic accuracy of different noninvasive screening tools in predicting PHG.

**Methods:** This cross-sectional study was conducted on 100 patients with LC who were divided into two groups based on EGD: group (A), 50 patients with LC with PHG, and group (B), 50 patients with LC without PHG. All patients were subjected to history taking, full clinical examination, laboratory investigations, abdominal–pelvic ultrasonography, and EGD.

**Results:** To predict PHG, the respective sensitivity and specificity of portal vein diameter (>10.5 mm) were 86 and 67%, of gallbladder wall thickness (GBWT) (>3.5 mm) were 64 and 68%, of platelets/GBWT (<40) were 68 and 78%, of aspartate aminotransferase (AST)/platelet ratio index (APRI) score (>1.1) were 60 and 66%, of platelet/spleen diameter (<1290) were 88 and 72%, of right liver lobe diameter/albumin ratio (>4) were 74 and 80%, and of AST/alanine aminotransferase (ALT) ratio (>1.1) were 50 and 58% ( $P = 0.353$ ).

**Conclusion:** Portal vein diameter, platelet/spleen diameter, and right liver lobe diameter/albumin ratio were independently associated with PHG and were good predictors of the PHG, whereas AST/ALT ratio and King score are poor predictors.

## Introduction

In Egypt, liver cirrhosis (LC) is a major cause of morbidity and mortality (0.727/1000).<sup>1</sup> In addition, LC leads to mortality in 18.1% of men aged 45–54 years.<sup>2</sup>

There are several complications of LC, and it leads to decreased life expectancy.<sup>3</sup> LC progresses rapidly to liver decompensation, which is manifested by ascites, spontaneous bacterial peritonitis, variceal bleeding (due to portal hypertension [PHTN]), hepatorenal syndrome, hepatic encephalopathy, liver failure, hepatocellular carcinoma (HCC), and death.<sup>4</sup>

PHTN usually leads to portal hypertensive gastropathy (PHG) and causes hemodynamic and mucosal changes in the entire gastrointestinal (GI) tract,<sup>5</sup> resulting in acute or subacute GI bleeding.<sup>6</sup> Acute upper GI bleeding occurs in 2–12% (up to 95% of patients had severe PHG), and chronic GI bleeding occurs in 3–26% and results in iron deficiency anemia. The mortality rate for PHG bleeding is approximately 12.5%.<sup>7</sup> Compared with patients without PHG or with mild PHG, severe PHG has a higher mortality rate and lower life expectancy.<sup>8</sup>

Esophagogastroduodenoscopy (EGD) is the gold standard in diagnosing PHG. Besides its invasiveness, EGD has other disadvantages, including psychological and financial challenges.<sup>9</sup>

Moreover, not all health-care centers, especially in rural areas, have such a facility. In addition, the competency of health-care providers to perform endoscopy is limited in those areas. These limitations have led many researchers to identify some parameters that can noninvasively predict the presence of PHG to avoid EGD.<sup>10</sup>

Recently, various noninvasive indicators are used to predict esophageal varices,<sup>11</sup> but to the best of our knowledge, this is the first study in Egypt to predict PHG by using noninvasive biomarkers.

This study aimed to evaluate the diagnostic accuracy of different noninvasive screening tools to predict PHG in Egyptian patients with LC and to reduce the use of unnecessary EGD screening to patients with LC without such a risk.

## Methods

This was a cross-sectional study conducted on 100 patients with LC admitted to the Endoscopy Unit at Kafrelsheikh University

for PHG screening from August 2019 to July 2020. The institutional ethical committee approved the study, and all patients signed an informed consent form. We maintained the privacy of participants and confidentiality of the data by providing a special file for each patient, and all research results were used for scientific purposes only.

Exclusion criteria were bleeding disorders; hepatic encephalopathy or coma; patients on prophylactic medications to lower PHTN, such as beta blockers or any medication that could affect platelet count or bilirubin levels; heart failure; renal failure; and HCC.

Patients were classified into two groups: group A, 50 patients with LC with PHG, and group B, 50 patients with LC without PHG.

All patients were subjected to (i) detailed history taking, (ii) full clinical examination, (iii) laboratory investigations (complete blood count [CBC], renal function tests [urea and creatinine], complete liver profile (total bilirubin, serum albumin, alanine aminotransferase [ALT], aspartate transaminase [AST]), prothrombin time and activity, and international normalized ratio [INR]), (iv) abdominal–pelvic ultrasonography (spleen diameter, right liver lobe diameter, portal vein [PV] assessment, and gallbladder [GB] wall thickness [GBWT]), and (v) EGD.

Pugh–Child score, right lobe liver diameter to albumin ratio, AST/ALT ratio, and AST/platelet ratio index (APRI) (AST [times above upper limit of normal]/[platelet count\*100]) were calculated.

### Upper GI tract endoscopy

**Before endoscopy.** Patients fasted for at least 6 h before the procedure after a review of their full laboratory investigations.

**During endoscopy.** The patients underwent the procedure under sedation in the endoscopy unit at the Kafrelsheikh University Hospital after signing the informed consent form for endoscopic intervention.

PHG was classified as mild and severe using the two-grading classification proposed by the Baveno III consensus.

PHG is classified as mild when the only change consists of a snakeskin mosaic pattern, and it is classified as severe when flat or bulging red or black-brown spots are seen in addition to the mosaic pattern and/or the presence of active hemorrhage.<sup>12</sup>

**After endoscopy.** The patients were observed for 2 h in the recovery room before discharge.

**Abdominal ultrasonography.** All patients fasted over the night before the examination. In an attempt to reduce the gas impacting good ultrasound quality, simethicone tablets were administered at least 1 day before examination. All ultrasound examinations were performed in the early morning before endoscopic examination or 1 day earlier.

The following parameters were assessed by ultrasonography:

- Diagnosis of cirrhosis (irregular liver surface, change in the liver echogenicity, nodular contour, caudate/right lobe ratio) and PV parameters.<sup>10</sup>
- GBWT measurement, spleen and PV diameters and patency, ascites, hepatic focal lesions, etc.

**Calculated scores:** The scores calculated included the Child–Pugh score, APRI score, right liver lobe diameter/albumin ratio, platelets/GBWT and platelet/spleen diameter, King score, Lok score, and Liaoning score according to previously published formulas:

- AST to platelets ratio index (APRI) = [(AST/ULN) × 100]/platelet count 109/L (ULN = the upper limit of normal)<sup>13</sup>;
- King score = Age × AST × INR/Platelets.<sup>14</sup>
- Lok score: log odds =  $-5.56 - 0.0089 \times \text{platelet count (103/mm}^3) + 1.26 \times (\text{AST/ALT}) + 5.27 \times \text{INR}$ ; Lok = [exp (log odds)]/[1 + exp (log odds)].<sup>15</sup>
- FIB-4 = (Age × AST)/(Platelets ×  $\sqrt{\text{ALT}}$ ).<sup>14</sup>

Liaoning score =  $0.466 + 1.0889 \times \text{AUGIB (1 = yes; 0 = no)} + 1.1479 \times \text{ascites (1 = yes; 0 = no)} - 0.0129 \times \text{PLT}$ .

**Sample size:** All patients who attended our unit during the study and fulfilled the diagnostic criteria were included.

**Ethics:** This study was performed in accordance with the Declaration of Helsinki, Good Clinical Practice, and applicable regulatory requirements. The study was approved by the faculty ethical committee at the Faculty of Medicine, Kafrelsheikh University.

**Statistical analysis.** Data were analyzed using SPSS v26 (IBM Inc., Chicago, IL, USA). Quantitative parametric variables were presented as mean and SD and compared using unpaired Student's *t*-test. Qualitative variables were presented as frequency (percentage) and compared using the Chi square test. The diagnostic performance of each test was evaluated using receiver operator characteristic curve analysis, and the area under the curve (AUC) was used to evaluate the overall test performance. *P* value <0.05 was considered significant.

## Results

During the study period, 100 patients were enrolled according to the inclusion criteria and underwent PHG screening from August 2019 to July 2020.

**Participant demographics.** Age, gender, and cause of LC were insignificantly different between both groups (*P* = 0.101, 0.383, >0.999) (Table 1).

**Laboratory and sonographic changes in participants.** AST, ALT, bilirubin, and serum creatinine were insignificantly different between both groups (*P* = 0.305, 0.692, 0.528, and 0.699, respectively). INR was significantly increased in group A than group B (*P* < 0.001). Hemoglobin, platelets, total leucocytic count, serum albumin and serum Na were significantly decreased in group A than group B (*P* = 0.003, <0.001, <0.001, <0.001, and 0.003, respectively) (Table 1).

In our study, we found that PV diameter, spleen size, right lobe liver diameter, and GBWT were significantly increased in group A than group B (*P* < 0.001, <0.001, 0.017, and <0.001, respectively). Ascites was present in 14 patients (28%) in group A and in 2 patients (4%) in group B, with a significant difference in *P* value (0.002). There was no statistical significance with regard to the presence of esophageal varices between both groups (Table 1).

**Table 1** Patients' characteristics, laboratory investigations, and ultrasound findings in both groups

|                                 | Group A (n = 50)  | Group B (n = 50)      | P value |
|---------------------------------|-------------------|-----------------------|---------|
| Age (years)                     | 51.44 ± 7.04      | 53.64 ± 6.22          | 0.101   |
| Gender                          |                   |                       |         |
| Male                            | 37 (74%)          | 33 (66%)              | 0.383   |
| Female                          | 13 (26%)          | 17 (34%)              |         |
| Cause of cirrhosis              |                   |                       |         |
| HCV                             | 47 (94%)          | 46 (92%)              | >0.999  |
| Others                          | 3 (6%)            | 4 (8%)                |         |
| Laboratory investigations       |                   |                       |         |
| Hemoglobin (g/L)                | 113.5 ± 6.4       | 117.9 ± 8.1           | 0.003*  |
| Platelets (*10 <sup>9</sup> /L) | 119.8 ± 33 563.31 | 167 170.3 ± 30 689.12 | <0.001* |
| TLC (*10 <sup>9</sup> /L)       | 7.07 ± 1.13       | 7.91 ± 1.06           | <0.001* |
| AST (IU)                        | 61.88 ± 19.13     | 58.1 ± 17.51          | 0.305   |
| ALT (IU)                        | 55.56 ± 19.56     | 54 ± 19.67            | 0.692   |
| Total bilirubin (mmol/L)        | 1.77 ± 0.59       | 1.88 ± 1.10           | 0.528   |
| Serum albumin (g/L)             | 3.28 ± 0.27       | 4.17 ± 0.48           | <0.001* |
| INR                             | 1.62 ± 0.27       | 1.31 ± 0.15           | <0.001* |
| Serum sodium (mmol/L)           | 133.52 ± 4.38     | 137 ± 6.7             | 0.003*  |
| Serum creatinine (mmol/L)       | 156.47 ± 69.8     | 111.38 ± 55.6         | <0.001* |
| Ultrasound findings             |                   |                       |         |
| Portal vein diameter (mm)       | 12.08 ± 1.32      | 9.99 ± 0.95           | <0.001* |
| Spleen size (cm)                | 14.21 ± 1.87      | 11.75 ± 1.18          | <0.001* |
| Right lobe liver diameter (cm)  | 13.54 ± 1.71      | 12.78 ± 1.45          | 0.017*  |
| GBWT (mm)                       | 4.2 ± 1.22        | 3.2 ± 0.81            | <0.001* |
| Ascites                         |                   |                       |         |
| Yes                             | 14 (28%)          | 2 (4%)                | 0.002*  |
| No                              | 36 (72%)          | 48 (96%)              |         |
| Associated esophageal varices   |                   |                       |         |
| Yes                             | 6 (12%)           | 4 (8%)                | 0.505   |
| No                              | 44 (88%)          | 46 (92%)              |         |

\*Significant as *P* value < 0.05.

Data are presented as mean ± SD or frequency (percentage).

ALT, alanine aminotransferase; AST, aspartate aminotransferase; GBWT, gall bladder wall thickness; HCV, hepatitis C virus; TLC, total leucocytic count.

### Calculated scores as non-invasive markers for portal hypertensive gastropathy.

Our study demonstrated that Child–Pugh score, APRI score, right liver lobe diameter/albumin ratio, King score, Lok score, Liaoning score, and fibrosis-4 index (FIB-4) were increased significantly in group A than group B (*P* < 0.001). Platelets/GBWT and platelet/spleen diameter were significantly decreased in group A than group B (*P* < 0.001). AST/ALT ratio was insignificantly different between both groups (*P* = 0.338) (Table 2).

### Comparison between scores and ultrasound findings in mild and severe cases of portal hypertensive gastropathy group.

In this study, we found that right liver lobe diameter/albumin ratio, King score, Lok score, and Liaoning score were significantly increased in group A than group B (*P* = 0.001, 0.026, 0.011, and < 0.001 respectively). Platelets/GBWT and platelet/spleen diameter were significantly decreased in the severe group than the mild group (*P* < 0.001). Child–Pugh score, APRI score, and AST/ALT ratio were insignificantly different between the mild and severe groups (*P* = 0.793, 0.243, and 0.338, respectively) (Table 3).

**Table 2** Scores in both groups

|   | Group A (n = 50) | Group B (n = 50) | P value |
|---|------------------|------------------|---------|
| Platelet/GBWT                           | 31.49 ± 13.33    | 56.11 ± 20.8     | <0.001* |
| Child–Pugh child score                  |                  |                  |         |
| 5                                       | 5 (10%)          | 32 (64%)         | <0.001* |
| ≥6                                      | 45 (90%)         | 18 (36%)         |         |
| APRI score                              | 1.4 ± 0.66       | 0.91 ± 0.34      | <0.001* |
| Platelet/spleen diameter                | 873.54 ± 334.4   | 1438.41 ± 320    | <0.001* |
| Right lobe liver diameter/albumin ratio | 4.15 ± 0.61      | 3.12 ± 0.3       | <0.001* |
| AST/ALT ratio                           | 1.23 ± 0.51      | 1.14 ± 0.35      | 0.338   |
| King score                              | 47.77 ± 28.59    | 25.88 ± 11.12    | <0.001* |
| Lok score                               | 0.92 ± 0.10      | 0.75 ± 0.15      | <0.001* |
| Liaoning score                          | 0.56 ± 0.08      | 0.45 ± 0.08      | <0.001* |
| FIB 4                                   | 4.01 ± 2.02      | 2.68 ± 0.87      | <0.001* |

\*Significant if *P* value < 0.05.

Data are presented as mean ± SD or frequency (percentage).

APRI, aspartate aminotransferase to platelet ratio index; GBWT, gall bladder wall thickness.

In this study, we found that PV diameter, spleen size, and GBWT were significantly increased in the severe group than the mild group ( $P < 0.001$ ,  $<0.001$ , and  $0.003$ , respectively) (Table 3).

With regard to PV diameter, using a cut-off  $>10.5$  mm to predict PHG, sensitivity was 86%, specificity was 67%, positive predictive value (PPV) was 72.9%, negative predictive value (NPV) was 82.9%, AUC was 0.890, and  $P$  value was  $<0.001$  (Table 4 and Fig. 1).

Our study showed that for GBWT, using a cut-off  $>3.5$  mm to predict PHG, sensitivity was 64%, specificity was 68%, PPV was 66.7%, NPV was 65.4%, AUC was 0.736, and  $P$  value was  $<0.001$  (Table 4).

**Table 3** Scores and ultrasound findings in mild and severe cases of portal hypertensive gastropathy group

|   | Mild group<br>( $n = 21$ ) | Severe group<br>( $n = 29$ ) | $P$ value  |
|---|----------------------------|------------------------------|------------|
| Scores                                  |                            |                              |            |
| Platelet/GBWT                           | 34.31 ± 9.55               | 24.69 ± 12.59                | 0.003*     |
| Pugh child score                        |                            |                              |            |
| 5                                       | 13 (61.9%)                 | 19 (65.5%)                   | 0.793      |
| ≥6                                      | 8 (38.1%)                  | 10 (34.5%)                   |            |
| APRI score                              | 1.38 ± 0.56                | 1.59 ± 0.68                  | 0.243      |
| Platelet/spleen diameter                | 895.33 ± 227.31            | 727.31 ± 226.96              | $<0.001$ * |
| Right lobe liver diameter/albumin ratio | 3.56 ± 0.766               | 4.24 ± 0.57                  | 0.001*     |
| AST/ALT ratio                           | 1.35 ± 0.75                | 1.29 ± 0.45                  | 0.338      |
| King score                              | 44.43 ± 23.19              | 61.22 ± 28.25                | 0.026*     |
| Lok score                               | 0.897 ± 0.121              | 0.969 ± 0.33                 | 0.011*     |
| Liaoning score                          | 0.520 ± 0.067              | 0.625 ± 0.052                | $<0.001$ * |
| Ultrasound findings                     |                            |                              |            |
| Portal vein diameter (mm)               | 11.27 ± 1.19               | 12.68 ± 1.08                 | $<0.001$ * |
| Spleen size (cm)                        | 11.96 ± 1.89               | 13.79 ± 1.32                 | $<0.001$ * |
| GBWT (mm)                               | 3.91 ± 1.06                | 4.9 ± 1.15                   | 0.003*     |

\*Significant as  $P$  value  $< 0.05$ .

APRI, aspartate aminotransferase to platelet ratio index; GBWT, gall bladder wall thickness.

Our study revealed that for platelets/GBWT, using a cut-off  $<40$  to predict PHG, sensitivity was 68%, specificity was 78%, PPV was 75.6%, NPV was 70.9%, AUC was 0.861, and  $P$  value was  $<0.001$ .

With regard to APRI score, using a cut-off  $>1.1$  to predict PHG, sensitivity was 60%, specificity was 66%, PPV was 63.8%, NPV was 62.3%, AUC was 0.738, and  $P$  value was  $<0.001$  (Table 4 and Fig. 1).

With regard to platelet/spleen diameter, using a cut-off  $<1290$  to predict PHG, sensitivity was 88%, specificity was 72%, PPV was 75.9%, NPV was 85.7%, AUC was 0.884, and  $P$  value was  $<0.001$  (Table 4 and Fig. 1).

With regard to right liver lobe diameter/albumin ratio, using a cut-off  $>4$  to predict PHG, sensitivity was 74%, specificity was 80%, PPV was 78.7%, NPV was 75.5%, AUC was 0.874, and  $P$  value was  $<0.001$  (Table 4 and Fig. 1).

Our result demonstrated that for AST/ALT ratio, using a cut-off  $>1.1$  to predict PHG, sensitivity was 50%, specificity was 58%, PPV was 54.3, NPV was 53.7, AUC was 0.554, and  $P$  value was 0.353 (Table 4).

Regarding the Liaoning Score, using a cut-off  $>0.483$  to predict PHG, sensitivity was 78%, specificity was 60%, PPV was 66.1%, NPV was 73.2%, AUC was 0.828, and  $P$  value was  $<0.001$ .

For the Lok score, using a cut-off  $>0.88$  to predict PHG, sensitivity was 76%, specificity was 74%, PPV was 74.5%, NPV was 75.5%, AUC was 0.872, and  $P$  value was  $<0.001$ .

With regard to King score, using a cut-off  $>28.4$  to predict PHG, sensitivity was 64%, specificity was 50%, PPV was 56.1%, NPV was 58.1%, AUC was 0.747, and  $P$  value was  $<0.001$ .

With regard to FIB-4 score, using a cut-off  $>3.3$  to predict PHG, sensitivity was 64%, specificity was 72%, PPV was 69.6%, NPV was 66.7%, AUC was 0.769, and  $P$  value was  $<0.001$ .

**Logistic regression analysis of scores for detection of portal hypertensive gastropathy.**

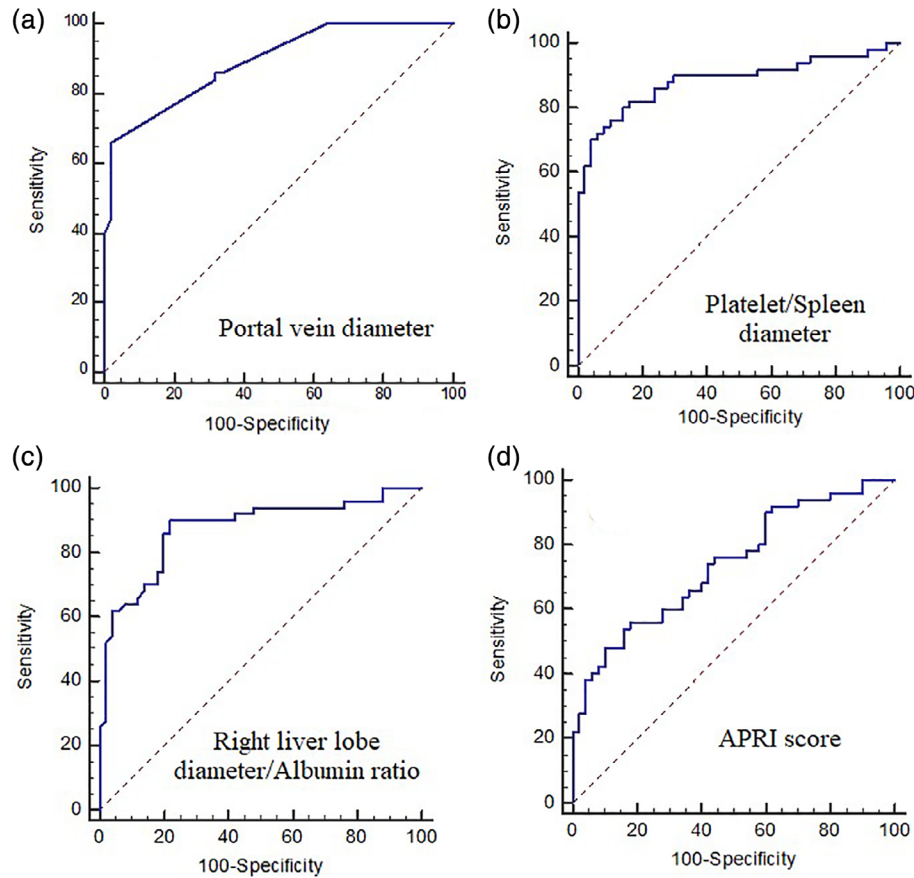
In all patients, univariate logistic regression analyses demonstrated that PV diameter, platelets/GBWT, platelet/spleen diameter, right

**Table 4** Comparison of serum markers for detection of portal hypertensive gastropathy

|   | Cut-off    | Sensitivity (%) | Specificity (%) | PPV (%) | NPV (%) | AUC   | $P$ value  |
|---|------------|-----------------|-----------------|---------|---------|-------|------------|
| Portal vein diameter                    | $>10.5$ mm | 86              | 67              | 72.9    | 82.9    | 0.890 | $<0.001$ * |
| GBWT                                    | $>3.5$ mm  | 64              | 68              | 66.7    | 65.4    | 0.736 | $<0.001$ * |
| Platelets/GBWT                          | $<40$      | 68              | 78              | 75.6    | 70.9    | 0.861 | $<0.001$ * |
| APRI score                              | $>1.1$     | 60              | 66              | 63.8    | 62.3    | 0.738 | $<0.001$ * |
| Platelet/Spleen diameter                | $<1290$    | 88              | 72              | 75.9    | 85.7    | 0.884 | $<0.001$ * |
| Right liver lobe diameter/Albumin ratio | $>4$       | 74              | 80              | 78.7    | 75.5    | 0.874 | $<0.001$ * |
| AST/ALT ratio                           | $>1.1$     | 50              | 58              | 54.3    | 53.7    | 0.554 | 0.353      |
| Liaoning Score                          | $>0.483$   | 78              | 60              | 66.1    | 73.2    | 0.828 | $<0.001$ * |
| Loke score                              | $>0.88$    | 76              | 74              | 74.5    | 75.5    | 0.872 | $<0.001$ * |
| King score                              | $>28.4$    | 64              | 50              | 56.1    | 58.1    | 0.747 | $<0.001$ * |
| FIB-4 score                             | $>3.3$     | 64              | 72              | 69.6    | 66.7    | 0.769 | $<0.001$ * |

\*Significant if  $P$  value  $<0.05$ .

ALT, Alanine aminotransferase; APRI, aspartate aminotransferase to platelet ratio index; AST, aspartate aminotransferase; AUC, area under the curve; GBWT, gall bladder wall thickness; NPV, negative predictive value; PPV, positive predictive value.



**Figure 1** Receiver operator curve (ROC) curves of portal vein diameter, platelet/spleen, and right lobe to albumin ratio aspartate aminotransferase/platelet ratio index score for detection of portal hypertensive gastropathy. AUC were 0.890, 0.884, 0.874, and 0.738.

**Table 5** Logistic regression analysis of scores for detection of portal hypertensive gastropathy

|   | Univariate analysis |             |         | Multivariate analysis |             |         |
|---|---------------------|-------------|---------|-----------------------|-------------|---------|
|   | OR                  | 95% CI      | P value | OR                    | 95% CI      | P value |
| Portal vein diameter                    | 0.199               | 0.105–0.376 | <0.001* | 0.441                 | 0.219–0.838 | <0.001* |
| GBWT                                    | 0.630               | 0.199–1.148 | 0.192   |                       |             |         |
| Platelets/GBWT                          | 1.145               | 1.084–1.209 | <0.001  | 1.015                 | 0.944–1.091 | 0.684   |
| APRI score                              | 0.420               | 0.004–1.015 | 0.417   |                       |             |         |
| Platelet/Spleen diameter                | 1.008               | 1.005–1.011 | <0.001* | 1.008                 | 1.003–1.012 | <0.001* |
| Right liver lobe diameter/Albumin ratio | 0.117               | 0.040–0.284 | <0.001* | 0.172                 | 0.056–0.531 | 0.002*  |
| AST/ALT ratio                           | 0.301               | 0.107–1.118 | 0.240   |                       |             |         |
| Liaoning score                          | 0.001               | 0.001–0.002 | <0.001* | 0.612                 | 0.391–1.114 | 0.721   |
| Lok score                               | 0.521               | 0.109–1.004 | 0.086   |                       |             |         |
| King score                              | 0.923               | 0.838–1.029 | 0.109   |                       |             |         |
| FIB-4 score                             | 0.420               | 0.114–1.027 | 0.267   |                       |             |         |

\*Significant if P value < 0.05.

ALT, alanine aminotransferase; APRI, aspartate aminotransferase to platelet ratio index; AST, aspartate aminotransferase; CI, confidence interval; GBWT, gall bladder wall thickness; OR, odds ratio.

liver lobe diameter/albumin ratio, and Liaoning score were significantly associated with PHG. Multivariate logistic regression analyses showed that PV diameter, platelet/spleen diameter, and right liver lobe diameter/albumin ratio were independently associated with PHG (Table 5).

## Discussion

PHG is an LC complication that leads to gastric mucosa changes. By using endoscopy, PHG is found in the gastric fundus and body and is seen as a “snakeskin-like appearance.”<sup>16</sup>

EGD is an invasive technique with several complications. Therefore, the use of noninvasive markers or techniques for the prediction of PHG is needed.<sup>9</sup>

Platelet count was significantly decreased in group A. Of the many mechanisms for thrombocytopenia in patients with PHTN, the main mechanism is splenic sequestration and pooling.<sup>17</sup>

In agreement with our results, Fontana *et al.*<sup>17</sup> and Ahmed *et al.*<sup>18</sup> showed that lower serum albumin and platelet were independent predictors of PHG. Tsaknakis *et al.*,<sup>19</sup> González-Ojeda *et al.*,<sup>20</sup> Esmat *et al.*,<sup>21</sup> and Nashaat *et al.*<sup>4</sup> also showed that platelet was significantly decreased in the esophageal varices (EV) group.

In our study, INR was significantly increased in group A. This was in line with Tsaknakis *et al.*<sup>19</sup> and Nashaat *et al.*,<sup>4</sup> who showed that INR was significantly higher with EV. AST and ALT were also insignificantly different between both groups, which was in line with Ahmed *et al.*<sup>18</sup> In addition, serum albumin was significantly decreased in group A, which was in line with Ahmed *et al.*<sup>18</sup>

In our study, portal vein diameter, spleen size, right lobe liver diameter, GBWT, and Child–Pugh score were significantly increased in group A, and platelets/GBWT was significantly decreased in group A. This was in line with Tsaknakis *et al.*,<sup>19</sup> who demonstrated that Child–Pugh Score, GBWT, spleen diameter, and portal vein diameter were significantly higher in the EV group. Moreover, Ahmed *et al.*<sup>18</sup> showed that Child pugh score, portal vein diameter, and spleen size were significantly increased among patients with PHG. Moreover, Nashaat *et al.* (2010)<sup>4</sup> showed that portal vein diameter and spleen size were higher in cases with esophageal varices. González-Ojeda *et al.*<sup>20</sup> and Esmat *et al.*<sup>21</sup> also showed that spleen diameters were significantly higher in the EV group.

In our study, right liver lobe diameter/albumin ratio were increased significantly in group A, and platelet/spleen diameter was significantly lower in group A.

In agreement with our results, Esmat *et al.*<sup>21</sup> and Nashaat *et al.*<sup>4</sup> showed that the values of right liver lobe diameter/albumin were significantly decreased with EV group.

In our study, PVD at a cut-off >10.5 mm can predict PHG significantly ( $P$  value <0.001), where sensitivity was 86%, specificity was 67%, PPV was 72.9%, NPV was 82.9%, and AUC was 0.890. This was in line with Nashaat *et al.*<sup>4</sup> who found that portal vein diameter (PVD) at a cut-off >13.5 mm can predict OV with 80% sensitivity and 55% specificity.

In our work, GBWT at a cut-off of >3.5 mm predicted PHG significantly ( $P$  < 0.001), with a sensitivity of 64%, specificity of 68%, PPV of 66.7%, NPV of 65.4, and AUC of 0.736.

GB is drained by small veins directly into the liver and cystic duct and then with vessels from the common bile duct, terminating in the portal venous system.<sup>22</sup> Due to the impairment in venous drainage, GBWT increases as an effect of PHTN.<sup>17</sup> This was in line with Tsaknakis *et al.*,<sup>19</sup> who showed that GBWT significantly predicted EV at a cut-off of  $\geq 4$  mm, with 46% sensitivity, 89% specificity, 70% PPV, and 73% NPV.

In our study, platelet/GBWT predicted PHG significantly at a cut-off of <40, with a sensitivity of 68%, specificity of 78%, PPV of 75.6%, NPV of 70.9%, AUC of 0.861, and  $P$  < 0.001. This was in the same line as Tsaknakis *et al.*,<sup>19</sup> who demonstrated that platelet/GBWT predicted EV significantly at a cut-off of > 46.2, with 78% sensitivity, 86% specificity, 76% PPV, 87% NPV, and an AUC of 0.864.

In our study, APRI score predicted PHG significantly at a cut-off >1.1, with 60% sensitivity, 66% specificity, 63.8% PPV, 62.3% NPV, AUC of 0.738, and  $P$  value of <0.001.

This was in line with Sebastiani *et al.*,<sup>23</sup> who showed that APRI score at a cut-off of >1.5 can predict PHG, with a sensitivity of 56.9%, specificity of 56.5%, PPV of 35.4%, NPV of 75.8%, and AUC of 0.57.

In our study, platelet/spleen diameter at a cut-off <1290 can predict PHG significantly ( $P$  value <0.001), where sensitivity was 88, specificity was 72, PPV was 75.9, NPV was 85.7, and AUC was 0.884. Splenomegaly is prevalent in patients with LC and PHTN.<sup>23</sup>

Mandhwani *et al.*<sup>9</sup> showed that the diagnostic accuracy of platelet/spleen diameter at a cut-off  $\leq 1326.58$  in the detection of PHG in patients with LC had 87.23% sensitivity, 5.88% specificity, 83.67% PPV, and 7.69% NPV. In this cross-sectional study, 111 patients aged 18–65 years who were screened using EGD to exclude EV were enrolled.

In addition, González-Ojeda *et al.*<sup>20</sup> showed that the diagnostic accuracy of platelet/spleen diameter to detect EV at a cut-off point >884 had 84% sensitivity, 70% specificity, 94% PPV, 40% NPV, and an AUC of 0.802.

In agreement with our results, Esmat *et al.*<sup>21</sup> showed that the platelet/spleen diameter at a cut-off 1326.6 can predict EV with 96.3% sensitivity, 83.3% specificity, 96.3% PPV, and 83.3% NPV.

In our study, right liver lobe diameter/albumin ratio at cut-off >4 can predict PHG significantly ( $P$  value <0.001), where sensitivity was 74, specificity was 80, PPV was 78.7, NPV was 75.5, and AUC was 0.874.

In agreement with our results, Esmat *et al.*<sup>21</sup> showed that the right liver lobe diameter/albumin ratio at a cut-off 4.442 can predict EV with 91.46% sensitivity, 77.78% specificity, 94.94% PPV, and 66.67% NPV. In addition, Mandhwani *et al.*<sup>9</sup> showed that the diagnostic accuracy of right liver lobe diameter/albumin ratio at a cut-off  $\geq 4.422$  for the detection of PHG in patients with LC had 28.72% sensitivity, 70.59% specificity, 84.38% PPV, and 15.19% NPV. Unlike our results, Alempijevic *et al.*<sup>24</sup> showed that the right liver lobe diameter/albumin ratio at a cut-off  $\geq 4.425$  for the presence of EV had 83.1% sensitivity and 73.9% specificity.

In our study, AST/ALT ratio at a cut-off >1.1 predicted PHG poorly ( $P$  = 0.353), where sensitivity was 50%, specificity was 58%, PPV was 54.3, NPV was 53.7, and AUC was 0.554. In agreement with our results, Kraja *et al.*<sup>25</sup> demonstrated that no association was found between esophageal varices and AST/ALT ratio and AST/ALT at a cut-off 1.71, with 59% sensitivity, 54% specificity, and an AUC of 0.53. This could be attributable to the effect of several variables on serum ALT, such as gender and body mass index, as well as hepatotoxic medications, which subsequently affect AST/ALT results.<sup>26</sup>

In our study, for the Liaoning score at a cut-off >0.483 used to predict PHG, sensitivity was 78%, specificity was 60%, PPV was 66.1%, NPV was 73.2%, AUC was 0.828, and  $P$  value was <0.001.

This was close to the results of Qi *et al.*,<sup>15</sup> who showed that the best cut-off value for the Liaoning score was >0.474, with a sensitivity of 70%, a specificity of 77.67%, a PPV of 88.8%, and an NPV of 50.6%.

In our study, for the Lok score at a cut-off >0.88, used to predict PHG, sensitivity was 76%, specificity was 74%, PPV was

74.5%, NPV was 75.5%, AUC was 0.872, and *P* value was <0.001.

This was in agreement with Sungkar *et al.*,<sup>27</sup> who showed that Lok score with a cut-off point of >0.9141 was highly predictive in the diagnosis of large EVs with a sensitivity of 74.5%, specificity of 72%, PPV of 84%, and NPV 58%. However, this was in disagreement with Sebastiani *et al.*,<sup>23</sup> who showed that for the Lok score at a cut-off >1.5, used to predict PHG, sensitivity was 71.3%, specificity was 68.3%, PPV was 50%, NPV was 84.2%, and AUC was 0.42. In addition, Farid K and his colleague mentioned that the combination of Lok index and Forns' index had an AUC of 0.80 with 90% NPV to exclude large OV or small OV.<sup>26</sup>

In our study, for the King score at a cut-off >28.4, used to predict PHG, sensitivity was 64%, specificity was 50%, PPV was 56.1%, NPV was 58.1%, AUC was 0.747, and *P* value was <0.001.

This was not in line with Kamel *et al.*,<sup>28</sup> who showed that the King score at a cut-off value of 12.11 could detect the presence of EVs with a sensitivity of 88.33% and specificity of 90%.

In our study, for the FIB-4 score at a cut-off >3.3, used to predict PHG, sensitivity was 64%, specificity was 72%, PPV was 69.6%, NPV was 66.7%, AUC was 0.769, and *P* value was <0.001.

This was in line with Sebastiani *et al.*,<sup>23</sup> who showed that for the FIB-4 score at a cut-off >4.3, used to predict PHG, sensitivity was 70.7%, specificity was 55.7%, PPV was 40.3%, NPV was 81.8%, and AUC was 0.53. In addition, Kamel *et al.*<sup>28</sup> showed that FIB-4 at a cut-off of 2.1 was used to predict the existence of EVs and demonstrated a sensitivity of 85%, a specificity of 83.3%, a PPV of 91%, and an NPV of 73.5%.

A limitation of this study was that the number of participants was relatively small.

On the other hand, we believe that some points in the methodology overcome some limitations in the previous studies. First, the same experienced hepatologists examined patients after at least one night of complete fasting. Second, both sonography and endoscopy were performed in the same day, limiting over-time changes in endoscopy and personnel changes in the sonographic findings. Third, we studied patients in a cross-sectional fashion and sometimes prospectively; consequently, we did not miss many of the important clinical and laboratory parameters. In conclusion, PV diameter, platelet/spleen diameter, and right liver lobe diameter/albumin ratio were independently associated with PHG and were good predictors of the PHG, whereas AST/ALT ratio and King score are poor predictors.

## Acknowledgment

To our families.

## References

- Wang H, Dwyer-Lindgren L, Lofgren KT *et al.* Age-specific and sex-specific mortality in 187 countries, 1970–2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet.* 2012; **380**: 2071–94.
- Mokdad AA, Lopez AD, Shahraz S *et al.* Liver cirrhosis mortality in 187 countries between 1980 and 2010: a systematic analysis. *BMC Med.* 2014; **12**: 145.
- Buti M, Fung S, Gane E *et al.* Long-term clinical outcomes in cirrhotic chronic hepatitis B patients treated with tenofovir disoproxil fumarate for up to 5 years. *Hepatol. Int.* 2015; **9**: 243–50.
- Nashaat EH, Abd-Elaziz H, Sabry M, Ibrahim A. Non-endoscopic predictors of esophageal varices and portal hypertensive gastropathy. *Nat. Sci.* 2010; **8**: 43–50.
- Heidelbaugh JJ, Bruderly M. Cirrhosis and chronic liver failure: part I. Diagnosis and evaluation. *Am. Fam. Physician.* 2006; **74**: 756–62.
- Primignani M, Carpinelli L, Preatoni P *et al.* Natural history of portal hypertensive gastropathy in patients with liver cirrhosis. The New Italian Endoscopic Club for the study and treatment of esophageal varices (NIEC). *Gastroenterology.* 2000; **119**: 181–7.
- Elgharably A, Gomaa AI, Crossey MM, Norsworthy PJ, Waked I, Taylor-Robinson SD. Hepatitis C in Egypt - past, present, and future. *Int. J. Gen. Med.* 2017; **10**: 1–6.
- Giannini E, Botta F, Borro P *et al.* Platelet count/spleen diameter ratio: proposal and validation of a non-invasive parameter to predict the presence of oesophageal varices in patients with liver cirrhosis. *Gut.* 2003; **52**: 1200–5.
- Mandhwani R, Hanif FM, Ul Haque MM, Wadhwa RK, Hassan Luck N, Mubarak M. Noninvasive clinical predictors of portal hypertensive gastropathy in patients with liver cirrhosis. *J. Transl. Int. Med.* 2017; **5**: 169–73.
- de Franchis R. Evolving consensus in portal hypertension. Report of the Baveno IV consensus workshop on methodology of diagnosis and therapy in portal hypertension. *J. Hepatol.* 2005; **43**: 167–76.
- Sherman DI, Jagtiani M, Shorvon P. Noninvasive predictors of portal hypertension. *Gastroenterology.* 2013; **144**: 1150–1.
- Wai CT, Greenson JK, Fontana RJ *et al.* A simple noninvasive index can predict both significant fibrosis and cirrhosis in patients with chronic hepatitis C. *Hepatology.* 2003; **38**: 518–26.
- Cross TJ, Rizzi P, Berry PA, Bruce M, Portmann B, Harrison PM. King's Score: an accurate marker of cirrhosis in chronic hepatitis C. *Eur. J. Gastroenterol. Hepatol.* 2009; **21**: 730–8.
- Lok AS, Ghany MG, Goodman ZD *et al.* Predicting cirrhosis in patients with hepatitis C based on standard laboratory tests: results of the HALT-C cohort. *Hepatology.* 2005; **42**: 282–92.
- Qi X, Li Y, Wang R *et al.* Liaoning score for prediction of esophageal varices in cirrhotic patients who had never undergone endoscopy: a multicenter cross-sectional study in Liaoning Province, China. *Adv. Ther.* 2019; **36**: 2167–78. <https://doi.org/10.1007/s12325-019-00967-w>. Epub 2019 May 15. Erratum in: *Adv Ther.* 2019 Jun 24; PMID: 31093864.
- Thomopoulos KC, Labropoulou-Karatzas C, Mimidis KP, Katsakoulis EC, Ionomou G, Nikolopoulou VN. Non-invasive predictors of the presence of large oesophageal varices in patients with cirrhosis. *Dig. Liver Dis.* 2003; **35**: 473–8.
- Fontana RJ, Sanyal AJ, Mehta S *et al.* Portal hypertensive gastropathy in chronic hepatitis C patients with bridging fibrosis and compensated cirrhosis: results from the HALT-C trial. *Am. J. Gastroenterol.* 2006; **101**: 983–92.
- Ahmed S, Mumtaz K, Ahmed US *et al.* Frequency and characteristic features of portal hypertensive gastropathy in patients with viral cirrhosis. *J. Coll. Physicians Surg. Pak.* 2010; **20**: 714–8.
- Tsaknakis B, Masri R, Amanzada A *et al.* Gall bladder wall thickening as non-invasive screening parameter for esophageal varices - a comparative endoscopic - sonographic study. *BMC Gastroenterol.* 2018; **18**: 123.
- González-Ojeda A, Cervantes-Guevara G, Chávez-Sánchez M *et al.* Platelet count/spleen diameter ratio to predict esophageal varices in Mexican patients with hepatic cirrhosis. *World J. Gastroenterol.* 2014; **20**: 2079–84.
- Esmat S, Omarn D, Rashid L. Can we consider the right hepatic lobe size/albumin ratio a noninvasive predictor of oesophageal varices in

- hepatitis C virus-related liver cirrhotic Egyptian patients? *Eur. J. Intern. Med.* 2012; **23**: 267–72.
- 22 Way L, Pellegrini C. *Surgery of the Gall Bladder and Bile Ducts*. Philadelphia, PA: Saunders, 1987.
- 23 Sebastiani G, Tempesta D, Fattovich G *et al.* Prediction of oesophageal varices in hepatic cirrhosis by simple serum non-invasive markers: results of a multicenter, large-scale study. *J. Hepatol.* 2010; **53**: 630–8.
- 24 Alempijevic T, Bulat V, Djuranovic S *et al.* Right liver lobe/albumin ratio: contribution to non-invasive assessment of portal hypertension. *World J. Gastroenterol.* 2007; **13**: 5331–5.
- 25 Kraja B, Mone I, Akshija I, Koçollari A, Prifti S, Burazeri G. Predictors of esophageal varices and first variceal bleeding in liver cirrhosis patients. *World J. Gastroenterol.* 2017; **23**: 4806–14.
- 26 Farid K, Omran MM, Farag RE, Arafa MM, Emran TM. Development and evaluation of a novel score for prediction of large oesophageal varices in patients with hepatitis c virus-induced liver cirrhosis. *Br. J. Biomed. Sci.* 2017; **74**: 138–43.
- 27 Sungkar I, Dairi LB, Siregar GA. Correlation between esophageal varices and lok score as a non-invasive parameter in liver cirrhosis patients. *Indones. J. Gastroenterol. Hepatol. Dig. Endosc.* 2016; **17**: 83.
- 28 Kamel AA, Ibrahim HM, Alaa FA, Ahmed GF. Assessment of different non-invasive score modalities in prediction of esophageal varices in patients with liver cirrhosis. *Zagazig Univ. Med. J.* 2019; **25**: 261–8.