Evaluation of PAPAS index (Platelet/Age/ Phosphatase/ AFP/ AST) as a Predictor for Esophagogastric Varices in HCVrelated Cirrhotic Patients

Thesis

Submitted for partial fulfillment of Master Degree in Tropical Medicine

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List of Abbreviations

Abb.	Meaning
AASLD	American Association for the Study of Liver Disease
AFP	Alp[ha Feto Protein
ALP	Alkaline phosphatase
ALT	Alanine Transaminase
APGA	AST/Platelet/GGT/AFP
APRI	Aspartate transaminase-to-Platelet Ratio Index
ARFI	Acoustic Radiation Force Impulse Imaging
AST	Aspartate Transaminase
AUC	Area Under The Curve
AUROC	Area Under The Receiving Operating Characteristics
BUN	Blood Urea Nitrogin
CBC	Complete Blood Count
CHC	Chronic Hepatitis C
CSPH	Clinically Significant Portal Hypertension
CT	Computed Tomography
CTP	Child-Turcotte-Pugh score
DA	Diagnostic Accuracy
DIA	Digital-Image Analysis
ECM	Extracellular Matrix
EGD	Esophagogastroduodenoscopy
ESR	Erythrocyte Sedimentation Rat
EV	Esophageal Varices
EVL	Endoscopic Variceal Ligation
FHVP	Free Hepatic Venous Pressure
GAVE	Gastric Antral Vascular Ectasia
GERD	Gastro Esophageal Reflux Disease

List of Abbreviations

Abb.	Meaning
GI	Gastrointestinal
GOV	Gastroesophageal Varices
GV	Gastric Varices
HB	Hemoglobin
HBV	Hepatitis B Virus
HBVsAg	Hepatitis B Virus surface antigen
HCV	Hepatitis C Virus
HCVAb	Hepatitis CVirus antibody
HCC	Hepatocellular Carcinoma
HREV	High Risk Esophageal Varices
HS	High Significant
HVPG	Hepatic Venous Pressure Gradient
IGV	Isolated Gastric Varices
INR	International Normalized Ratio
IVC	Inferior Vena Cava
LC	Liver Cell
LOV	Large Osephageal Varices
LS	Liver Stiffness
MLP	Mosaic Like Pattern
MMPs	Matrix Metalloproteinases
MRE	Magnetic Resonance Imaging Elastography
MRI	Magnetic Resonance Imaging
NASH	Non-Alcoholic Steatohepatitis
NIEC	North Italian Endoscopic Club
NPV	Negative Predictive Value

List of Abbreviations

Abb.	Meaning
NSAIDs	Non-Steroidal Anti-Inflammatory Drugs
OGD	Oesophago gastro duodenopathy
OV	Oesophageal Varices
P/A ratio	Platelet count/spleen Area ratio
P/D ratio	Platelet count/spleen Diameter ratio
PBC	Primary Biliary Cirrhosis
PHG	Portal Hypertensive Gastropathy
PPG	Portal Pressure Gradient
PPV	Positive Predictive Value
PT	Prothrombin Time
PTFE	Polytetrafluoroethylene
PV	Portal Vein
PVD	Portal Vein Diameter
PVT	Portal Vein Thrombosis
ROC	Receiver Operator Characteristics
S	Significant
S. Alb	Serum Albumin
S.creat	Serum creatinine
S.K	Serum Potassium level
S.Na	Serum Sodium level
SEMS	Self-Expandable Metal Stents
SV	Splenic Vein
TB	Total Bilirubin
TE	Transient Elastography
TIMPs	Tissue Inhibitor of Metalloproteinase
TIPS	Transjugular Intrahepatic Portosystemic Shunt

List of Abbreviations

Abb.	Meaning
US	Ultrasonography
ULN	Upper Limit of Normal
VBL	Variceal Band Ligation
VEGF	Vascular Endothelial Growth Factor
VHS	Very Highly Significant
WBCs	White Blood Cells
WHVP	Wedged Hepatic Venous Pressure

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Protocol of Thesis

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Introduction

Portal hypertension commonly accompanies the presence of liver cirrhosis, and the development of esophageal varices (EV) is one of its major complications. The prevalence of esophageal varices in cirrhotic patients ranges between 24% and 69% according to the degree of liver dysfunction ***(De Franchis and Primignani, 2001).*** The incidence of EV development is approximately 5% per year in patients with cirrhosis and the progression from small to large varices occur in 10% to 20% of cases after 1 year ***(De Franchis, 2003).*** In Egypt, it was found that the incidence of varices among portal hypertension patients was 77% ***(Hunter et al., 1998).***

Variceal haemorrhage occurs in 25 to 40% of patients with cirrhosis and varices ***(Grace, 1992),*** the frequency of bleeding from large varices is 30%-53% compared with 5%-18% for small varices ***(De Franchis, 2003).*** Bleeding esophageal varices is the most common cause of upper GI haemorrhage in Egypt as it represented 53.3% of total bleeding cases ***(Esmat et al., 2004).***

The mortality from each episode of variceal bleeding is estimated to be 17-57 % ***(Jensen, 2002).*** Within the first two years of detection of varices, the incidence of the first attack of bleeding ranges from 20 to 40 % of all cases. This makes the prevention of esophageal variceal bleeding is the cornerstone of long-term management of patients with liver cirrhosis ***(D'Amico et al., 2001).***

The American Association for the Study of Liver Disease (AASLD) and the Baveno V Consensus Conference on portal hypertension recommended that cirrhotic patients should be screened by esophago-gastro-duodenoscopy (EGD) for the presence of EV when liver cirrhosis is diagnosed ***(Garcia-Tsao et al., 2007 and De Franchis, 2010).***

In addition, repeated EGD is recommended at 3 year intervals in patients without varices and compensated cirrhosis and at 2 year intervals in patients with small varices so as to evaluate the development or progression of this feature. Furthermore, if there is evidence of hepatic decompensation, EGD should be repeated annually ***(De Franchis, 2000).***

These recommendations imply a considerable burden on endoscopies and related costs as they require that patients repeatedly undergo an unpleasant invasive procedure, even though the majority of subjects undergoing screening EGD either do not have varices or have varices that do not require prophylactic therapy ***(D'Amico and Morabito, 2004).*** On the other hand, many patients refuse repeated endoscopies because of discomfort and fear of transmission of or contribution to infection as it is associated with disruption of the natural barriers ***(Bosch et al., 2003).*** Moreover, sedation of a cirrhotic patient to perform endoscopy may be hazardous ***(McGuire, 2001).***Therefore, considerable interest in developing models to predict the presence of esophageal varices especially high risk varices by non-endoscopic methods.

The PAPAS index, a newly-designed predictive model using routinely-available clinical parameters has moderate diagnostic utility for the prediction of fibrosis in patients CHC and the diagnostic accuracy of PAPAS was equal to that of other noninvasive markers ***(Ozel et al, 2015).***

Aim of the Work

The aim of this study is to evaluate the usefulness of PAPAS index (Platelet/Age/ Phosphatase/AFP/AST) to predict for the presence of EV in HCV related cirrhotic patients.

Patients and Methods

- ***Study design:*** Cross-sectional study.
- ***Sampling:***
  a- **Sample size:** one hundred (100) patients. [Calculated by Epi Info program (version 6) at 95% Confidence Limit, Power of the Test is 80% and Alpha Set at 0.05 (Type I error)].
  b- **Sampling method:** Patients with HCV related chronic liver disease admitted to Ain Shams University Hospitals, Tropical Medicine Department or attending the outpatient clinics and endoscopy unit will be enrolled in this study.

Inclusion criteria:

Patients with stigmata of chronic liver disease based on clinical, laboratory and sonographic data.

Our exclusion criteria:

- Patients who refuse to be enrolled in the study.
- Patients with active gastrointestinal bleeding.
- Patients who underwent previous band ligation or variceal sclerotherapy.
- Patients who underwent Transjugular intrahepatic Portosystemic stent shunt, or surgery for portal hypertension.
- Presence of portal vein thrombosis.
- Presence of Hepatocellular carcinoma.
- Patients taking drugs for primary prophylaxis of variceal bleeding.
- Patients with active (< 6 months of alcohol abstinence) alcohol abuse.

- Patients with history of canal water exposure or bilhariziasis.
- Advanced other organ malignancy.
- Other severe medical condition (end stage renal disease, congestive heart failure or severe respiratory syndrome).
- Patients with other causes of splenomegaly or thrombocytopenia (hematological disease).

All participants in the study will be subjected to the following:

1. **Informed consent:** all patients must give their informed consent to participate. The study will be accepted by ethical research committee in Ain Shams University Medical School.

2.

3. **Full history taking.**

4. **A complete clinical examination.**

5. **Laboratory investigations including.**

   - Complete blood count.

   - Liver profile tests (ALT, AST, Albumin, PT, alkaline phosphatase, total bilirubin, INR& AFP).

   - Serum creatinine.

5. Ultrasonography of the abdomen with stress on: liver size and echogenicity, presence of periportal thickening, portal vein (PV) diameter & patency, splenic size splenic vein (SV) diameter & patency, status of ascites and presence of portosystemic collaterals.

Criteria suggestive of chronic liver disease and cirrhosis:

Increased liver echogenicity: loss of homogenous texture to be replaced by speckled coarse texture, irregular liver margins,