FIB-4 and platelet indices as non invasive predictors of liver fibrosis in Egyptian patients with chronic hepatitis C virus infection

Thesis

Submitted for partial fulfillment of
Master Degree in Tropical Medicine

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Introduction

Due to the invasive nature of liver biopsy, there has been extensive interest in developing non-invasive tests to measure liver fibrosis. These alternatives can be used in clinical practice, with benefits in terms of cost, risk, and patient convenience ***(Lai et al., 2011)***. Clinically applicable non-invasive tests include radiological studies, transient elastography (TE), and serum markers.

Most noninvasive tests of liver fibrosis were developed with the aim of discriminating between "insignificant", (F0-F1) by METAVIR and clinically "significant" fibrosis (≥ F2) by METAVIR or for identifying or excluding established cirrhosis in patients with well compensated chronic liver disease. Both these aims are clinically the most relevant ***(Strader et al., 2004)***. Diagnosing or excluding cirrhosis has major implications for patient outcomes and mandates radiological screening every six months for hepatocellular carcinoma and endoscopy to rule out portal hypertension ***(Schuppan and Afdhal, 2008)***.

A variety of direct serum markers of fibrosis, reflecting either the deposition or the removal of extracellular matrix in the liver, as alpha-2-macroglobulin,

serum hyaluronate, laminin, collagenases and their inhibitors such as matrix metalloproteases and tissue inhibitory metalloprotease-1 (etc..). Indirect serum markers including prothrombin index, platelet count, and AST/ALT ratio have also been proposed ***(Castera, 2009)***.

The limitations of individual markers to assess liver fibrosis have led to the development of more sophisticated algorithms or indices combining the results of panels of markers as FibroTest. AST-to-Platelet Ratio Index (APRI), FibroIndex , FibroMeter, Forns, Hepascore (***Castera, 2009)***, Fibro-α score ***(Omran et al., 2011)*** and Fib-4 ***(Sterling et al., 2006)***.

Mean platelet volume (MPV) and mean platelet diameter (MPD) are laboratory markers obtained from complete blood count (CBC) analysers in routine clinical practice. In the past, these were unnoticed indicators in CBC analysis. However, recent studies have yielded promising results for the effective use of these parameters. These studies have looked for a possible link between MPV and several inflammatory diseases such as myocardial infarction ***(Chu et., 2010)***, cerebrovascular disease ***(Mayda-Domac et al., 2010)***, ulcerative colitis ***(Yuksel et., 2009)***, shronic hepatitis B ***(Ceylan et al., 2013)*** and C infection ***(Purnak et al., 2013)*** and others.

Aim of the work:

The goal of the present study is to evaluate whether Fib 4 and other platelet indices would be useful in predicting degree of liver fibrosis in chronic hepatitis C infected patients.

Patients and methods:

This prospective cross sectional study will be conducted at Tropical Medicine department at Ain-Shams University Hospitals and the Police Hospital. Sixty patients with chronic hepatitis C (CHC) infection, undergoing liver biopsy as prerequisite before combined pegylated interferon and ribavirin treatment for HCV infection, will be recruited.

Exclusion criteria:

1- Other causes of chronic hepatitis, including autoimmune hepatitis, Wilson's disease and hemochromatosis, other viral hepatitis causes and HIV infection.
2- Alcohol use (≥ 20 g/day).
3- Patients with conditions that might affect MPV and platelet count, including splenectomised patients, acute and chronic renal failure, chronic obstructive lung disease, hematologic disorders and malignancies were excluded from the study.

4- Patients receiving drugs such as inhibitors of platelet function including aspirin, ticlopidine, clopidogrel, non-steroid anti-inflammatory drugs.
5- Patients with low mean corpuscular volume in CBC analysis (MCV < 80 fL) since small red blood cells might be counted mistakenly as platelets by the analyser.

Methods:

All the following parameters will be done for all patients.

1. Full personal history taking and thorough clinical examination including measurement of body mass index.
2. Complete blood picture
3. Liver profile including alanine aminotransferase (ALT), aspartate aminotransferase (AST). Serum bilirubin, serum albumin, serum alkaline phosphatase and prothrombin time (PT).
4. HCV Ab and HBs Ag.
5. Random blood sugar
6. Renal function tests.
7. Alpha fetoprotein (AFP) level.
8. HCV RNA quantitative.
9. Abdominal ultrasound.

10. Liver biopsy and histopathological assessment

The following parameters will be studied as Noninvasive assessment of liver fibrosis:

- Mean platelet volume (MPV) and platelet distribution width (PDW) from the CBC.
- APRI test will be calculated using the following formula ***(Wai et al., 3002)***: APRI = [(AST of the sample/normal upper limit AST) /platelets count (this should be in the range 0 to 500 or so – if there are extra zeros, delete these before computing)]×100.
- FIB-4 index will be calculated using the following formula ***(Sterling et al., 2006)***: FIB-4 index = age (years) × AST (IU/L)/Platelet count (×109/L) × (ALT [IU/L])$^{1/2}$.

Statistical analysis:

The data will be tabulated data analysis will be performed to formulate the results.

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