

# Fibrogenesis Markers and Hepatic Histopathology : What is the Role?

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## Background

HCV infection has an estimated prevalence of 3% around the world [1], and Egypt is among the highest prevalence [2]. Asymptomatic HCV patients are underrepresented. Unfortunately, many persons with HCV infection are asymptomatic [3]. Many asymptomatic seropositive donors have clinically significant liver disease [4]. The progression to severe fibrosis and occurrence of HCC were reported [1, 2]. Patients with normal enzymes may have definite chances of chronic hepatitis on histological examination [6].

Percutaneous liver biopsy, is the gold standard for grading and staging liver diseases [7], but it is invasive, has limitations [8], and asymptomatic patients may not accept.

The matrix metalloproteinases (MMPs), and their inhibitors are groups of proteins involved in controlling matrix degradation. Therefore, it seems that imbalance between MMPs and TIMPs affects rate of fibrosis progression, and their estimation was correlated with the stage of fibrosis [9].

Aspartate aminotransferase to platelet ratio (APRI Score) was also proved useful to stage liver fibrosis [10]. It is an easy and validated predictor of hepatic fibrosis in chronic hepatitis C [11].

Non invasive diagnosis of liver fibrosis and cirrhosis in chronic hepatitis C, is required in pre-treatment and follow up [12].

## Summary of paper

The paper entitled " Can fibrogenesis markers reflect early hepatic histopathology in chronic hepatitis C?" published in this issue of the Afro-Egyptian journal of infectious and Endemic Diseases by Abou El-Azm et al., aimed at evaluating individual and combined non invasive indicators of fibrogenesis (MMP-2, TIMP1 and

APRI score) to assess early hepatic histopathology, and developing cirrhosis in chronic HCV patients with and without symptoms. The authors enrolled 344 patients (Group I: 129 asymptomatic chronic-HCV, Group II: 135 with symptoms and Group III: 80 patients with compensated HCV-related cirrhosis). For each patient, APRI-Score was evaluated. Quantitative immunoassay measured serum MMP-2 and TIMP-1. Guided liver biopsy for histopathology staging and grading was done. The results imply that combination of markers raised the sensitivity, specificity and correlations. It could reflect early hepatic histopathology, developing cirrhosis and potentially could replace liver biopsies in pre-treatment and follow up of chronic HCV.

## Comment on the study

The current study showed a significant correlation of AST with the stage of fibrosis in the studied patients. This finding is consistent with the results mentioned that liver fibrosis severity and subsequent cirrhosis were correlated with high AST levels [13].

The current study showed that platelets decreased significantly in severe fibrosis or cirrhosis and these results are in agreement with previous results [14]. Decreased platelet count was the earliest indicator of cirrhosis [15].

As regard to direct serum fibrogenesis markers which reflect extracellular matrix turnover, MMP-2 & TIMP-1 were measured and correlated to the stage of fibrosis in liver biopsy. There was a significant positive correlation between serum MMP-2 and serum TIMP-1 and the stage of fibrosis. These results are in accordance with the results of Abdel-Samea et al. [14].

APRI score was reported to have correlations with the stages of histological fibrosis [16], in agreement with the present results. While Khairy M et al, showed that APRI score had moderate degree of accuracy [10]. Ma et al. considered it

as a tool with limited expense, widespread availability, a promising noninvasive alternative to liver biopsy for detecting hepatic fibrosis and treatment response in patients with chronic hepatitis C [17].

Although the outcome of non-invasive markers in different studies is not the same but multiplicity of markers can give more accuracy. The combined indicators of fibrosis: TIMP-1, MMP-2 and APRI score in the current study showed a higher sensitivity, specificity, and strong correlations with histopathology staging of liver fibrosis.

### Recommendations:

Serum markers of hepatic fibrosis are to replace liver biopsy - especially in the presence of obstacles – in assessment of patients with HCV related liver disease and in follow up of these patients post-treatment.

Further serum markers of liver fibrosis are to be determined individually or in combination to replace liver biopsy. These markers include procollagen type III N-terminal peptide (PIIINP) [18], procollagen type I N-terminal peptide (PINP) [19], type IV collagen [20], procollagen V C-terminal peptide (PVCP) [21], hyaluronic acid [22], matrix metalloproteinase 1 (MMP 1) and matrix metalloproteinase 9 (MMP 9) [23].

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