Mean Platelet Volume and Hepatic Stellate Cells Activity as Fibrosis Markers in Egyptian Patients with Chronic Hepatitis C

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Abstract

**Background and Aims:** Liver biopsy is the gold standard in assessing liver histology and stellate cells activation by specific markers as alpha-smooth muscle actin (α-SMA). However, this procedure is invasive and costly, hence, non invasive tests have been proposed to assess the severity of hepatic fibrosis. Mean platelet volume (MPV) is a laboratory marker obtained from complete blood count (CBC) analyzer in routine clinical practice. The goal of the present study was to investigate whether MPV, hepatic stellate cells activity could be markers for fibrosis in chronic hepatitis C (CHC) patients.

**Methods:** A total of 83 patients with CHC and 20 control subjects were included in this study. MPV was recorded at the time of admission. Activated hepatic stellate cells were identified immunohistochemically using antibody to α-SMA immunostaining in 53 of studied cases of CHC and 10 control samples. The clinical characteristics of chronic hepatitis C patients including demographics, laboratory findings were reviewed and liver biopsies were scored for fibrosis in Early Cancer Detection Unit-Benha University and Pathology Department of Faculty of Medicine, Benha University.

**Results:** Statistically significant increase in MPV values was observed in CHC patients (9.006±1.71) compared to healthy controls (8.01±0.97) (p<0.01). MPV values also were higher among patients with severe fibrosis as compared to those with mild fibrosis (9.62±2.34 vs 8.85±1.49) but without statistically significant difference (p=0.098). On the other hand, there is statistically significant correlation between α-SMA expression and stage of fibrosis (p<0.001). While, MPV was increasing with increased α-SMA expression but without statistically significant difference (p=0.3).

**Conclusion:** The present study showed that MPV increased in CHC patients with severe fibrosis but MPV is not specific marker for fibrosis in relation to stellate cell activity which is directly correlated with stage of fibrosis.

**Key Words:** Liver biopsy – Platelet volume – Chronic hepatitis C – Hepatic stellate cells – Egyptian patients.

Introduction

**HCV** is a global disease whose morbidity and mortality are increasing. The world health organization estimated that 3% of the world’s population or approximately 130-170 million people were chronically infected with HCV at the end of the 20th century, and 2.4-4.7 million new infections per year [1].

Egypt has the highest prevalence of antibodies to HCV in the world, estimated nationally at 14.7% and an estimated 9.8% are chronically infected [2]. The Egyptian Ministry of Health and Population (MOHP) estimated that more than half a million people are newly infected each year [3].

In early stage of HCV infection, the immune system generates antibodies to eradicate the virus and, once the infection becomes chronic, it inflicts hepatocyte damage through direct cellular toxicity and local stimulation of inflammatory cytokine expression, which triggers liver fibrosis by activating hepatic stellate cells (HSCs) [4,5].

Some patients with CHC will develop cirrhosis in a short period of time “fast fibrosers”, some will have very slow progression of the disease “slow fibrosers” and the rest belong to a category named as “intermediate fibrosers” [6]. It is well known that hepatic stellate cells (HSCs) play an important role in development of fibrosis and its progression to cirrhosis [7].

Normally, HSCs are quiescent, store vitamin A and synthesize collagen types III, IV and, in small quantities, type I [8,9]. Under conditions of stress and injury, such as in CCH, HSCs undergo “activation” or transdifferentiation, from a quiescent, to a myofibroblast-like cell, contributing to excessive extracellular matrix deposition [7-10,11].
HSCs activation consists of two major stages: Initiation triggered by chronic hepatic injury and inflammation mediated through a series of signaling molecules released by inflammatory cells, damaged hepatocytes, as well as other non-parenchymatous cells, mainly kupffer cells and sinusoidal endothelial cells. The second stage-perpetuation-is defined by HSCs proliferation, followed by an increase in type I collagen synthesis and extracellular matrix (ECM) accumulation, with a reduction in its degradation. Activated HSCs lose their cytoplasmic lipid droplets, forming multiple microfilaments that consist mainly of alpha-smooth muscle actin (α-SMA). Although activated HSCs may be immuno-histochemically stained with a series of antibodies, α-SMA represents a trustworthy marker in emphasizing their filaments [12,13].

Chronic HCV infection is responsible for chronic hepatitis, which results in cirrhosis in approximately 20% of cases. Patients with cirrhosis are exposed to life-threatening complications, including end-stage liver disease, peritonitis, esophageal variceal hemorrhage, and the development of hepatocellular carcinoma, which occurs at an incidence of 4%-5% per year [14].

Liver biopsy is the gold standard for the assessment of stage of fibrosis in hepatic diseases which has a high value, not only for the diagnosis and prognosis of disease, but also for the therapeutic decision and for the monitoring of the natural history or the evolution under treatment [15]. But the biopsy has some problems, such as bleeding, poor patient compliance, sampling error, and coagulation problems. Because of these problems, there is always an effort to find a method or a laboratory test for predicting the stage of fibrosis stage in CHC patients [16].

Mean platelet volume (MPV) is a laboratory marker obtained from complete blood count (CBC) analysers in routine clinical practice. Almost all hospitalised patients have this easily available parameter. In the past, this was an unnoticed indicator in CBC analysis [17]. Platelet volume is an indicator of platelet function and activation [18]. Platelet activity and aggregation capacity can be easily determined by measuring mean platelet volume (MPV) [19]. Recent studies have yielded promising results for the effective use of this parameter. These studies have looked for a possible link between MPV and several inflammatory diseases such as myocardial infarction, cerebrovascular disease, diabetes, ulcerative colitis, CHB, acute pancreatitis, celiac disease and rheumatoid arthritis [17,20-24].

In the present study we aimed to evaluate the value of MPV and HSCs activity in predicting the stage of fibrosis in patients with chronic hepatitis C (CHC) in comparison to liver biopsy.

Patients and Methods

We performed a prospective analysis of baseline clinical, laboratory and histological parameters in HCV infected patients in our hepatology, gastroenterology and infectious diseases department. Between January 2012 to 2013. The study groups consisted of 83 naïve HCV patients and twenty age and sex matched healthy controls. Diagnosis of CHC was confirmed by detectable HCV antibody for 6 months and serum HCVRNA positivity. Exclusion criteria were decompensated cirrhotic patients diagnosed clinically and laboratory, hepatocellular carcinoma, alcohol use, other diseases can cause chronic hepatitis as autoimmune hepatitis, HIV co infection, HBV infection.

Also we exclude from the study patients with conditions that might affect MPV and platelet count, including splenectomised patients, patients with atherosclerotic heart disease, celiac disease, diabetes mellitus, acute and chronic renal failure, hyperlipidemia, chronic obstructive lung disease, hematologic disorders and malignancies were excluded from the study. Patients receiving drugs such as inhibitors of platelet function including aspirin, ticlopidine, clopidogrel, non-steroid anti-inflammatory drugs and any other drugs that might potentially interact with platelet function and size were also excluded from the study. Moreover, patients with low mean corpuscular volume in CBC analysis (MCV <80 fl) were excluded from the study since small red blood cells might be counted mistakenly as platelets by the analyser.

Clinical and laboratory assessment:

All CBC analysis was performed in the hematology laboratory of our hospital. CBC analysis was performed with the same analyzer within 2 hours after collection of blood samples with the use of a Beckman Coulter (High Wycombe, UK) Gen-S automated analyzer. Platelet count and MPV were recorded at the time of admission. Venous blood samples were obtained between 8.00-9.00 am after an overnight fast of 8-12 hours. Serum levels of ALT, AST, total alkaline phosphatase (ALP) and creatinine were determined by automated techniques (Roch Modular System). HCV-RNA levels were determined using the Roche COBAS Ampliprep/COBAS TaqMan HCV amplification test. The associated range of detection of HCV-RNA levels was from 100-25,000,000 IU/ml.
**Histopathological assessment of liver fibrosis:**

The prospective study based on 83 naïve HCV patients and 20 cases of normal liver were taken as control. Cases were collected in the period between January 2012 to 2013. They were selected from files of Early Cancer Detection Unit-Benha University and Pathology Department of Faculty of Medicine, Benha University. Cases were selected according the availability of clinical and follow-up data.

Sections of 4-5 μm were cut from the paraffin blocks and were stained using Hematoxylin and Eosin (H&E) for assessment of fibrosis. Fibrosis staging was assessed in accordance to the METAVIR system. LFSs were defined as follow: Score for fibrosis (F): F0, no fibrosis; F1, portal fibrosis without septa F2, portal fibrosis with rare septa; F3, numerous septa without cirrhosis; and F4, cirrhosis [25]. According to the METAVIR scoring system, patients were divided into 2 groups: patients without significant fibrosis (F0, F 1, or F2) (Group 1) and patients with advanced fibrosis and cirrhosis (F3, F4) (Group 2).

**Immunohistochemical study:**

This study included 53 cases of CHC including 3 non-consecutive retrospective selected cases of stage 0, 7 of stage 1, 26 of stage 2, 10 of stage 3 and 7 of stage 4, 10 cases of normal liver were taken as control. Cases were collected in the period between January 2012 to 2013.

One section of 4 micron thickness was obtained from each case and was mounted on positively-charged slides. Paraffin sections 3-5 μm were deparaffinized in the oven at 56°C for 30 minutes, and inserted in xylene for 30 minutes. Tissues were dehydrated in ascending grades of alcohol 95%, 85%, then 75% for 5 minutes each. Slides were rinsed with distilled water for 5 minutes. Antigen retrieval was performed by boiling in sodium citrate buffer (0.001 M, pH 6) for 15 minutes in microwave. Endogenous peroxidase activity was blocked by incubation with hydrogen peroxide for 10 minutes. Then rinse with distilled water. Apply primary antibodies 2-3 drops of diluted (1:50) mouse anti-human monoclonal antibody α-SMA (cattlog no. MS-113-P0; Lab Vision Corporation, Fremont, CA, USA) on each slide to cover the specimen overnight at 4°C. After 3 wash with phosphate buffer saline (PBS) and sections were incubated with biotinylated secondary antibodies at for 30 min. This is followed by incubation by streptavidin-biotin-peroxidase complex. After 3 rinses with PBS, The slides were incubated with diaminobenzidine for 15min. The slides were rinsed with H2O and counterstained with hematoxylin for 3 minutes. This was followed by washing in cold running water, then wash in distilled water. Sections were dehydrated in ascending grades of alcohol and cleared with xylene, then coverslipped and examined. Muscle cells of small arterial blood vessels in portal tracts served as a positive internal control. Negative control was performed by leaving out the primary antibody during the staining procedure.

**Scoring criteria:** α-SMA immunostaining was demonstrated as yellow/reddish brown granules in the cytoplasm of stellate cells. The expression was evaluated semi-quantitatively based on the staining extent by determining the percentage of positive cells on a x100 magnification in at least 5 areas. The percentage of immunoreactive cells was grouped as follows: Negative: Up to 3% (0), mild: 3-33% (1), moderate: 34-66% (2) and strong: More than 66% (3) of mesenchymal cells in the portal tracts and fibrous septae. The SMA-positive vascular smooth muscle cells were excluded from α-SMA scoring [9].

**Statistical analysis:**

Statistical analysis was performed using SPSS software version 18. The degree of correlation between different parameters was evaluated by using the chi-square test. Results were expressed as frequencies and percentages, mean±standard deviation. A difference of \( p<0.05 \) between groups was considered significant and \( p<0.01 \) was considered highly significant.

**Results**

Demographic data and laboratory findings of control and patients groups are reported in Table 1. There was highly statistically significant difference between patients with CHC and healthy control group as regards Age \( (p=0.002) \), ALT \( (p=0.001) \), AST \( (p=0.001) \), Albumin \( (p=0.002) \), Platelet Count \( (x103/UL) (p=0.042) \), MPV \( (p=0.014) \) and very high statistically significant difference between the 2 groups as regard Age, PT \( (p=0.000) \), Serum AST, ALT, Albumin, WBCS, HB%.

In Table (2) there was very high statistically significant difference between group I (Mild fibrosis F0, F 1, F2) and group II (severe fibrosis F3, F4) as regard Age \( (p=0.005) \), AST \( (p=0.007) \), HB \( (p=0.007) \), Albumin, Platelet count, PT, Total Bilirubin, Direct Bilirubin, Spleen Diameter, PV \( (p-value for each of them=0.000) \). There was statistically significant difference between group I and
group II as regard Serum ALT \((p=0.02)\) and WBCS \((p=0.038)\). While, MPV was higher group of severe fibrosis \((9.6\pm2.33)\) compared to Mild fibrosis \((8.84\pm1.49)\) but without statistical significant difference \((p=0.098)\).

**Immunohistochemical results:** Table (3):

In the control group, very few \(\alpha\)-SMA-positive HSCs were found only along the sinusoids, mostly in the peripheral zones of the hepatic lobule close to the portal spaces. In the HCV group, there is negative \(\alpha\)-SMA expression in all cases without hepatic fibrosis with increasing score of \(\alpha\)-SMA towards severe fibrosis. There was highly significant difference in \(\alpha\)-SMA score between control cases and different stages of fibrosis where all cases of control and those without fibrosis are negative while 71.4% of stages 1 have mild expression in relation to 85.7% of stage 4 which have marked expression \((p<0.01)\).

### Table (1): Demographic parameters and laboratory findings of control and patient groups.

<table>
<thead>
<tr>
<th></th>
<th>Control (n=20)</th>
<th>CHC (n=83)</th>
<th>(p)-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>29.3±9.02</td>
<td>37.9±10.96</td>
<td>0.002**</td>
</tr>
<tr>
<td>ALT</td>
<td>21.35±6.18</td>
<td>52.5±39.82</td>
<td>0.001**</td>
</tr>
<tr>
<td>AST</td>
<td>22.15±6.13</td>
<td>45.7±30.25</td>
<td>0.001**</td>
</tr>
<tr>
<td>Alb</td>
<td>4.72±0.26</td>
<td>4.2±0.68</td>
<td>0.002**</td>
</tr>
<tr>
<td>Bilirubin T</td>
<td>0.76±0.17</td>
<td>0.85±0.42</td>
<td>0.308</td>
</tr>
<tr>
<td>Bilirubin D</td>
<td>0.17±0.09</td>
<td>0.29±0.35</td>
<td>0.127</td>
</tr>
<tr>
<td>PT</td>
<td>12.0±0.46</td>
<td>14.0±1.32</td>
<td>0.0000</td>
</tr>
<tr>
<td>Hb</td>
<td>12.59±1.47</td>
<td>13.4±1.76</td>
<td>0.07</td>
</tr>
<tr>
<td>PC (x10³)</td>
<td>232.45±67.11</td>
<td>196.4±70.91</td>
<td>0.042*</td>
</tr>
<tr>
<td>MPV (fL)</td>
<td>8.01±0.97</td>
<td>9.01±1.71</td>
<td>0.014*</td>
</tr>
</tbody>
</table>

AST : Aspartate aminotransferase. ALT : Alanine aminotransferase. PT : Prothrombin time. PV : Portal vein diameter. BIL : Bilirubin. ALB : Albumin. PC : Platelet count. Values are expressed as mean±SD. ** : \(p\)-value <0.01. * : \(p\)-value <0.05.

### Table (2): Demographic characteristics and laboratory findings of CHC patients.

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (n=66)</th>
<th>Group 2 (n=17)</th>
<th>(p)-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>36.2±10.03</td>
<td>44.4±12.2</td>
<td>0.005**</td>
</tr>
<tr>
<td>ALT</td>
<td>47.6±32.22</td>
<td>71.7±58.47</td>
<td>0.025*</td>
</tr>
<tr>
<td>AST</td>
<td>41.3±25.24</td>
<td>63.0±41.25</td>
<td>0.007**</td>
</tr>
<tr>
<td>Alb</td>
<td>4.4±0.56</td>
<td>3.7±0.83</td>
<td>0.002**</td>
</tr>
<tr>
<td>Total Bil</td>
<td>0.76±0.29</td>
<td>1.25±0.59</td>
<td>0.000**</td>
</tr>
<tr>
<td>Direct Bil</td>
<td>0.23±0.22</td>
<td>0.55±0.59</td>
<td>0.001**</td>
</tr>
<tr>
<td>PT</td>
<td>13.7±1.03</td>
<td>15.3±1.62</td>
<td>0.000**</td>
</tr>
<tr>
<td>Hb</td>
<td>13.6±1.45</td>
<td>12.4±2.43</td>
<td>0.007**</td>
</tr>
<tr>
<td>WBCs/cmm PC x10³</td>
<td>6304.4±207.002</td>
<td>5173.8±1810.99</td>
<td>0.038*</td>
</tr>
<tr>
<td>PT</td>
<td>211.9±65.14</td>
<td>136.1±60.57</td>
<td>0.000**</td>
</tr>
<tr>
<td>MPV</td>
<td>8.9±1.49</td>
<td>9.6±2.34</td>
<td>0.098</td>
</tr>
<tr>
<td>Spleen diameter</td>
<td>11.7±1.07</td>
<td>13.9±1.26</td>
<td>0.000**</td>
</tr>
<tr>
<td>PV</td>
<td>11.7±1.17</td>
<td>13.5±1.55</td>
<td>0.000**</td>
</tr>
<tr>
<td>PCR</td>
<td>4.44E5±7.921E5</td>
<td>5.526E5±4.60E5</td>
<td>0.698</td>
</tr>
</tbody>
</table>

Values are expressed as mean±SD.

### Table (3): Alpha-smooth muscle actin (\(\alpha\)-SMA) immunoreactivity in relation to different stages (Metavir score) and MPV in the studied cases of chronic hepatitis C.

<table>
<thead>
<tr>
<th>No.</th>
<th>Negative (&lt;3%)</th>
<th>Positive Mild (3-33%)</th>
<th>Positive Moderate (34-66%)</th>
<th>Positive Marked (&gt;66%)</th>
<th>(p)-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage of fibrosis:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>10</td>
<td>10 (100%)</td>
<td>–</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>Stage 0 (F0)</td>
<td>3</td>
<td>3 (100%)</td>
<td>–</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>Stage 1 (F1)</td>
<td>7</td>
<td>2 (28.6%)</td>
<td>5 (71.4%)</td>
<td>–</td>
<td>0.002**</td>
</tr>
<tr>
<td>Stage 2 (F2)</td>
<td>26</td>
<td>6 (23.1%)</td>
<td>20 (76.9%)</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>Stage 3 (F3)</td>
<td>10</td>
<td>–</td>
<td>9 (90%)</td>
<td>1 (10%)</td>
<td></td>
</tr>
<tr>
<td>Stage 4 (F4)</td>
<td>7</td>
<td>–</td>
<td>1 (14.3%)</td>
<td>6 (85.7%)</td>
<td></td>
</tr>
<tr>
<td>MPV</td>
<td>63</td>
<td>9.0±6±1.67</td>
<td>9.15±1.53</td>
<td>9.4±2.02</td>
<td>9.93±2.87</td>
</tr>
</tbody>
</table>

N.B.: From the table, there was highly significant difference in stellate cells activity (\(\alpha\)-SMA expression) between control cases and different stages of fibrosis \((p<0.01)\). While, there was positive correlation between \(\alpha\)-SMA expression and MPV but with no statistical significance difference \((p>0.05)\).
Fig. (1): C viral hepatitis with: A- Mild fibrosis showed mild α-SMA immunoreactivity of activated hepatic stellate cells within portal spaces and fibrous septa (streptavidin biotin x400). B- Moderate fibrosis showed moderate α-SMA immunoreactivity of activated hepatic stellate cells within portal spaces and fibrous septa (streptavidin biotin x400). C- Cirrhosis showed strong α-SMA immunoreactivity of activated hepatic stellate cells within portal spaces and fibrous septa (streptavidin biotin x400).

Discussion

The assessment of the stage of liver fibrosis is essential for prognosis and for deciding on antiviral treatment [26]. The gold standard in assessing the stage of liver fibrosis is the histological evaluation of a biopsy. However, the procedure carries a moderate risk of complications, including bleeding and a small risk of death [27].

Laboratory markers of liver fibrosis may be the ideal diagnostic tool to assess the grade of fibrosis. They are supposed to provide accurate and reliable results in a simple, fast and cost-effective manner [28].

MPV gives information about platelet production in bone marrow. When platelets decrease in number, bone marrow megakaryocytes are stimulated by thrombopoietin, and their nucleus becomes hyperlobulated, with much higher deoxyribonucleic acid content. These stimulated megakaryocytes produce larger platelets. Thus, platelets with a higher MPV are expected to be seen in destructive thrombocytopenia when megakaryocytic stimulation is present. Conversely, platelets with a lower MPV are expected in thrombocytopenic states associated with marrow hypoplasia or aplasia. There is an inverse relationship between platelet count and MPV, resulting in a roughly constant circulating platelet mass [29].

Platelet count is known to decrease in proportion to the advancement of the stage of liver disease in chronic hepatitis C virus infection. Related to progression of thrombocytopenia, MPV may be increased in patients with chronic hepatitis C with advanced fibrosis, and this can explain our results as we have demonstrated that patients with CHC have significantly higher MPV values compared with control subjects. Also, patients with advanced liver fibrosis have higher MPV values compared to other patients with mild fibrosis [30].

In this study, our aim was to investigate whether MPV could be a marker for fibrosis in CHC patients. We found that MPV was significantly higher in patients with CHC compared to control subjects. In contrast, PC was significantly lower in CHC patients. Portal hypertension and hypersplenism in some of the subjects with advanced fibrosis may be the cause of this significant difference.

Patients were divided into 2 groups according to severity of fibrosis. AST, ALT, ALB, PT and PC were significantly different between the groups. Therefore, we suggest that these parameters are affected by the degree of fibrosis in CHC. Kandemir, et al., [31] reported that PC and the GUCI (Goteborg University Cirrhosis Index, calculated using AST, PC, and PT) can discriminate to some degree of accuracy patients with severe fibrosis. Karaman, et al., [16] also found AST, ALT, PT to be helpful in identifying severity of fibrosis.

While, MPV values also were higher among patients with severe fibrosis as compared to those
with mild fibrosis but without statistically significant difference which was confirmed by the statistically insignificant correlation between MPV and $\alpha$-SMA immunostaining. Low platelet count (PC) of patients with advanced fibrosis could be one reason for the higher MPV ratio in patients with advanced fibrosis [16]. This results in agreement with the study of Purnak et al., [17] and Karaman, et al., [16]. Also, MPV was reported to be independently associated with advanced fibrosis in patient with chronic hepatitis B, the authors hypothesized that increased levels of IL-6 production secondary to inflammation in the fibrosis process may cause elevated circulating young platelets that are responsible for increased MPV in CHB with advanced fibrosis [32].

We believe that two main mechanisms are responsible for increased MPV in CHC patients. One of them is inflammation, which is the important cause of metabolic syndrome and its complication, and the other one is secondary to chronic changes due to liver pathology in CHC. It is also important to remember that MPV can both decrease and increase in pathological diseases [33]. Therefore, it should be evaluated in the appropriate clinical context.

Also, inflammation and increased release of proinflammatory cytokines, including the monocyte chemoattractant protein and TNF-$\alpha$, is one mechanism of Hepatic stellate cells (HSCs) activation which is initiated on the other hand by Kupffer cells that amplify the activity of nuclear factor kappa-B [34]. The activation of hepatic myofibroblasts, including HSCs, plays a major role in the feedback mechanism that regulates injury and tissular regeneration.

In this study, the control group, showed very few $\alpha$-SMA immunostained HSCs along the sinusoids, especially in the peripheral areas of the hepatic lobule, in the proximity of portal spaces, in terminal venules and in perivascular areas. There was a strong correlation between the stellate cell activity ($\alpha$-SMA expression) and the stage of fibrosis in patients with chronic viral hepatitis C ($p<0.001$). This data may suggest the roles of stellate cell activation in initiation and progression on liver fibrosis.

Using $\alpha$-SMA immunostaining techniques, several studies have emphasized an increase in the number of activated HSCs according to the severity of chronic liver injury, in patients infected with HCV, emphasizing a correlation between HSCs activity and the degree of liver fibrosis [9,11,13,35,36].

HSCs represent the most important cells that play a major role in the development of liver fibrosis. Identifying the main phenomena modulating physiopathological mechanisms involved in early stages of liver injury, which leads to HSC activation, followed by the initiation and development of liver fibrosis, new antifibrotic therapies can be developed. A potential therapeutic strategy may target the inhibition of activated HSCs response to inflammatory cytokine and growth factor stimulation, with a subsequent reduction in ECM production and an improvement in the severity of liver fibrosis and possible implications in the prevention of HCC [37].

Conclusion:

In conclusion, elevated MPV values might be a warning sign for forthcoming decompensation in patients with CHC but not a specific marker for fibrosis.

Alpha-SMA proves to be a very accurate marker for HSC differentiation to myofibroblast-like cells. The stellate cell activity is directly correlated with the stage of fibrosis. Identifying the activated stellate cell opens new perspectives in early diagnosis of liver fibrosis, as well as in future antifibrinogenic therapies.

References


