Biomarkers in Liver Disease: From Diagnosis to Prognosis

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INTRODUCTION

Hepatitis C is a global health problem which can trigger a chronic inflammatory disease process that might lead to liver fibrosis, cirrhosis and even hepatocellular carcinoma [1]. Patients with cirrhosis can be asymptomatic or symptomatic, depending on whether their cirrhosis is clinically compensated or decompensated. In compensated cirrhosis, patients are usually asymptomatic. On the other hand, patients with decompensated cirrhosis usually present with a wide range of signs and symptoms arising from a combination of liver dysfunction and portal hypertension. Multiple organs are affected with gastrointestinal, renal, pulmonary, cardiological and endocrine manifestations [2].

Furthermore, bacterial infections can occur in nearly one quarter of hospitalized decompensated cirrhotic patients [3] which trigger inflammatory response that causes progression of liver failure and development of complications; hence increases morbidity and mortality [4]. Consequently, early diagnosis of chronic viral hepatitis and as well as early detection of superadded bacterial infections may play an important role in hepatitis treatment, inhibits disease progression, and reduces morbidity and mortality.

Increasing evidence suggests that miRNAs are essential for the regulation of liver development, regeneration and metabolic functions [5]. Hence, alterations in intrahepatic miRNA networks have been associated with all aspects of liver disease, including hepatitis, cirrhosis and HCC [6]. miR-122 is the most frequent miRNA in the adult liver [7,8]. Interestingly, miR-122 can be detected in the circulation and serum miR-122 has been shown to serve as a biomarker of liver injury including chronic hepatitis B or C [9-11].

miR-122 has a liver-enriched expression and is one of the most abundant miRNAs in the liver, accounting for about 52% of the whole hepatic miRNome in adult human [7].

A study published in Afro-Egypt J Infect Endem Dis under the title of "Serum MiRNA-122 as a Diagnostic Marker in HCV Related Liver Cirrhosis" aimed to evaluate serum miRNA-122 expression as a potential biomarker for diagnosis and monitoring different stages of disease in chronic hepatitis C patients.

The study revealed that miRNA-122 expression levels were significantly increased among liver disease patients than healthy controls. Furthermore, miRNA-122 expression levels were significantly higher in the compensated patients compared to the decompensated patients. Also, this study elucidated that serum miRNA-122 levels were decreased with the progression of liver disease (from Child-Pugh class A to C) but without reaching to a significant difference .

Additionally, patients with ascites had a significantly lower expression of miR-122 compared to those without ascites, while patients with gastrointestinal bleeding and hepatic encephalopathy had statistically

insignificant lower expression of miRNA 122 compared to subjects without these complications. A significant positive correlation between miRNA-122 expression and (AST, ALT, albumin, and viral load) were detected as well as a significant negative correlation as regard INR .

Collectively, the study figured out the role of serum miRNA-122 expression in the progression of liver disease and its potential usage as a new diagnostic marker in hepatitis C patients with different stages of the disease.

Infected patients with cirrhosis can be asymptomatic at initial stages, but highly susceptible to dissemination of infections due to their immunocompromised state that often leads to development of severe disease specific complications with significant mortality rate[12,13]. Therefore, early recognition of bacterial infections is essential, however, in the clinical practice their accurate identification is challenging from both the clinical[14] and the laboratory point of view[15]. Currently C ¬reactive protein (CRP) and procalcitonin (PCT) are broadly used in the clinical practice to aid the early diagnosis of bacterial infection[16]. Consequently, finding out accurate laboratory markers is a must to maximize the efficacy of diagnostic procedure of bacterial infections and thus making early intervention possible.

Presepsin (soluble CD14 subtype, sCD14¬ST) is a 13¬kD a cleavage product of CD14 receptor that recognizes different cell surface structure of both Gram-negative and positive bacteria. Presepsin in the circulation can be perceived as a witness of activated monocyte-macrophage in response to pathogens[17]. Several recent clinical studies have shown that presepsin is a specific and sensitive novel marker for the diagnosis of sepsis [18], for evaluating the severity of sepsis and for predicting the outcome[19,20]. Beyond sepsis, presepsin is worthy of studying in those clinical settings, where systemic infections are frequently associated with severe diseases course such in cirrhosis [acute decompensation (AD), organ failure]. Contributive role of presepsin for the diagnosis and prognosis of cirrhosis associated bacterial infection has not been assessed extensively so far.

Resistin, an insulin resistance-modulating hormone, is secreted by adipocytes and macrophages. It has a novel proinflammatory function that enhances the neutrophil response to LPS stimulation. Elevated serum levels of resistin were detected in severe sepsis and septic shock [21-22]. Besides, in liver cirrhosis, resistin positively correlates with disease stage, and negatively correlates with survival [23].

According to an interesting study published in the current issue of the Afro-Egyptian Journal of Infectious and Endemic Disease " Presepsin and Resistin as Diagnostic Markers for Bacterial Infection in Patients with Decompensated Cirrhosis"Presepsin and resistin were significantly higher among patients with infection and positively correlated with Model for End-stage Liver Disease score (MELD), Child-pough score (CPS), CRP and PCT. At 1205 pg/ml as cutoff, Presepsin could predict infection at sensitivity 83.8%, specificity 93% and accuracy 88.7%. While using 21ng/ml as cutoff, Resistin could predict infection at sensitivity 64.6%, specificity 68.4% and accuracy 66.7%. Adding CRP to PCT or presepsin increased sensitivity to 99%, specificity 73.7%, and accuracy 85.4%. Adding presepsin to PCT or resistin increased sensitivity to 94.9%. Yet combined presepsin and PCT had higher specificity than combined presepsin and resistin. Conclusion: Presepsin has comparable diagnostic performances to CRP and PCT for bacterial infection in decompensated cirrhosis while resistin has poor sensitivity and specificity. Adding presepsin to CRP yields the same diagnostic performance as combined CRP and PCT. So, combining any of them to CRP helps to early diagnose bacterial infection in those patients.

Finally, serum miRNA-122 seems to be a useful new diagnostic marker in hepatitis C patients with different stages of the disease. Furthermore, the present study suggests that presepsin is a promising biomarker during diagnostic procedure of bacterial infections in cirrhosis by enhancing the diagnostic capacity of CRP and reflecting more accurately the severity of infections. The main limitation of these studies is being carried in a single center with a relatively small sample size consequently further studies are needed in large scale to establish these findings

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