

INTRODUCTION

Any patient with chronic liver disease might develop liver fibrosis. Accurate estimation of the disease severity is helpful for evaluation of the therapeutic effect and prognosis of the disease (*Luo, 1996 and Wang, 1998*).

There are three ways for this purpose histology, serology and imaging. Liver histological diagnosis based on needle biopsy is a gold standard to evaluate the degree of liver fibrosis. However, liver biopsy can not be done routinely because of its invasiveness (*Xu, 1999 and Colli, 2003*).

Imaging technologies such as ultrasonography has become the most common and valuable method because of its low cost, easy performance and high acceptability by the patient, it could provide not only valuable information on morphological change of the liver but also liver haemodynamics by color Doppler flow imaging. Also several biochemical indicators have been discussed as potential non invasive serum/ plasma markers of fibroproliferation. Among them are the matrix metalloproteinases (MMPs) and their tissue inhibitors (TIMPs) haptoglobin, gamma glutamyl transpeptidase (GGT) and total bilirubin (*Lichtinghagen et al. 2000, Imbert-Bismut et al., 2001*).

Other maker of fibrosis include fibronectin ,N terminal peptide of type III procollagen , hyaluronic acid , collagen IV and laminin P₁ may reliably distinguish between early and late stages of fibrosis (*Rosenberg et al.,2000*).

Matrix metalloproteinases (MMPs) are impotent zinc containing enzymes that degrade such components of the extracellular matrix as collagen, gelatin, laminin and proteoglycan core protein.

They form a gene family and each MMP degrades specific substrates. Gelatinases (type IV collagenases) may be especially important for the development of liver fibrosis because they degrade type IV (basal membrane) collagen and thus are involved in the early steps of tissue remodeling that characterize chronic liver disease (*Benyon et al., 1996, Ebata et al., 1997*).

On the other hand, tissue inhibitors of metalloproteinases (TIMPs) act as regulatory factors for MMPs, they are involved in liver fibrosis through impaired matrix degradation (*Ebata et al., 1997*).

Haptoglobin is a glycoprotein that is largely synthesized by hepatocytes. Low values are found in severe chronic hepatocellular disease, haemolytic crises and is negatively associated with fibrosis (*Sherlock and Dooley, 2002*).

GGT and total bilirubin are associated with fibrosis and have been used as a serum markers of fibrosis (*Naveu et al., 1994*).

The increase in GGT level with the stage of hepatic fibrosis is associated with hepatocyte growth factor which rises as fibrosis progress (*Potder et al., 1997 and Dluzniowska et al. 2002*).

The damage of liver cells is associated with an increase in conjugated and unconjugated bilirubin. Hepatitis, fibrosis and cirrhosis are the most common disorders that produce liver cell injury and jaundice (*Imbert-Bismut et al., 2001 and Rossi et al., 2003*).

If markers with high positive or negative predictive values of fibrosis can be obtained, fewer liver biopsies would need to be done and thus the cost and risk of liver biopsy would be lessened (*Cadranel et al., 2003*). Combined application of the three methods is hopeful to improve diagnostic accuracy (*Arda et al., 1997 and Tchelepi et al., 2002*).