INTRODUCTION

Chronic liver diseases constitute the most common health problem in Egypt. This is simply due to the endemicity of schistsomiasis and viral hepatitis. The end-results of these disorders are usually the development of fibrosis, cirrhosis and portal hypertension which can lead to bleeding varices and finally hepatocellular carcinoma (HCC) (Abdel Ghaffar et al., 1994).

Tumours of the liver represent one of the most common malignancies in the world. The annual international incidence of the disease is about one million cases, with a male to female ratio of about 4:1 (Parker et al., 1996).

The 60% to 80% association of hepatoeellular carcinoma (HCC) with underlying cirrhosis has long been recognized (Tiribell et al., 1989), more typically with macronodular cirrhosis in south East Asia, but also with micronodular cirrhosis in Europe and the United State. It is still not clear whether cirrhosis itself is a predisposing factor to the development of HCC or whether the underlying causes of the cirrhosis are actually the carcinogenic factors. However, approximately 20% of North American patients with HCC do not have underlying cirrhosis (Carr et al., 1997).

The first serologic assay for detection and clinical follow up of patients with hepatocellular carcinoma was α-fetoprotein (AFP). It is found in the serum of animals bearing transplantable hepatomas (Abelev et al., 1963) and was later detected in humans (Tatarinov, 1964). Improvements in this assay, including the development of radioimmunoassays for AFP (Waldman and McIntire, 1974 and Matsumato et al., 1982) allowed sequential studies in high-risk patients and patients being treated either with surgical resection or chemotherapy. False-positive elevations in AFP levels may be found in pregnancy, germ cell tumours and acute or chronic viral hepatitis. Serum AFP levels may be normal or slightly raised in the presence of HCC, and therefore, alternative tumour markers are being sought (Khakoo et al., 1996).

Intercellular adhesion molecule-I (ICAM-1) is an 80-110 KDa, transmembrane glycoprotein. It is constitiutionally expressed on the cell surface, or its expression can be induced by inflammatory cytokines such as interferon-gamma (IFN-γ) and tumour necrosis factor-α (TNF-α) (Dustin et al., 1986 and Rothlein et al., 1988). A soluble form of ICAM-I has been found in the serum of normal individuals (Rothlein et al., 1991). This form includes almost the whole extracellular domain of the membrane-bound molecule and is able to bind with lymphocyte function associated antigen-1 (LFA-1) on

T-cells (LFA- I). Furthermore, high concentrations of the circulating form of ICAM-1 (cICAM-1) have been reported in various malignant diseases, and its usefulness as a diagnostic marker for some malignancies has been suggested (Tsujisaki et al., 1991).

In a previous study carried out by (Hyodo et al., 1993), they found that serum levels of cICAM-1 were significantly increased in the patients with chronic liver diseases when compared to healthy controls and were higher in liver cirrhosis (LC) than in chronic hepatitis (CH). Thus cICAM-1 levels rose along with disease progression.

Hyaluronic acid, type IV collagen and the N-terminal propeptide of type III procollagen peptide (PIIIP) have been reported as markers of liver dysfunction and fibrosis (Fabris et al., 1997).

PIIIP is liberated during the conversion of type III procollagen into collagen (Suou et al., 1995). The serum concentration of PIIIP is elevated in many acute and chronic liver diseases and is considered to mainly reflect inflammatory activity and active fibrogenesis (Teare et al., 1993).

Matrix metalloproteinase-9 (MMP-9) (92-kd gelatinase/ type IV collagenase, gelatinase B) is a member of the matrix

metalloproteinase gene family (Birkedal-Hansen et al., 1993) and is implicated in tissue destruction in various pathophysiological conditions including tumor invasion (French et al., 1994). The enzyme has a wide range of substrate specificity against interstitial fibrillar collagens (Collagen types III and V) and against their gelatins as well as type IV collagen (Watanabe et al., 1993).

Human and rat Kupffer cells in a primary cell culture have been shown to synthesize and release MMP-9 which was localized in kupffer cells by the immunofluorescence method (Winwood et al., 1993) Thus, Kupffer cells could be a source of MMP-9 in patients with HCC.