INTRODUCTION

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Human hepatocyte growth factor was first identified and cloned as a mitogen for mature hepatocytes .It is a heterodimeric molecule of a 69 kDa α –chain and a 34 kDa β-chain ,and the receptor for HGF is the c-met protooncogene product of heterodimeric tyrosine kinase. Specific binding of HGF to the c-Met/HGF receptor induces tyrosine phosphorylation of the receptor and activates intracellular signaling cascades ***(Matsumoto K et al.,1998)*** .

HGF exhibits multiple biological activities on a wide variety of cells and has mitogenic, motogenic (enhancement of cell motility), morphogenic, and anti-apoptotic activities. These biological activities are important for organization of tissue structures during development and regeneration. Several lines of evidence indicate an important role for HGF in development and morphogenesis of epithelial organs, including the liver, placenta, lung, tooth , mammary gland and kidney. Essential roles of HGF in the development of mammalian fetal tissues were also defined by disruption of HGF or the c-Met gene in mice. These mice with targeted mutation of the HGF or c-Met gene died at embryonic day 13 to 15 due to impaired organogenesis of the placenta and liver. Together with respective expression of HGF and the c-Met receptor in mesenchyme and epithelia , HGF functions as a mediator of epithelia – mesenchymal interactions for organogenesis ***(Matsumoto K et al.,1998)*** .

Production of human hepatocyte growth factor in the liver occurs in Kupffer cells, sinusoidal endothelial cells and Ito cells (fat

storing cells), but not in hepatocytes ***(Matsumoto and Nakamura., 1992).***

human hepatocyte growth factor act as a hepatotrophic factor for liver regeneration through two mechanisms : a paracrine mechanism and an endocrine mechanism. The paracrine mechanism involving HGF was derived from the neighboring nonparenchymal liver cells such as Kupffer cells and Ito cells. The other endocrine mechanism involving HGF was derived from extrahepatic organs such as the lung , kidney and spleen ***(Tsubouchi et al., 1993).***

In experimental animal, human hepatocyte growth factor activity increases markedly in the liver of rat, after various liver injuries such as hepatitis, ischaemia, physical crush and partial hepatectomy ***(Matsumoto and Nakmura., 1992).***

Also hepatocyte growth factor (HGF) act as a renotropic factor . It has mitogenic, motogenic, anti–apoptotic, and morphogenic(induction of branching tubulogenesis) activities for renal tubular cells , while it has angiogenic and angioprotective actions for endothelial cells . Stromal cells such as mesangial cells, endothelial cells , and macrophages are sources of renal HGF . In response to acute renal injury , the expression of HGF increase in the injured kidney and in distant intact organs such as the lung and spleen .Locally and systemically increased HGF supports renal regeneration , possibly not only by enhancing cell growth but also by promoting morphogenesis of renal tissue ***(Kunio M . et al ., 2001).***

Hioki et at., (1993) reported that the human hepatocyte growth factor levels increased significantly in the sera of patients with acute hepatitis, fulminant hepatitis, chronic hepatitis and liver cirrhosis. They concluded that serum levels of human hepatocyte growth factor could be used as an index of the severity of liver dysfunction in various liver diseases.

Serum hHGF levels were markedly higher in patients with fulminant hepatic failure than in those with chronic hepatic failure irrespective of severity of hepatic failure .The difference of serum hHGF levels between two types would be due to the difference in the extent of hepatocellular necrosis.This difference of serum hHGF levels may provide a useful tool to differentiate fulminant and chronic types of hepatic failure . ***(Kinoshta . T et al ., 1990) .***

Malatino et al.,(2000) suggested that HGF is a pleiotropic factor involved in tissue protection and repair in the endothelium and various organ systems.

Ho R . T. et al., (1999) reported that HGF is a multipotent factor involved in tissue regeneration, and a lot of cellular repair processes.

In our country chronic liver diseases represent a very special and important problem because of endemicity of bilharziasis and its complications. So, HGF is of particular interest because of its high potency as a hepatotrophic factor.