

## SUMMARY

Cytokines mediate the body's response to infection and inflammation. Tumor necrosis factor alpha, a monocyte macrophage derived cytokine, was initially identified because of its ability to lyse certain malignant cells.  $\text{TNF-}\alpha$ , is a major product of activated macrophages, including Kupffer cells, and has a variety of effects on the immune system including recruitment of immune cells to sites of inflammation, activation of lymphoid cells and induction of other cytokines.

Tumor necrosis factor-alpha, causes a wide variety of systemic effects such as fever, anorexia, muscle wasting and hyperlipidemia. Recent studies have demonstrated that  $\text{TNF-}\alpha$  has a variety of effects on neoplastic and normal cells. The close relationship between the septic state and coagulation abnormalities and hemorrhagic nature of lesion in the tumor bed induced by  $\text{TNF-}\alpha$  which, also, stimulates the production of acute-phase proteins and enhances amino acid uptake by hepatocytes.

Increased production of  $\text{TNF-}\alpha$  by monocyte/macrophage has been observed in patients with a variety of liver diseases including cirrhosis, alcoholic hepatitis, bilharzial hepatic fibrosis and chronic active hepatitis. The liver represents an important site of synthesis and also a major clearance organ for several cytokines. Many biological effects to be mediated by

inflammatory cytokines such as fever, malaise, cachexia, and cholestasis are observed in chronic liver disease.

The present study was conducted on 146 subjects, 116 with different chronic liver diseases and 30 healthy controls. All subjects were chosen and selected to fit one of the following groups:

- 1) Normal control.
- 2) Chronic active hepatitis.
- 3) Chronic persistent hepatitis.
- 4) Cirrhosis.
- 5) Bilharzial hepatic fibrosis.

All subjects were performed to the following investigations :

- 1) Clinical examination.
- 2) Abdominal ultrasonography.
- 3) Liver biopsy.
- 4) Liver function tests.
- 5) Total and differential leukocytic counts.
- 6) Viral markers (HBs Ag, HBc Ab and Anti-HCV).
- 7) Auto-antibodies (ANA, ASMA, and AMA).

All subjects included in our study has been studied to assess their serum levels of the following parameters:

- 1) Tumour necrosis factor- $\alpha$
- 2) Interleukin -1 $\beta$ .
- 3) Interleukin-6
- 4) C-Reactive protein.

Serum levels of the proinflammatory cytokines TNF- $\alpha$ , IL-1 $\beta$ , and IL-6 are significantly elevated in patients with chronic liver diseases. CRP, a key acute-phase protein mainly controlled by IL-6, was also increased in all patient groups compared to control. Serum levels of TNF- $\alpha$ , IL-1 $\beta$ , IL-6, and CRP in cirrhotic group where elevated compared to other groups.

The serum levels of cytokines and CRP were significantly elevated in patients with decompensated cirrhosis than with compensated and in patients with severe chronic active hepatitis than with mild degree.

Good positive correlation between cytokine /CRP and AST/ALT was found in patients with chronic active hepatitis and a negative correlations with prothrombin time and serum albumin in patients with cirrhosis and hepatic fibrosis.

Total serum bilirubin showed positive correlation with TNF- $\alpha$ , IL-1 $\beta$ , IL-6 and CRP in cirrhotic group of patients. There are a

good correlation among cytokines and between cytokines and CRP in all patient groups.

We can concluded that serum levels of  $\text{TNF-}\alpha$ ,  $\text{IL1}\beta$ ,  $\text{IL-6}$  and CRP were elevated in patients with chronic liver diseases. Endogenous cytokine patterns in chronic liver diseases were stage dependent and only marginally affected by the type of underlying disease. Elevated concentrations of cytokines represent a characteristic feature of chronic liver diseases regardless of underlying etiology.

This and the apparent stage-dependency suggest that enhanced endogenous cytokines levels represent a consequence of liver dysfunction rather than of inflammatory diseases.