

by the infection itself which down regulates the requisite signaling between macrophage and T cells<sup>(8)</sup>.

Gamma interferon (IFN- $\gamma$ ) secreted by Th1 cells is the most potent macrophage-activating cytokine, leading to the host resistance to infection with *Leishmania* parasite<sup>(12)</sup>. A marked decrease in the production of IFN- $\gamma$  was observed in patients group (Table 1). The deficient production of IFN- $\gamma$  after exposure to *Leishmania* antigens is one of the commonly reported factors which associated with increase expression of CD4+ T cells. The disease susceptibility is associated with the inability to produce macrophage-stimulating profile including IFN- $\gamma$ , IL-2, and IL-12<sup>(13)</sup>. Coutinho et al.<sup>(14)</sup> detected a decrease in the level of *Leishmania* in supernatants from *Leishmania* stimulated cell cultures 2255 $\pm$ 653 pg/ml before antimonial therapy and 3005 $\pm$ 900 pg/ml at the end of the treatment. A significant increase in the level of IFN- $\gamma$  was detected in the serum of patients during treatment with pentostam when compared to its level before treatment, this explain that a successful drug therapy were restored T-cell proliferation and IL-2, IFN- $\gamma$  production in response to *Leishmania* antigen<sup>(15)</sup>. Furthermore, these findings confirmed the role of IFN- $\gamma$  in the healing of the lesion due to involvement of CD4+ T cells in the healing process and elevated IFN- $\gamma$  production at the end of the treatment in human<sup>(16)</sup>. Also, IFN- $\gamma$  could be used as immunopotentiator for augmenting the capacity of macrophages to eliminate *Leishmania* infection<sup>(17)</sup>.

Transforming growth factor (TGF- $\beta$ ) is a multipotential cytokine with diverse effects on immune cells, including the down-regulation of certain macrophages and the blockade of IFN- $\gamma$  induced macrophages activation<sup>(18,19)</sup>. In this study the concentrations of TGF- $\beta$  in patients and

treated groups decreased significantly as compared to controls (30.4 $\pm$ 4.15 pg/ml and 37.8 $\pm$ 1.48 respectively). Li et al.<sup>(20)</sup> showed that using anti-TGF- $\beta$  treatment promotes rapid healing of murine leishmaniasis through enhancing *in vivo* nitric oxide (NO) production by activated macrophages.

In this study, TNF- $\alpha$  and IL-1 levels were found to be significantly higher for CL patients than for control group, and during therapy their concentrations were significantly elevated also.

T cells mediate activation of macrophages to produce NO, resulting in killing or control *L. major* parasites and the secretion of TNF- $\alpha$  by macrophages is sufficient to mediate production of NO and killing of *L. major* parasites<sup>(21)</sup>. Melby et al.<sup>(22)</sup> found significant increase in the expression of IL-1 $\beta$ , TNF- $\alpha$ , IL-10 and TGF- $\beta$  in late lesions compared with that in early lesions, these finding were in agreement with our study.

IL-1 is primarily produced by cells of the mononuclear phagocytic lineage but is also produced by endothelial cells, keratinocytes, synovial cells, astrocytes, osteoblasts, neutrophils, glial cells, and numerous other cells. IL-1 production may be stimulated by a variety of agents, including endotoxins and other cytokines, microorganisms, and antigens. IL-1 is also cytotoxic to cancerous and virus – infected cells<sup>(8)</sup>. Sodhi et al.<sup>(23)</sup> demonstrated that IL-1 levels were significantly increased when *L. donovani* infected animals were treated with antimony salts 14 days post infection; their findings appear to support our study. It is thought that TNF- $\alpha$  and IL-1 levels increase as a part of host defense strategies, and induction of the cytokines by antimonial therapy might be dependent on macrophage activation.

T cells, monocytes and fibroblast produces IL-6, which is a major cytokine involved in T and B cell regulation and also in some aspects of the inflammatory response<sup>(24)</sup>. Serum IL-6 levels were significantly