SERUM TUMOR NECROSIS FACTOR-α IN CHILDREN WITH TYPHOID FEVER

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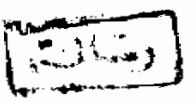

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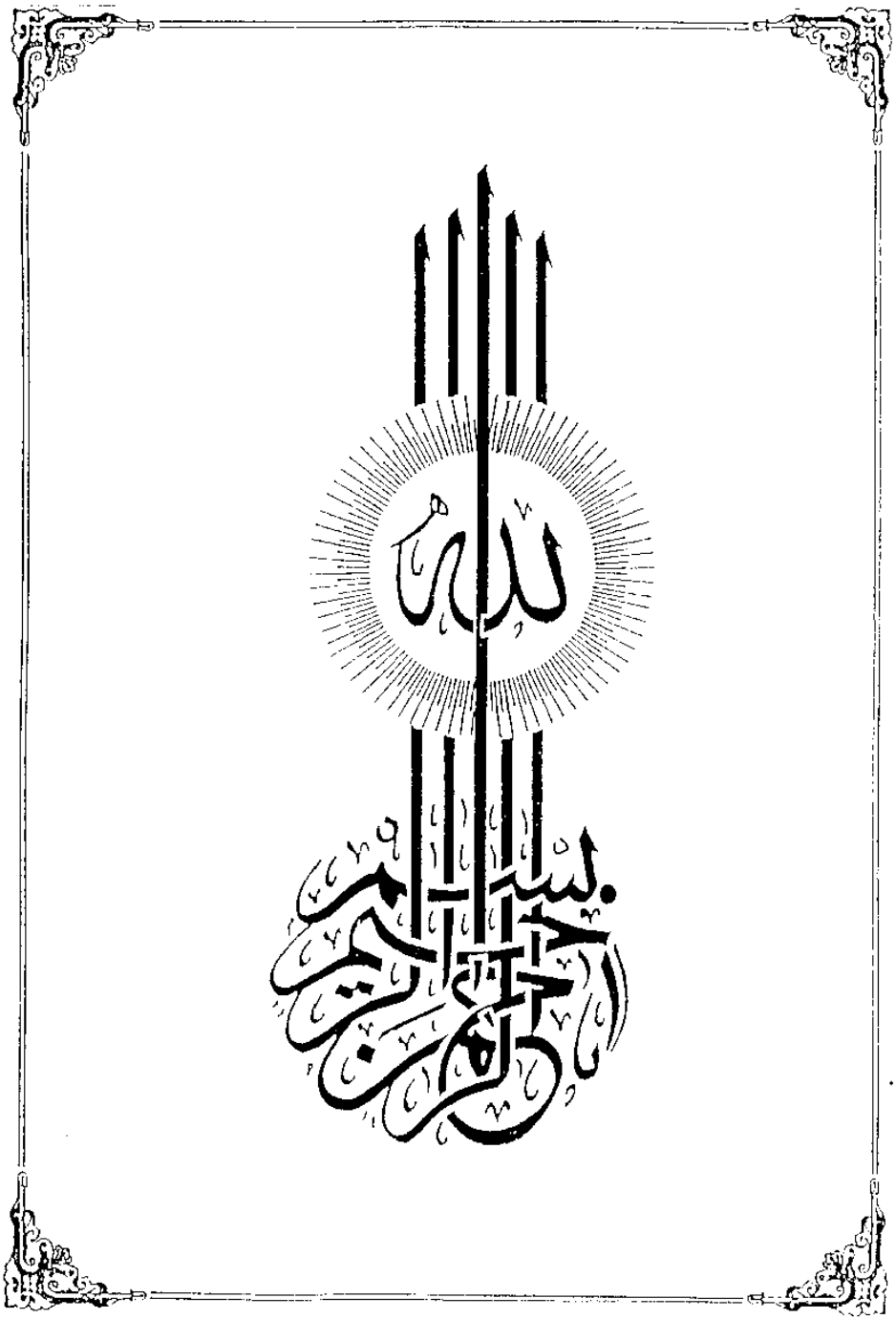

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INTRODUCTION AND AIM OF THE WORK

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Typhoid fever is an acute infectious communicable disease. t continues to occur as an endemic disease in several parts of the world including Egypt ***(Kamal, 1975)***.

Typhoid fever in children had various clinical manifestations and so it must be considered in any acute disease. Definitive diagnosis of typhoid fever requires isolation of the organism from blood, bone marrow, faeces or urine, techniques that are not always practicable particularly in the rural areas ***(Mandal, 1994)***.

The Widal serodiagnostic test has many limitations ***(Anonymous, 1978)*** but continues to be widely used. Cytokines are hormone-like polypeptides of glycoproteins synthesized and secreted from activated lymphocytes and monocytes that participate in a variety of cellular responses including the regulation of immune system ***(Oppenheim et al, 1991)***.

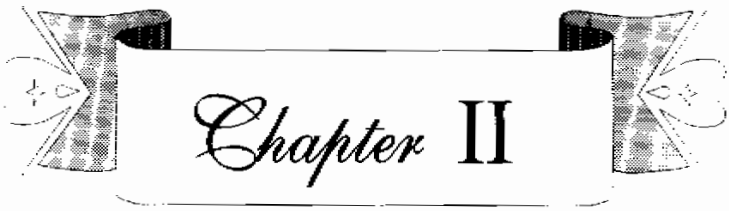
Tumor necrosis factor-α is a cytokine predominantly released by cells of the monocyte-macrophage lineage in response to activation and it acts via specific cellular receptors

that also mediate uptake and degradation of the proteins ***(Petersen et al, 1989)***.

The pro-inflammatory cytokines including tumor necrosis factor-α have been implicated in the pathogenesis of sepsis caused by Gram-negative microorganisms ***(Cannon et al, 1990)***.

The role of tumor necrosis factor-α in the pathogenesis of inflammatory reaction of typhoid fever and its relation to the outcome of the disease was studied in adults ***(Keuter et al, 1994)*** but not well studied in children.

The aim of the present work is to determine the level of tumor necrosis factor-α in the serum of children suffering form typhoid fever at different intervals (before therapy and after one week from the start of therapy) in order to investigate the association of serum TNF-α concentration with the severity of the disease and also to assess its value in predicting the outcome of the disease.



Chapter II

REVIEW OF LITERATURE

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TYPHOID FEVER

Typhoid fever is an acute infectious disease. It is a disease of world wide prevalence especially in Asia, Africa and North America. Typhoid fever is endemosporadic in Egypt. It could occur all the year round, but it runs a yearly seasonal rise during the months May to October reaching its peak in August ***(Kamal AM, 1958)***.

The incidence of the disease is higher in urban than rural areas due to presence of communal catering in towns, or to better notification in towns with more developed health services ***(Kamal Moussa, 1970)***.

Typhoid fever can affect any age but the morbidity rate is higher in the age group from five to twenty years, while the mortality rate is higher under five years of age ***(World Health Statistics, 1981)***.

Etiology :

In Egypt; typhoid fever represents about 75% of cases of enteric fevers (typhoid and paratyphoid fevers), followed by paratyphoid A that forms about 20% of the cases, then

paratyphoid B that forms about 5% of the cases, whereas parathyroid C is very rare ***(El-Akkad AM, 1970)***.

Salmonella typhi are Gram negative, non spore forming, motile bacilli ***(Jawetz E et al, 1978)***. they possess three antigens; O or somatic antigen, H or flagellar antigen and Vi or second somatic antigen responsible for the virulence of the organism ***(Wilson and Miles, 1975)***.

Salmonella organisms are killed by temperature 60°C for 15-30 minutes but they resist cold and can survive for a long time in frozen water and are easily destroyed by chlorination of water, pasteurization of milk and cooking of food ***(Wilson and Miles, 1975)***.

Pathogenesis :

Typhoid fever is primarily an infection of the hemopoietic tissue ***(Boyd W., 1961)***. The source of infection is always human either patients or carriers, and infection occurs by ingestion of the micro-organisms. After oral ingestion of the bacilli; most of them are destroyed by the high gastric acidity. The bacilli that escaped proliferate rapidly in the second part of the duodenum where bile gives a favourable alkaline medium for bacterial growth ***(Huckstep, 1962)***.

The bacilli pass through the intestinal mucosa of the lower ileum to the lymphoid tissue (Peyer's patches); producing a mild inflammatory reaction which is accompanied by infiltration of histiocytes, plasma cells, lymphocytes and polymorphonuclear leukocytes. The bacilli pass via the lymphatics to the mesenteric lymph nodes, and after multiplication they invade the blood stream via the thoracic duct resulting in primary bacteremia.

The blood stream becomes rapidly cleared from the bacilli by the phagocytic reticulo-endothelial cells of the spleen, liver, lymph nodes and bone marrow. In these cells; the bacilli undergo proliferation and finally the cells rupture and the blood stream is flooded with large number of bacilli producing secondary bacteremia, which starts at the end of the incubation period.

The organisms soon reach the bile; either directly from the capillaries in the gall bladder wall, or indirectly by the liver capillaries into the bile canaliculi and flourish in it. A second and heavier invasion of the intestine through the infected bile takes place. It is the second invasion which is responsible for the lesions occurring in the small intestine in the form of ulceration of the mucosa over the inflamed Peyer's patches together with mesenteric adenitis. When these intestinal lesions appear; the gross clinical manifestations of the disease become evident ***(Walter and Israel, 1979)***.

The typhoid bacillus exerts its main effects by an endotoxin which is not released until the death of the bacteria. The constitutional upsets are due mainly to this general toxaemia, while the local changes in tissue are due to both toxin and bacteremia. Therefore, every organ may be affected by toxaemia, bacteremia or by a combination of both ***(Huckstep, 1962)***.

Typhoid ulcers usually vary greatly in number and extent according to the severity of the disease, mainly they are long oval ulcers in the lower ileum, parallel to the long axis of the bowel and correspond in shape and arrangement to the Peyer's patches but may be high up in the small intestine and lower down in the large intestine. The appendix is frequently found to be affected with typhoid ulcers and a fair number of cases of peritonitis are found to be due to perforated typhoid appendix ***(Abu-Gharreeb, 1968)***.

The liver is hyperaemic, soft and enlarged in the early stages, microscopically; it shows the cloudy swelling of toxaemia with fatty changes in the liver cells. It can be involved by single or multiple typhoid abscesses ***(Huckstep, 1962)***.

The spleen is hyperaemic and enlarged especially in the early stages, it is soft and friable but rupture is rare, microscopically; small infarcts may be found with mononuclear cells and clumps of typhoid bacilli, the lymphoid follicles are packed with large mononuclear cells ***(Huckstep, 1962)***.