# CEREBROSPINAL FLUID TUMOR NECROSIS FACTOR - α IN CHILDREN WITH MENINGITIS

**THESIS**

**Submitted in Partial Fulfilment of Master Degree in Pediatrics**

By

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بسم الله الرحمن الرحيم

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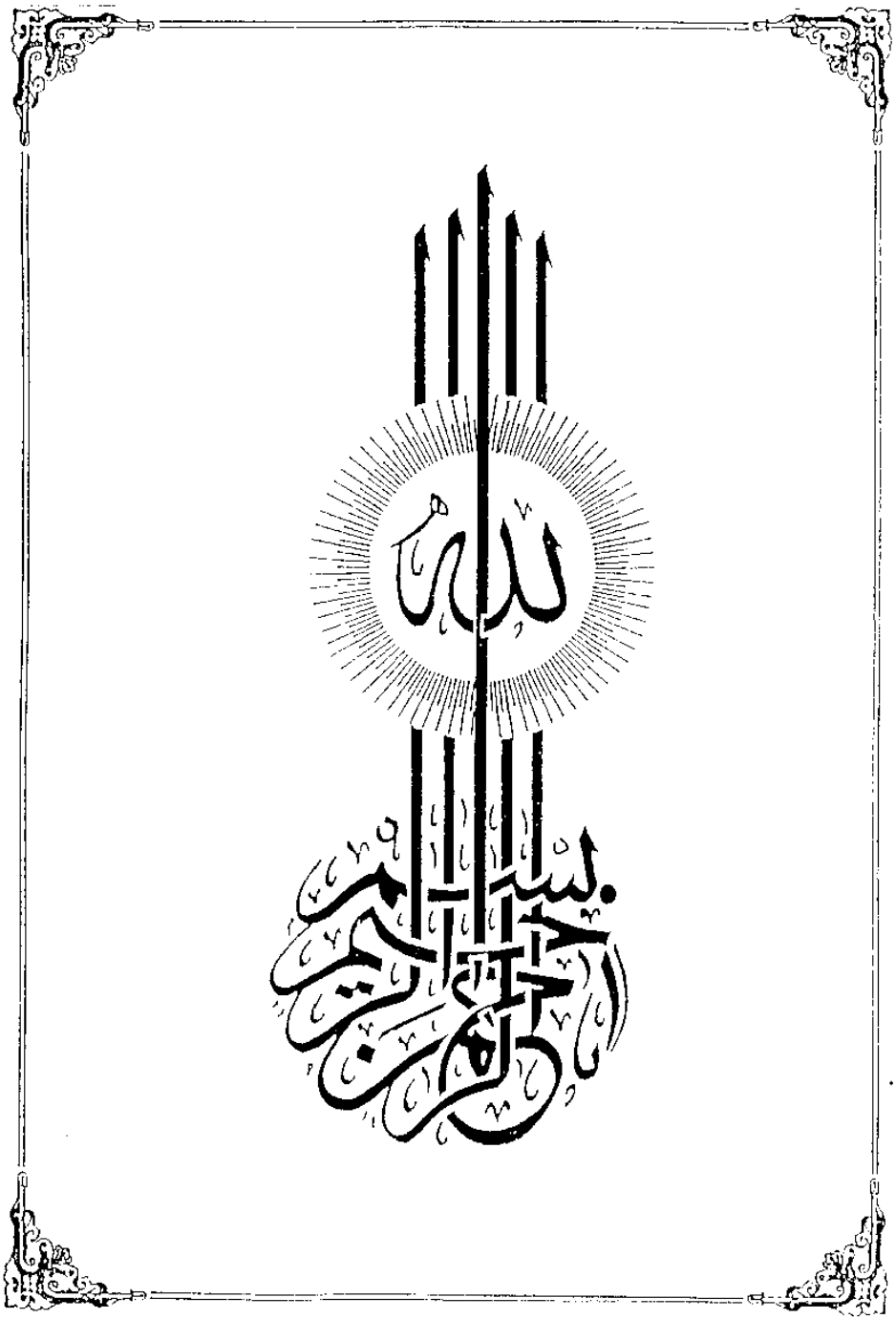
صدق الله العظيم

البقرة - ٣٢ -



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Hesham Salama

*THIS WORK IS DEDICATED TO . . .*

*MY LOVELY PARENTS*

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# LIST OF ABBREVIATIONS

| | |
|---|---|
| ADH | Antidiuretic hormone . |
| CBC | Complete blood count. |
| CIE | Counter immunoelectrophoresis . |
| CNS | Centeral nervous system . |
| CRP | C-reactive protein . |
| CSF | Cerebrospinal fluid . |
| CT | Computerized tomography . |
| DNA | Deoxyribonucleic acid. |
| EBV | Epstein -Barr virus . |
| ELISA | Enzyme linked immunosorbant assay . |
| ESR | Erythrocyte sedemintation rate . |
| GM-CSF | Granulocyte macrophage-colony stimulating factor. |
| H.R/min | Heart rate per minute . |
| IFN | Interferons . |
| IgM | Immunoglobulin M . |
| IL | Interleukins . |
| KD | Kilo dalton . |
| LPS | Lipopolysaccharide . |
| mg/dl | Milligram per deciliter . |
| µg | Microgram . |
| mRNA | Messenger ribonucleic acid. |
| PAF | Platelet activating factor . |
| pg/ml | Picogram per milliliter . |
| PMNL | Polymorphonuclear leucocytes . |
| R.R/min | Respiratory rate per minute . |
| r-TNF | Recombinant tumor necrosis factor . |
| SLE | Systemic lupus erythromatosus . |
| TCC | Total cell count . |
| TLC | Total leucocytic count . |
| TNF | Tumor necrosis factor . |

# INTRODUCTION

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The morbidity and mortality associated with bacterial meningitis have remained, distressingly, high decades after the introduction of antibiotics **(Schlech et al., 1985)** and the advent of newer, more potent antibiotics has not substantially improved the outcome of this disease **(Yogev , 1985)** .

One explanation is that the pathologic consequences of the disease beyond the leptomeninges, but within the central nervous system (CNS), progress despite the bacteriologic cure **(Swartz, 1984)** .

During the course of bacterial meningitis, bacterial cell wall products including peptidoglycan, techoic acid or the endotoxin lipopolysaccharide (LPS) which are generated in vivo or released during antibiotic therapy **(Täuber et al., 1987)** induce an intense host inflammatory response in the subarachnoid space **(Tuomanen et al., 1985 )** .

The resulting inflammatory response includes, not only the well-known cytochemical abnormalities, but also activation of the complement cascade **( Ernst et al., 1984 )** increase in arachidonate metabolism **( Tuomanen et al., 1985 )** release of a

complex network of inflammatory cytokines and other mediators (**Mustafa et al., 1989**) and activation of granulocytes and platelets ( **Täuber et al., 1988** ) .

The specific pathophysiologic changes leading to cerebral dysfunction and damage during bacterial meningitis ( **Scheld et al., 1987** ) are most probobaly induced by both bacterial products and the host inflammatory response ( **Tuomanen , 1988** ) and are well underway by the time the diagnosis of bacterial meningitis is made.

The induction and amplification of these host inflammatory responses, to control locally the infectious process may actually exert a destructive effect on the CNS and thus may contribute to the morbidity and mortality of meningitis (**Tuomanen , 1988**) .

The pathophysiologic effects of LPS are mediated by endogenous factors, such as cachectin/tumor necrosis factor-α (TNFα), interleukin-1 (IL-1), and platelet activating factor (PAF) ( **Beutler and Cerami , 1986** ) .

Recent studies have shown that local overproduction of cytokines, especially if prolonged, sustain the inflammatory response and induce consequences potentially detrimental to the host (**Dinarello , 1989**).

Evidence obtained from experimental meningitis suggests that components of bacterial cell wall stimulate local production and release of inflammatory mediators such as TNF α and IL-1 in the cerebrospinal fluid (CSF) ( **Mustafa et al., 1989** ) .

The complex interactions among the host and bacterial determinants of the CNS damage in bacterial meningitis are incompletely defined, and further understanding and identification of these interactions are essential before significant improvement in prognosis can be expected.

**Thus, the goal of this study is to assess the magnitude of involvement of TNF α in cases of meningitis by measurment of its level in CSF. Addingly, trial would be exerted to correlate between its level versus etiology of meningitis.**

# REVIEW OF LITERATURE

**CSF Circulation :**

The CSF circulates from the lateral to the third ventricle through the "Foramina of Monro", then to the fourth ventricle through the "Aqueduct of Sylvius". The fourth ventricle is connected with the subarachnoid space through a central foramen "Foramen of Magendie" and two lateral foramina "Foramina of Luschka". The CSF is reabsorbed from the subarachnoid space by the arachnoid villi to reach the venous circulation. So, it is in a dynamic state and replaced several times daily **(Romanes, 1981)**.

**Functions of CSF :**

1 - Protective function : the CSF is a medium that baths the brain and spinal cord. It regulates the pressure changes in the skull and acts as a protective agent against heat to which the central nervous system is extremely sensitive.

2 - Nourishment to the nerve cells : this is not accepted by many authors in view of the fact that the different components of the CSF are too small, though some authors have the openion that the composition of the CSF might be the most useful for the function of the nerve cells.

3 - A mean of removal of metabolic waste products : the CSF cooperates in removal of metabolic waste products and various poisnous substances from the central nervous system **(Ganong, 1983)**.

**Normal Values of CSF :** ( Table 1 )