SERUM TUMOR NECROSIS FACTOR-ALPHA IN CHILDREN WITH MENINGITIS

Thesis
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Master Degree in Pediatrics

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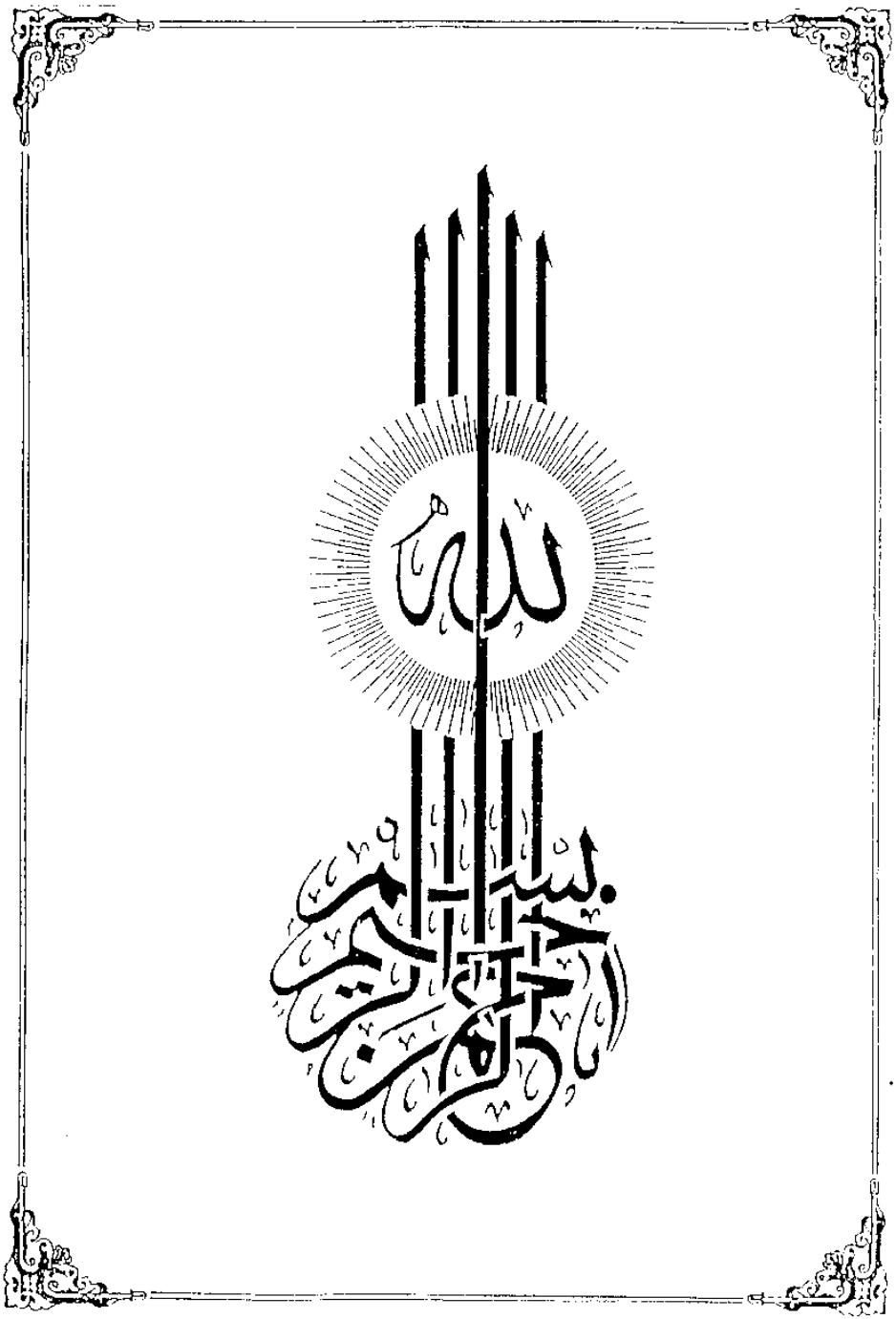
بسم الله الرحمن الرحيم

« الله لا إله إلا هو الحي القيوم لا تأخذه سنه ولا نوم له ما في السموات وما في الأرض من ذا الذي يشفع عنده إلا بإذنه يعلم ما بين أيديهم وما خلفهم ولا يحيطون بشئ من علمه إلا بما شاء وسع كرسيه السموات والأرض ولا يؤده حفظهما وهو العلي العظيم »

صدق الله العظيم

سورة البقرة الآية ٢٥٥



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Nahla Ahmed

TO

MY

FAMILY

LIST OF ABBREVIATIONS

TNF-α	= Tumor Necrosis Factor - alpha.
TNF-β	= Tumor Necrosis Factor - Beta.
IL-1	= Interleukin-1.
IL-6	= Interleukin-6.
IL-8	= Interleukin-8.
C.S.F.	= Cerebro - Spinal Fluid.
CNS	= Central Nervous System.
TLC	= Total Leucocytic Count.
PMNL	= Poly Morphe Nuclear Leucocyte.
C.B.C.	= Complete Blood Count.
ESR	= Erythrocyte Sedmintation Rate.
DIC	= Disseminated Intravascular Coagulation.
CRP	= C-Reactive Protein.
SIADH	= Syndrome of Inappropriate Secretion of Anti-Diuretic Hormone.
SLE	= Systemic Lupus Erythematosus.
PAF	= Platelet Activating Factor.
LPS	= Lipo-Polysaccharide.
CIE	= Counter Immune Electrophoresis.
ELISA	= Enzyme Linked Immune Sorbant Assay.
I.V.	= Intra - Venous.
I.M.	= Intra - Muscular.
O.	= Oral.
(CFU)/ml	= Colony Forming Units/milliliter.
GM-CSF	= Granulocyte - Monocyte Colony Stimulating Factor.
S.	= Significant.
N.S.	= Not Significant.
P.	= Prevalence.
S.D.	= Standard Deviation.
M.r.	= relative Molecular Mass.
A.	= Adenosine.
U.	= Uridine.
s.	= species.
r.	= range.

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INTRODUCTION
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AIM OF THE WORK

Meningitis is defined as the inflammatory process occurring in the leptomeninges, i.e pia-arachnoid ***(Feigin and Dodge, 1976).***

Increased susceptibility of the children in general and newborn infants in particular to meningitis might be due to the relatively high vascularity of their brains, and because of low levels of immunity against some organisms especially Escherichia coli, Haemophilus influenzae and group B-beta streptococci ***(Feigin and Dodge, 1976)***.

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 antibiotics has not substantially improved the outcome of this disease ***(Yogev, 1985)***.

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 ***(Tauber 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 ***(Bell, 1982),*** increase in arachnoid 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 ***(Tauber et al., 1988)***.

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

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-alpha (TNF-alpha), interleukin-1 (IL-1), and platelet activating factor (PAF) ***(Beutler and Cerami, 1986)***. Other studies have shown that local overproduction of cytokines, especially if prolonged, sustain the inflammatory response and induce consequences potentially detrimental to the host ***(Dinarello, 1988)***.

Evidence obtained from experimental meningitis suggests that components of bacterial cell wall stimulate local production and release of inflammatory mediators such as TNF-alpha and IL-1 in the serum ***(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 aim of this study was to assess the magnitude of involvement of TNF-Alpha in cases of meningitis by measurement of its level in serum. Addingly, trial would be exerted to correlate between its level versus etiology of meningitis.