Levels of Cytokines, Interleukin-1β & Interlukin-6 (IL-1β, IL-6) in Chronic Myelogenous Leukaemia (CML) patients: Relationship with Intercellular Adhesion Molecule-1 (ICAM-1) and Neutrophil Alkaline Phosphatase

Thesis
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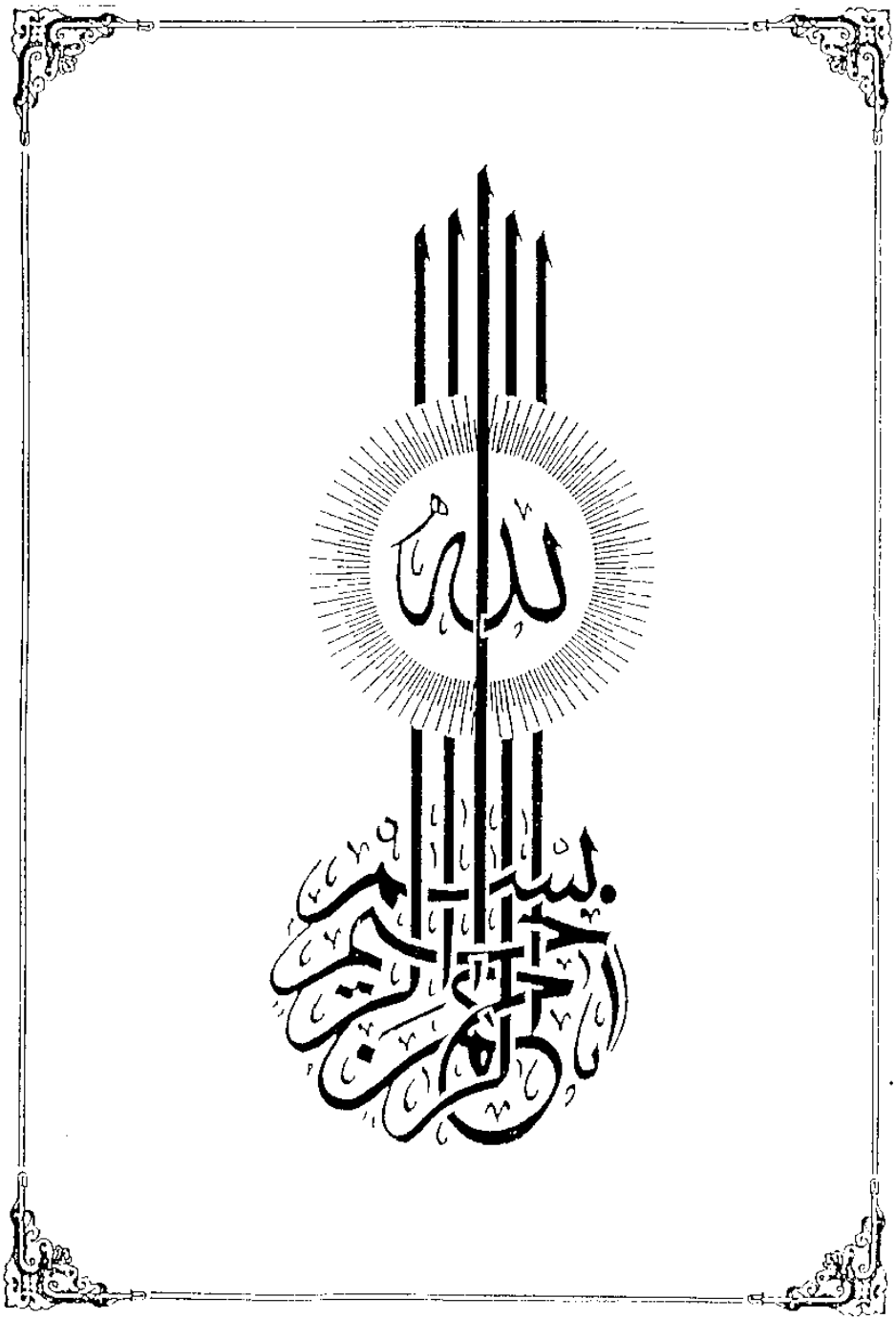

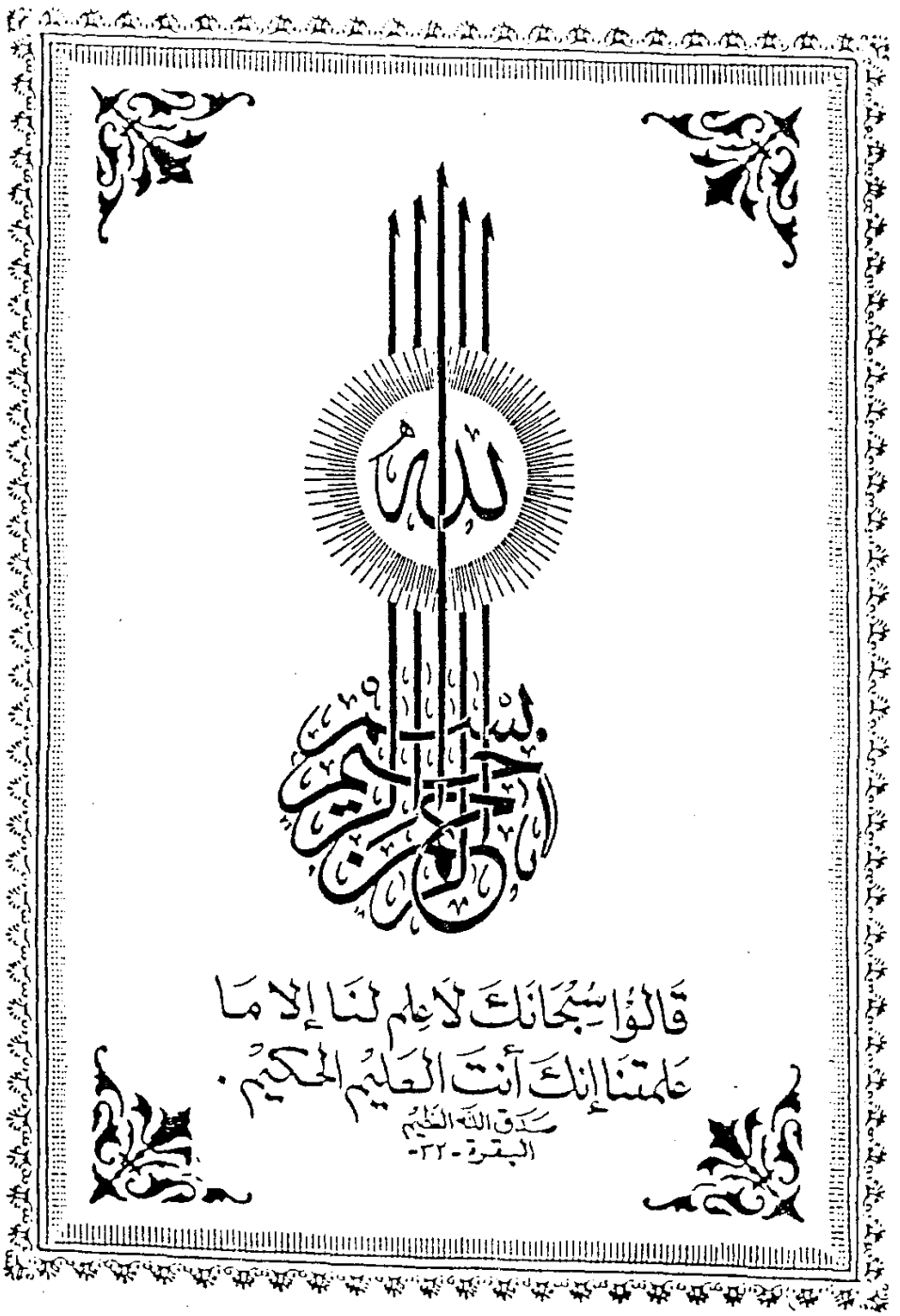

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LIST OF ABBREVIATIONS

ABL:	Abelson Protooncogene.
Acc :	Accelerated.
ADCC:	Antibody depenent cell mediated cytotoxicity.
Ag :	Antigen.
AML:	Acute myelogenous leukaemia.
APC:	Antigen presenting cell.
BC:	Blastic crisis.
BCR-ABL:	Breakpoint cluter region-ABL.
BFU-E:	Burst forming unit-Erythroid.
BFU-MK:	Burst forming unit-Megakaryocyte.
BL:	Basophilic leukaemia.
BM:	Bone marrow.
BMT:	Bone marrow transplantation.
CD4:	T-helper (TH).
CD8:	T-suppressor.
CD56:	Natural Killer.
CFC:	Colony forming cells.
CFMs:	Colony stimulating factor receptor.
CFU-GEMM:	Colony forming unit-granulocyte erythroid macrophage megakaryocyte.
CGL:	Chronic granulocytic leukaemia.
CHO:	Carbohydrate.
CHR:	Complete haematological remission.
C-Kit:	Stem cell factor receptor.
CML:	Chronic myelogenous leukaemia.
CNTF:	Ciliary neutrophilic factor.
CMML:	Chronic myelomonocytic leukaemia.
CMoL:	Chronic monocytic leukaemia.
CSF:	Colony stimulating factor.

CSF-G:	CSF-granulocyte.
CSF-GM:	CSF-granulocyte macrophage.
CSF-M:	CSF-monocyte.
CSF-Meg:	CSF-megakaryocyte.
α :	Alpha.
CSA:	Colony stimulating activity.
CSIF:	Cytokine synthesis inhibitory factor.
EDTA:	Ethylene diamine tetraacetate.
EL:	Eosinophilic leukaemia.
ELAM-1:	Endothelial adhesion molecule-1.
EPo:	Erythropoietin.
FAB:	French American British.
FACS:	Fluorescence activated cells.
HA:	Hyaluronic acid.
HEK:	Human embryonic kidney.
HEV:	High endothelial venules.
HTLV:	Human T-cell leukaemia.
ICAM:	Intercellular adhesion molecule.
Ig:	Immunoglobulin.
IL:	Interleukin.
IL-1RA:	Interleukin-1 receptor antagonist.
IFN-γ:	Interferon-γ.
KD:	Kilo Dalton.
LAD:	Leucocyte adhesion deficiency.
LAF:	Lymphocyte activating factor.
LAK:	Lymphokine activated killer.
LFA:	Leucocyte function associated antigen.
LIF:	Leucocyte inhibitory factor.
LPS:	Lipopolysaccharide.
MHC:	Major hitocompatibility complex.
MIP-1α:	Macrophage inflammatory protein-1α.
MM:	Multiple myeloma.

MW:	Molecular weight.
NAP:	Neutrophil alkaline phosphatase.
NAP-2:	Neutrophil activating peptide-2
NCAM:	Neutral cell adhesion molecule.
NK-SF:	Natural killer cell stimulatory factor.
OSM:	Oncostatin-M.
PADGEM:	Platelet activation dependent granule to external membrane.
PDGF:	Platelet derived growth factor. Ph-chromosome: Philadelphia chromosome.
SCF:	Stem cell factor.
SIL-6R:	Soluble interleuin-6 receptor.
TH:	T-helper.
TCR:	T-cell receptor.
TGF:	Transforming growth factor.
TNF-α:	Tumour necrosis factor-α.
TSH:	Thrombopoietin.
TSF:	Thrombocytopoiesis stimulating factor.
VLA:	Very late activation.

ABSTRACT

Chronic myelogenous leukaemia (CML) is characterized by metamorphosis of the chronic phase to blastic crisis. However, cellular events associated with this transition are not well understood. To examine the possible participation of cytokines and adhesion molecules in this process, we studied the levels of IL-1β, IL-6 and ICAM-1in serum and supernatant of in-vitro culture for a series of CML patients and normal controls and correlated their levels with neutrophil alkaline phosphatase (NAP) score on one hand and other studied haematological parameters on the other hand. Both IL-1β and IL-6 as well as ICAM-1 were associated with the disease progression as they were markedly elevated in accelerated/ blastic crisis (Acc/BC) phases compared to chronic (Chr) phase or control group ($P<0.001$). High IL-1β, IL-6 and ICAM-1 levels were highly associated with increased marrow and peripheral blast cells as well as with NAP score. In contrast, no significant correlation could be detected between the three studied parameters and Hb level, TLC and platelets. Both IL-1β and IL-6 were significantly decreased in the supernatant of in-vitro culture compared to their levels in serum while IL-6 is sharply increased. Finally, IL-1β values were directly correlated with IL-6 and ICAM-1 indicating that IL-1β is a pleotropic cytokine that has an obvious role in induction of other cytokines and adhesion molecules which clarifies its pivotal role in the pathophysiology of CML and as an essential molecular master switch in the whole process.