STUDY OF PLASMA ENDOTHELIN-1 LEVEL IN LIVER CIRRHOSIS AND HEPATORENAL SYNDROME

THESIS
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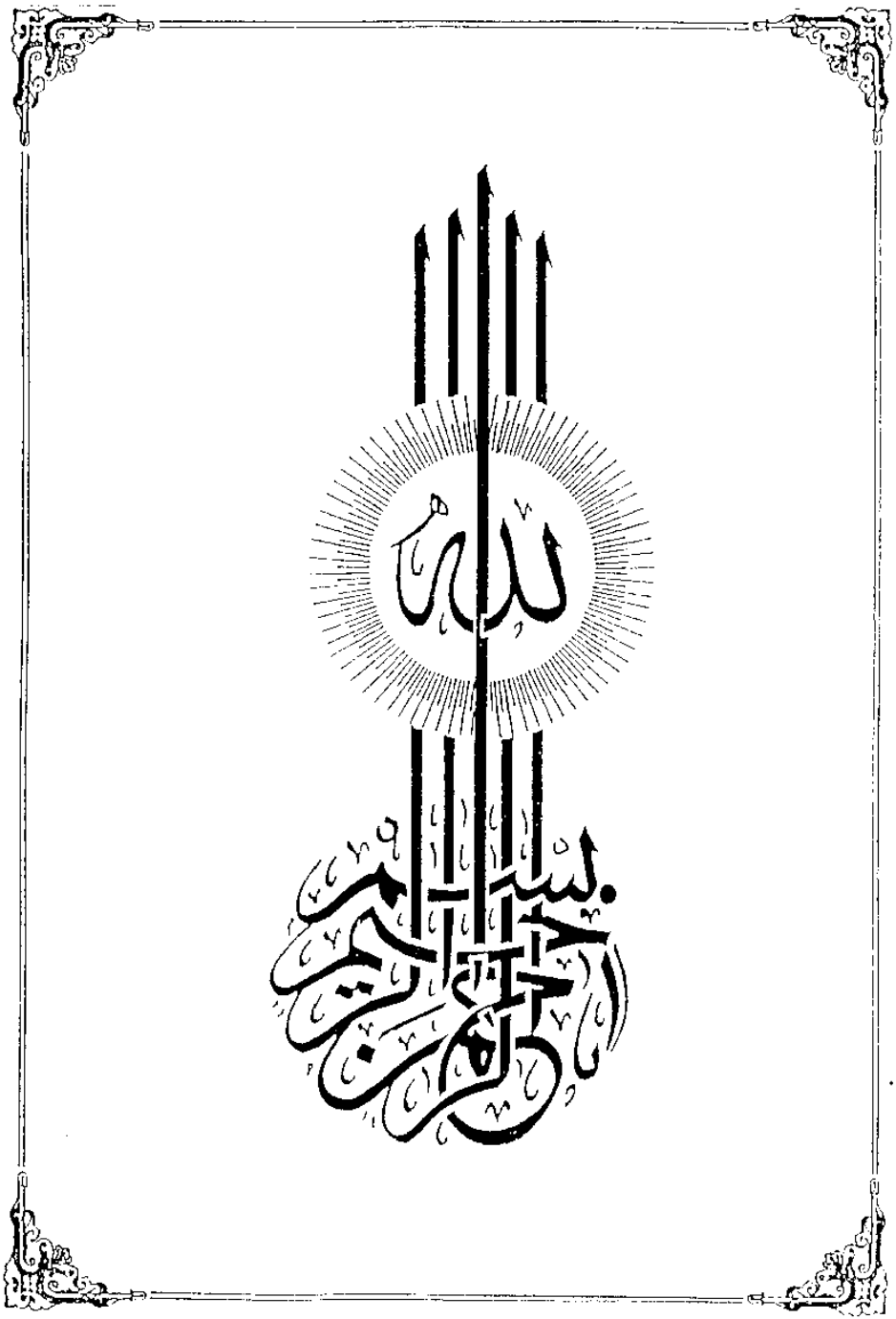

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ABBREVIATIONS

ET	Endothelin
PGI_2	Prostacyclin
ATP	Adenyl triphosphate
ADP	Adenyl diphosphate
NO	Nitric oxide
EDRF	Endothelium derived relaxing factor
cGMP	Cyclic guanosine monophosphate
cAMP	Cyclic adenosine monophosphate
A-II	Angiotensin-II
t-PA	Tissue plasminogen activator
EDHF	Endothelium-derived hyperpolarizing factor
ACE	Angiotensin converting enzyme
PAF	Platelet activating factor
$[Ca^{2+}]i$	Intracellular calcium
$[Ca^{2+}]$	Ionized calcium
GFR	Glomerular filtration rate
RBF	Renal blood flow
TXA_2	Thromboxane A2
VIC	Vasoactive intestinal contractor
S6b	Sarafotoxin 6 b
APR	Acute phase reactant
TGF-ß	Transforming growth factor ß
AU	Adenosine uracil
Lys	lysine
Arg	Arginine
Cys	Cysteine
Met	Methionine
Tryp	Tryptophan
Ile	Isoleucine
ECE	Endothelin converting enzyme
ET-1-LI	Endothelin-1 like immunoreactivity
PMN	Polymorphonuclear
ANP	Atrial natriuretic peptide
TNF	Tumor necrosis factor
IL-1	Interleukin-1
PLC	Phospholipase C
PI	Phosphatidyl inositide
IP	Inositol phosphate
PKC	Protein kinase C

EC	Extracellular
IC	Intracellular
EGTA	Ethyl glycol tetra-acetic acid
ROC	Receptor operated channel
VOC	Voltage operated channel
PLA2	Phospholipase A2
NEP	Neutral endopeptidase
SNFR	Single nephron filtration rate
RAS	Renin angiotensin system
ADH	Antidiuretic hormone
EDCF	Endothelium derived contracting factor
ARF	Acute renal failure
RIA	Radioimmunoassay
EIA	Enzyme immunoassay
CLIA	Chemiluminescence immunoassay
POD	Peroxidase
TFA	Trifloro acetic acid
HPLC	High performance liquid chromatography
ATN	Acute tubular necrosis
AST	Aspartate amino transferase
ALT	Alanine amino transferase
ALP	Alkaline phosphatase
GGT	Gammaglutamyl transferase
HRS	Hepatorenal syndrome
FeNa	Fractional excretion of sodium
COP	Cardiac output
GIT	Gastrointestinal tract
MAO	Monoamine oxidase
AV	Arteriovenous
EDTA	Ethylene diamine tetra acetic acid
KIU	Kallikrein inhibitory unit

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INTRODUCTION
AND
AIM OF THE WORK

Introduction:

Endothelin (ET) is a recently discovered circulating polypeptide consisting of 21 amino acids. Three isoforms have been identified; ET (1,2,3) ***(Inoue et al., 1989)a***.

Endothelial cells produce exclusively ET-1 ***(Saito et al., 1989)***. ET-1 produces a profound and sustained contractile response ***(Yanagisawa et al., 1988)***. This effect occurs through rising of the intracellular free Ca^{++} and increasing the inositol phosphate turnover ***(Marsden et al., 1989)***.

Elevated plasma concentrations of endothelin have been reported in patients with acute renal failure ***(Firth et al., 1988)***, subarachnoid hemorrhage ***(Masaoka et al., 1989)***, myocardial infarction ***(Miyauchi et al., 1989)***, chronic renal failure, hypertension ***(Shichiri et al., 1990)*** and sepsis ***(Pittet et al., 1991)***.

Endothelial cells of various origin synthesize endothelin. It is therefore likely that the hepatic endothelial and Kupffer cells, which are the predominant cell types constituting liver sinusoids also synthesize this peptide ***(Yanagisawa et al., 1988 and Takahashi et al., 1989)***.

Under conditions of hypoxia and vascular tissue damage, endothelial cells are stimulated to synthesize and secrete endothelin ***(Firth et al., 1988)***. Accordingly, in cases of liver injury leading to hepatic hypoxia, the hepatic endothelial cells also generate this peptide. Since this peptide produces a powerful renal and systemic vasoconstriction, such effects may mediate the development of renal failure in patients with severe liver disease ***(King et al., 1989)***.

Aim of the work:

The aim of the present work is to study plasma endothelin levels in patients with liver cirrhosis with and without ascites, acute renal failure and hepatorenal syndrome in a trial to find out the clinical significance of endothelin in the various studied diseased groups as well as its possible role in the pathogenesis of the hepatorenal syndrome.