Assessment of Nitric Oxide in Exhaled Air in Children with Liver Cirrhosis

Thesis
Submitted in partial fulfillment for
M.Sc. Degree in Pediatrics

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FACULTY OF MEDICINE
Ain Shams UNIVERSITY
1997

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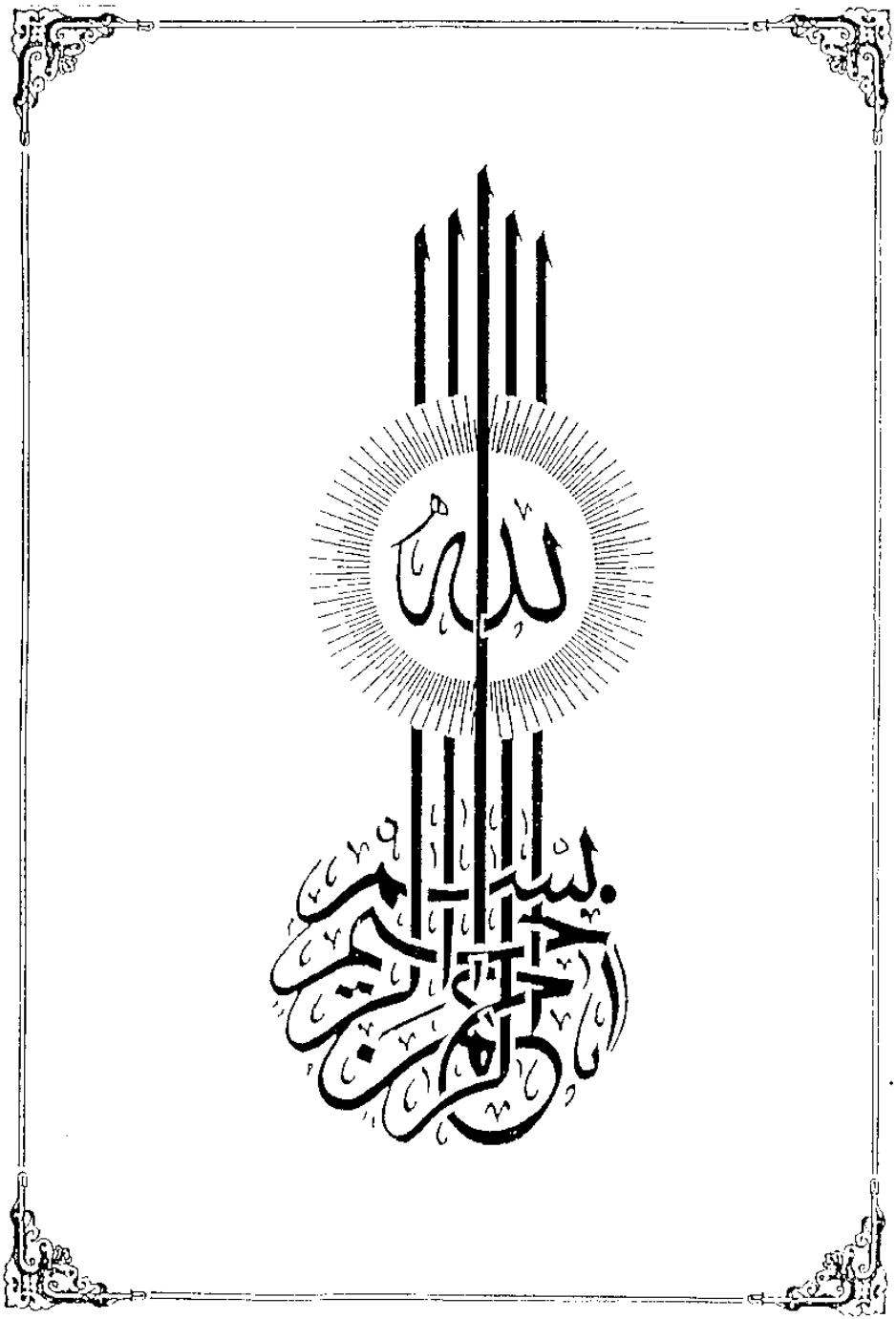

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LIST OF ABBREVIATIONS

ADMA	Asymmetric dimethyl arginine
Alk Ph	Alkaline phosphatase
ALT	Alanin transaminase
AST	Aspartat transaminase
CGRP	Calcitonin gene related peptide
CI	Cardiac index
DCM	Dilated cardiomyopathy
ED	Endothelial dysfunction
EDRF	Endothelium derived relaxing factor
eNOS	endothelial nitric oxide synthase
ET-1	Endothelin 1
GSD	Glycogen storage disease
HBV	Hepatitis B virus
HCV	Hepatitis C virus
HGF	Hepatocyte growth factor
HPV	Hypoxic pulmonary vasoconstriction
HRS	Hepatorenal syndrome
HSC	Hepatic stellate cell
HSCs	Hepatic stellate cells
IL-1	Interleukin-1
IL-6	Interleukin-6

LIST OF ABBREVIATIONS (CONT.)

INF	Interferon
iNOS	inducible nitric oxide synthase
L-NAME	Nitroglycerine L-arginine methyl ester
L-NMMA	Nitroglycerine monomethyl L-arginine
Lam-PI	Laminin
LDL	Low density lipoprotein
LPS	Lipopolysaccharides
NO	Nitric oxide
nNOS	Neuronal nitric oxide synthase
NO2	Nitrite
NO3	Nitrate
NOS	Nitric oxide synthase
NOSS	Nitric oxide synthases
ONOO	Peroxynitrite
P III P	Procollagen III
PDGF	Platelet derived growth factor
PET	Posetron emmersion tomography
ppb	part per billion
ppm	part per milion
TGF-B	Transforming growth factor B
TNF	Tumor necrosis factor

LIST OF ABBREVIATIONS (CONT.)

TNF alpha	Tumor necrosis factor alpha
UK	United Kingdom
VIP	Vasoactive intestinal peptide

Acknowledgement

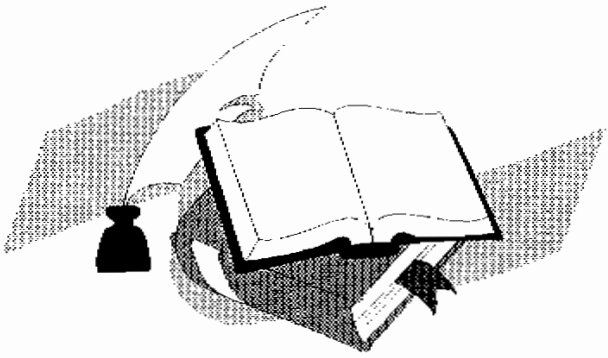
I would like to express my deepest thanks and grateful appreciation to **Prof. Dr. Zeinab Anwar El-Kabbany,** *Professor of Pediatrics, Ain Shams University, to whom I owe more than words can express her limitless help, valuable advice and kind encouragement are beyond acknowledgement.*

I would like to express my sincere appreciation and deep gratitude to **Dr. Eman Monir Sherif,** *Lecturer of Pediatrics, Ain Shams University, for her valuable guidance and suggestions. Her cooperative attitude was of great help to complete the work.*

I owe special gratefulness and much regards to **Prof. Dr. Ahmed Hussein Abdel Karim,** *Prof. of Occupational and Environmental Health, Ain Shams University. His encouragement, guidance and valuable advice were behind the accomplishment of this work.*

Thanks to all staff members and to all patients who shared a lot in this work.

Magda Erian Badrous, 1997



Introduction &
Aim of the Work

INTRODUCTION

Patients with liver cirrhosis exhibit circulatory derangement characterized by peripheral vasodilatation mainly in the splanchnic bed, tendency towards hypotension, increased cardiac output and hyperdynamic circulation.

This peripheral vasodilatation is clinically important, as it is thought to be responsible for the pathogenesis of complications that may be encountered in these patients such as ascites and hepatorenal syndrome **[Michielsen and Pelckmans, 1994]**.

The precise mechanisms of these hemodynamic disorders have not yet been clearly elucidated. Excessive production of vasodilators, such as prostacyclin, bradykinin, substance P, and atrial natriuretic peptide has been proposed , but there is no clear evidence to show that vasodilators are involved **[Bosch et al., 1988].**

Vallance and Moncada [1991] hypothesized that nitric oxide (NO), originally discovered as an endothelium derived relaxing factor, may be a causative factor in hemodynamic disorders in patients with liver cirrhosis.

High concentration of circulating endotoxins are frequently found in patients with cirrhosis who have no clinical evidence of infection **[Lumsden et al., 1988]**.

Thus, the endotoxemia of liver cirrhosis may induce nitric oxide synthase directly in blood vessels or indirectly through

cytokines, including interleukin -1, tumor necrosis factor, bradykinine, histamine and thrombin **[Ignarro, 1989]**, leading to increased synthesis and release of nitric oxide that may account for the hemodynamic abnormalities **[Tilg et al., 1992]**.

Aim of the work

The aim of this work is to determine nitric oxide output in exhaled air in children with liver cirrhosis and to examine the correlation between systemic hemodynamics and nitric oxide production in these patients.