

بسم الله الرحمن الرحيم





شبكة المعلومات الجامعية التوثيق الالكتروني والميكرو فيلم



جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

قسم

نقسم بالله العظيم أن المادة التي تم توثيقها وتسجيلها
علي هذه الأقراص المدمجة قد أعدت دون أية تغيرات



يجب أن

تحفظ هذه الأقراص المدمجة بعيدا عن الغبار





بعض الوثائق الأصلية تالفة





بالرسالة صفحات
لم ترد بالأصل



B1NCA7

PLASMA ENDOTHELIN I CONCENTRATION IN PATIENTS WITH CONGENITAL HEART DISEASES

Thesis

Submitted for partial fulfillment of M.D. degree
In PEDIATRICS



By

Ahmed Anwar Attia Khattab

M.B. B.Ch., M.Sc. Pediatrics

Supervised by

Dr. Fahima
Prof. Dr.

Fahima Mohamed Hassane

Professor of Pediatrics
Faculty of Medicine, Minufiya University

Dr. Soheir
Prof. Dr.

Soheir Sayed Abou El-Ella

Professor of Pediatrics and Vice Dean
Faculty of Medicine, Minufiya University

Dr. Ahmed
Prof. Dr.

Ahmed Abbas Raouf

Professor and Head of Biochemistry Dept.,
Liver Institute, Minufiya University

Dr. Fady
Dr.

Fady Mohamed El-Gendy

Assistant Professor of Pediatrics
Faculty of Medicine, Minufiya University

Dr. Tarek
Dr.

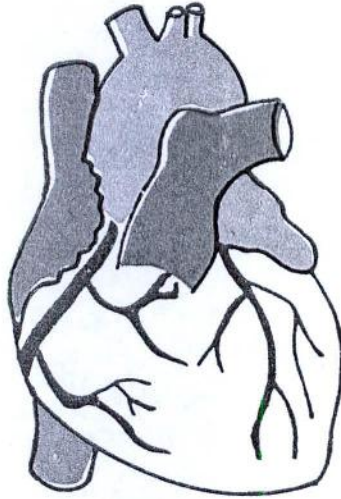
Dr. Tarek Khaliel

Assistant Professor of Cardiology,
Faculty of Medicine, Minufiya University

FACULTY OF MEDICINE
MINUFIYA UNIVERSITY
2000

Dr. el sh
Dr. el sh

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ



"قالوا سبحانك لا علم لنا إلا ما علمتنا
إنك أنت العزيز الحكيم"

صدق الله العظيم

(البقرة ٢٢)

Acknowledgement

*I would like to express my sincere gratitude to **Prof. Dr. Fahima Mohamed Hassane**, Professor of Pediatrics, Faculty of Medicine, Minufiya University whose guidance, help and sincere supervision were the cornerstone in the building up of this thesis. She kindly supervised all the details of this work and revised all the work throughout its various steps.*

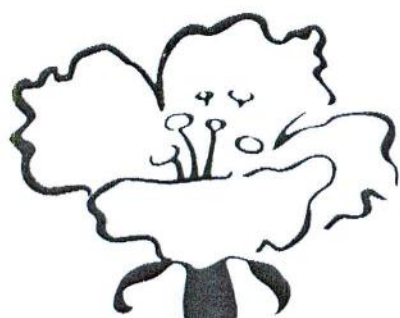
*I would like to express sincere gratitude to **Dr. Soheir Sayed Abou El-Ella**, Professor of Pediatrics, Faculty of Medicine, Minufiya University for her generous advice, kind supervision, continuous encouragement and huge assistance in this work. She offered me much of her unlimited experience in this research.*

*I would like to express my gratitude to **Prof. Dr. Ahmed Abbass Raouf**, Professor and Head of Biochemistry Department, Liver Institute, Minufiya University, for his valuable help, cooperation, encouragement, accurate revision, continuous support, and helpful guidance during all steps of this thesis.*

*My sincere appreciation to **Dr. Fady Mohamed El-Gendy**, Assistant Professor of Pediatrics, Faculty of Medicine, Minufiya University for his kind moral support and encouragement.*

*Deep thanks to **Prof. Dr. Tarek Khaliel**, Assistant Professor of Cardiology, Faculty of Medicine, Minufiya University for his encouragement, accurate supervision and kind cooperation,*

Lastly and not the least .. deep thaks to all people who participated in this work.



To

My beloved family

CONTENTS

	<i>Page</i>
- LIST OF ABBREVIATIONS	I
- LIST OF TABLES	II
- LIST OF FIGURES	IV
- INTRODUCTION	1
- AIM OF THE WORK	3
- REVIEW OF LITERATURE	4
* Congenital Heart Diseases:	4
• Definition	
• Prevalence	
• Fetal circulation	
• Etiology	
• Classifications	
• Diagnosis	
* Pulmonary Hypertension:	48
• Definition	
• Etiology	
• Pathogenesis	
• Pathology	
• Diagnosis	
• Treatment	
* Endothelin-1:	68
• Definition and origin	
• Structure and types	
• Endothelin receptors	
• Endothelin release and control	
• Mechanism of action	

- Pathophysiologic roles of ET1 in different pathological conditions

- Endothelin antagonists

- SUBJECTS AND METHODS	92
- RESULTS	109
- DISCUSSION	135
- SUMMARY	146
- CONCLUSION	149
- RECOMMENDATIONS	150
- APPENDIX	151
- REFERENCES	160
- ARABIC SUMMARY	

LIST OF ABBREVIATIONS

• A.S.D. :	Atrial septal defect
• Bivent. ++ :	Biventricular enlargement
• C.A.V.C. :	Common atrioventricular canal
• C.H.D. :	Congenital heart disease
• C.I. :	Cardiac index
• C.O.P. :	Cardiac output
• E.C.G. :	Electrocardiography
• Echo :	Echocardiography
• ET-1 :	Endothelin-1
• F4 :	Fallot's tetralogy
• LBBB :	Left bundle branch block
• LSH :	Left side of the heart
• Lt. V. :	Left ventricle
• Lt. vent. ++ :	Left ventricular enlargement
• MPAP :	Mean pulmonary artery pressure
• O ₂ sat. :	Oxygen saturation
• P.A. :	Pulmonary artery
• P.D.A. :	Patent ductus arteriosus
• P.S. :	Pulmonary stenosis
• P.V.R. :	Pulmonary vascular resistance
• pH :	Pulmonary hypertension
• RBBB :	Right bundle branch block
• RSH :	Right side of the heart
• Rt. V. :	Right ventricle
• Rt. vent. ++ :	Right ventricular enlargement
• T.G.A. :	Transposition of the great vessels
• V.S.D. :	Ventricular septal defect
• ♂ :	Male
• ♀ :	Female

LIST OF TABLES

Page

Tables in Review:

Table 1: Incidence of specific congenital heart defects	2
Table 2: Most important genes involved in cardiovascular morphogenesis	11
Table 3: Applications of catheterization in establishing etiologic diagnosis of pulmonary hypertension	62
Table 4: Endothelin receptor affinities	73
Table 5: Two distinct pharmacologic activities of endothelins	75
Table 6: Factors known to release endothelin	77
Table 7: Endothelin receptor antagonists	91
Table 8: Non-specific endothelin antagonists	91

Tables in Results:

• Table (1): Congenital heart cases included in the study	115
• Table (2): Age, sex, weight and height of studied groups.	116
• Table (3): Distribution of age groups among the studied groups	117
• Table (4): Comparison between MPAP measured by catheter and Echo among group I and group II.	120
• Table (5): Comparison between group I and group II regarding O ₂ saturation, C.I. and P.V.R.	122
• Table (6): Rt. S. ET1, P.A. ET1 and Lt. S. ET1 among the studied groups.	124
• Table (7): Plasma ET1 level in group I and group II distributed by ECG data of both groups	125
• Table (8): Correlation matrix between ET1 and other variables among group I.	128

	<i>Page</i>
• Table (9): Correlation matrix between ET1 and other variables among group II.	129
• Table (10): Correlation of P.V.R. with some variables among group I and group II.	130
• Table (11): Correlation of C.I. with some variables among group I and group II.	131
• Table (12): Right sided ET1, P.A. ET1 and left sided ET1 profiles among group I variables (irreversible versus reversible pulmonary hypertension).	132
• Table (13): Comparison between MPAP measured by catheterization before and after giving O ₂ 100% in group I.	133

LIST OF FIGURES

	<i>Page</i>
Figures in Review:	
Fig. (1): Structure of human endothelins and one of the snake venom sarafotoxins	69
Fig. (2): Proteolytic processing of preproendothelin and proendothelin in biosynthesis of mature endothelin-1	78
Fig. (3): Intracellular transduction pathways activated by endothelin	80
Figures in Results:	
Fig. (1): Age distribution among the studied groups	121
Fig. (2): Sex distribution among the studied groups	119
Fig. (3): Comparison between main pulmonary artery pressure measured by catheter and echo among group I and group II	121
Fig. (4): Comparison between group I and group II regarding O ₂ saturation, cardiac index and pulmonary vascular resistance	126
Fig. (5): Plasma endothelin-1 level in patients of group I with left ventricular enlargement and biventricular enlargement detected by ECG	126
Fig. (6): Plasma ET-1 level in patients of group II distributed by ECG data	127
Fig. (7): Comparison between mean pulmonary artery pressure measured by catheterization before and after giving oxygen 100% in group I	134