

شبكة المعلومات الجامعية التوثيق الإلكتروني والميكروفيلو

بسم الله الرحمن الرحيم





MONA MAGHRABY



شبكة المعلومات الجامعية التوثيق الإلكتروني والميكروفيلو



شبكة المعلومات الجامعية التوثيق الالكتروني والميكروفيلم



MONA MAGHRABY



شبكة المعلومات الجامعية التوثيق الإلكترونى والميكروفيلم

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



MONA MAGHRABY



Screening for Microvascular and Macrovascular Complications using Echocardiography and Cathelicidin in Children and Adolescents with Type 1 Diabetes

Thesis

Submitted for Partial Fulfillment of Master Degree of **Pediatrics**

By

Reham Mohamed Shiba Alhamd

M.B.,B.Ch (2013)
Faculty of Medicine, Ain Shams University

Under Supervision of

Prof. Dr. Randa Mahmoud Asaad Sayed Matter

Professor of Pediatrics Faculty of Medicine, Ain Shams University

Dr. Rasha Adel Fathy Thabet

Lecturer of Pediatrics
Faculty of Medicine, Ain Shams University

Dr. Marwa Waheed Abd Elhady Nasef

Lecturer of Pediatrics
Faculty of Medicine, Ain Shams University

Faculty of Medicine Ain Shams University

2021



سورة البقرة الآية: ٣٢

Acknowledgments

First and foremost, I feel always indebted to **Allah** the Most Beneficent and Merciful.

I wish to express my deepest thanks, gratitude and appreciation to **Prof. Dr. Randa Mahmoud Asaad Sayed Matter**, Professor of Pediatrics, Faculty of Medicine, Ain Shams University, for her meticulous supervision, kind guidance, valuable instructions and generous help.

Special thanks are due to **Dr. Rasha Adel Fathy Thabet**, Lecturer of Pediatrics, Faculty of Medicine, Ain
Shams University, for her sincere efforts, fruitful
encouragement.

I am deeply thankful to **Dr. Marwa Waheed Abd Elhady Masef**, Lecturer of Pediatrics, Faculty of
Medicine, Ain Shams University, for her great help,
outstanding support, active participation and guidance.

I would like to express my hearty thanks to all my family for their support till this work was completed.

Last but not least my sincere thanks and appreciation to all patients and their families participated in this study.

Reham Mohamed Shiba Alhamd

Tist of Contents

Title	Page No.
List of Tables	i
List of Figures	iii
List of Abbreviations	vii
Introduction	1
Aim of the Work	3
Review of Literature	
Type 1 Diabetes Mellitus	4
Complications and Comorbidities of Type 1 Diabete Mellitus	
Left Ventricular Diastolic Dysfunction (LVDD)	35
Cathelicidin as a Marker	50
Patients and Methods	55
Results	71
Discussion	95
Summary	107
Conclusion	111
Recommendations	112
References	114
Appendix	136
Arabic Summary	

Tist of Tables

Table No.	Title	Page No.
Table 1:	Criteria for the Diagnosis of Diabetes	s7
Table 2:	Types of insulin preparations and action profiles for S.C. administration	
Table 3:	ISPAD, Screening recommendations factors for vascular complications	
Table 4:	ISPAD, Recommended threshold different parameters for interver primary prevention of microvascular in children and adolescents with diabetes:	ntion and and CVD h type 1
Table 5:	Descriptive data for studied groups sociodemographic data, anth measures and diabetic history	ropometric
Table 6:	Shows incidence of mic complications among the study group	
Table 7:	Comparison between 3 groups socioeconomic and anthropometric m	_
Table 8:	Comparison between three groups history, glycemic control and diabet acute complications.	tes related
Table 9:	Comparison between three groups lipid profile, presence of mic complication and cathelicidin level	rovascular
Table 10:	Shows comparison between three regarding echocardiographic examinations and the comparison between three regarding echocardiographic examinations.	· -
Table 11:	Correlation between cathelicidin lev clinical, laboratory parameters, r characteristics of the studied groups.	adiological

Tist of Tables cont...

Table No.	Title	Page No.
Table 12:	Shows relation between cath different variants including acute complications of type 1 diabetes i groups.	e and chronic n the studied
Table 13:	Correlation between CIMT and clinical, laboratory parameters, characteristics of the studied grou	radiological
Table 14:	Shows relation between CIMT variables of the studied groumicrovascular and not complications	ps including nacrovascular
Table 15:	Comparison between all studied and without diastolic dysfunctio different studied variables	n as regards

Tist of Figures

Fig. No.	Title	Page No.
Figure 1: Figure 2:	Pathogenesis of type 1 diabetes mellity Adverse micro-vascular and macro- complications of diabetes leading to nephropathy, retinopathy, and neurop	-vascular diabetic
Figure 3:	Evaluation of left-ventricular diastolic using echocardiography	function
Figure 4:	Pulsed-wave Doppler imaging of the valve shows peak <i>E</i> wave velocity (<i>A</i>), and decomposed of the peak <i>A</i> wave velocity (<i>A</i>), and decomposed of the peak <i>A</i> wave velocity (<i>A</i>), and decomposed of the peak <i>A</i> wave velocity (<i>A</i>), and decomposed of the peak <i>A</i> wave velocity (<i>A</i>), and decomposed of the peak <i>A</i> wave velocity (<i>A</i>), and decomposed of the peak <i>A</i> wave velocity (<i>A</i>), and decomposed of the peak <i>A</i> wave velocity (<i>A</i>), and decomposed of the peak <i>A</i> wave velocity (<i>A</i>), and decomposed of the peak <i>A</i> wave velocity (<i>A</i>), and decomposed of the peak <i>A</i> wave velocity (<i>A</i>), and decomposed of the peak <i>A</i> wave velocity (<i>A</i>), and decomposed of the peak <i>A</i> wave velocity (<i>A</i>), and decomposed of the peak <i>A</i> wave velocity (<i>A</i>), and decomposed of the peak <i>A</i> wave velocity (<i>A</i>), and decomposed of the peak <i>A</i> wave velocity (<i>A</i>), and decomposed of the peak <i>A</i> wave velocity (<i>A</i>), and decomposed of the peak <i>A</i> wave velocity (<i>A</i>), and decomposed of the peak <i>A</i> wave velocity (<i>A</i>), and decomposed of the peak <i>A</i> wave velocity (<i>A</i>), and decomposed of the peak <i>A</i> wave velocity (<i>A</i>), and decomposed of the peak <i>A</i> wave velocity (<i>A</i>).	e mitral ity (E) , eleration
Figure 5:	time (DT)	iography Ea wave
Figure 6:	Progression from normal diastolic fur worsening degrees of left ventricular dysfunction (LVDD)	nction to diastolic
Figure 7:	Algorithm for grading of left verdiastolic dysfunction (LVDD) in our according to the 2016 American Section Cardiography and European Assof Cardiovascular Imaging (ASE)	ntricular tpatients ociety of sociation
Figure 8:	guidelines	41 ging from from the Tissue
Figure 9:	view sampling from the septal mitral a Recordings of velocity–time curves b tissue Doppler imaging from the basa and lateral wall	annulus 42 y pulsed l septum 43
Figure 10:	Mechanisms of diabetic cardiomyopath	ıy46

Tist of Figures cont...

Fig.	No.	Title	Page No.
Figu	ıre 11:	General pathogenesis of cardiomyopathy (DCM) and its relevant to heart failure (HF)	evolution
Figu	ıre 12:	Summary of cathelicidin functions	50
Figu	ıre 13:	Cathelicidins have multiple mic	crobicidal,
		immune modulatory & inflammo m	odulatory
		properties	51
Figu	ıre 14:	Philips Ultrasound EPIQ CV	$f_{\mathbf{x}}$ with
		Ultrasound transducer L12-4 (12-4 N	1Hz). 63
Figu	ıre 15:	Pulsed wave tissue Doppler Imaging	from the
		apical 4 chamber view from the sep	tal mitral
		annulus	65
Figu	ıre 16:	Pulsed wave tissue Doppler Imaging	from the
		apical 4 chamber view from the late	ral mitral
		annulus	65
Figu	ıre 17:	Shows M-mode echocardiograp	ohy for
		calculation of aorta to left atrial ratio	66
Figu	ıre 18:	Shows M-mode echocardiograp	ohy for
		calculation of ejection fraction	66
Figu	ıre 19:	Measurement of carotid intima	a media
		thickness in one of the study patients	68
Figu	ıre 20:	Shows significant difference between	een three
		groups regarding their age, patie	ents with
		complications are older than those	e without
		complication and newly diagnosed pa	teints74
Figu	ıre 21:	<u>-</u>	~ -
		regarding their body mass index being	ng normal
		in the three groups	
Figu	ıre 22:	Shows that patients with complica	
		higher level of cathelicidin than other	groups 77

Tist of Figures cont...

Fig. No.	Title	Page No.
Figure 23:	Comparison between three group their carotid intima media thic higher in the group of T complications.	ekness being F1DM with
Figure 24:	Shows that percentage of diastolic was higher in the group with microvascular complications that	c dysfunction T1DM with n the other
Figure 25:	groups	abnormality T1DM with
Figure 26:	© 1	between ima media
Figure 27:	·	between A ratio in the
Figure 28:	Shows difference between patient without complications as regarded cathelicidin level	its with and gard serum
Figure 29:	Shows difference between patient without diastolic dysfunction as reathelicidin level.	egard serum
Figure 30:	Positive correlation between camedia thickness and E/A ratio groups	of the study
Figure 31:	Shows that patients with n complications have higher car media thickness.	nicrovascular otid intima
Figure 32:	Shows higher Carotid intima med among patients with diastolic dysf	lia thickness

Tist of Figures cont...

Fig. No.	Title	Page No.
Figure 33:	ROC curve for Cathclicidin and CIMT	
Figure 34:	Newly diagnosed type 1 diabetes an diabetes without complications	90 S between
Figure 25.	Type 1 diabetes without complicat Type 1 diabetes with complications ROC curve for predictors of	90
rigure 50:	dysfunction	

Tist of Abbreviations

Abb.	Full term
2D	Two-dimensional
A	Late diastolic filling velocity
A' lat	Peak late diastolic tissue velocity at lateral
	mitral annulus;
A' sep	Peak late diastolic tissue velocity at medial
_	mitral annulus
ACE	Angiotensin converting enzyme
ADA	American Diabetes Association
ADs	Autoimmune diseases
AGE	Advanced glycation end products
AMPs	Antimicrobial peptides
	One-way analysis of variance
ARB	Angiotensin receptor blocker
	American Society of Echocardiography/
	European Association of Cardiovascular
	Imaging
BMI	Body mass index
CAD	Coronary artery disease
	Cathelicidin antimicrobial peptide
CAN	Cardiac autonomic neuropathy
	Continuous Glucose Monitoring
	Carotid intima media thickness
cm	Centimeters
CRAMP	Cathelicidin-related antimicrobial peptide
	in mice
CSII	Continuous subcutaneous insulin infusion
CTDI	Color Tissue Doppler imaging
	Cardiovascular disease
DAFNE	Dose Adjustment for Regular Eating
	Diabetes Control and Complications Trial
DCM	Diabetic cardiomyopathy
	Diastolic dysfunction
	Diabetic ketoacidosis
DKD	Diabetic kidney disease

Tist of Abbreviations cont...

DM	Abb.	Full term
DN	DM	Diahotos mollitus
E		
E/A ratio Mitral inflow early-to-late diastolic flow E/E'lat ratio Ratio is a marker of elevated diastolic left ventricle and left atrium pressure E'lat Peak early diastolic tissue velocity at lateral mitral annulus; E'sep Peak early diastolic tissue velocity at medial mitral annulus EF Ejection fraction ER Endoplasmic reticulum ESC/EASD European Society of Cardiology/European Association for Study Diabetes) guidelines Fiasp Faster acting insulin aspart FMASU REC Research Committee of Faculty of Medicine, Ain Shams University FPG Fasting plasma glucose GCK Glucokinase HbA1c Hemoglobin A1c HF Heart failure HFrEF Heart failure with preserved ejection fraction HHS Hyperglycemic hyperosmolar state HNF Hepatic nuclear factor ICH International Council on Harmonization IOMS Islamic Organization for Medical Science IVRT Isovolumetric relaxation time		·
E/E'lat ratio Ratio is a marker of elevated diastolic left ventricle and left atrium pressure E'lat Peak early diastolic tissue velocity at lateral mitral annulus; E'sep Peak early diastolic tissue velocity at medial mitral annulus EF Ejection fraction ER Endoplasmic reticulum ESC/EASD European Society of Cardiology/European Association for Study Diabetes) guidelines Fiasp Faster acting insulin aspart FMASU REC Research Committee of Faculty of Medicine, Ain Shams University FPG Fasting plasma glucose GCK Glucokinase HbA1c Hemoglobin A1c HF Heart failure HFrEF Heart failure with preserved ejection fraction HHS Hyperglycemic hyperosmolar state HNF Hepatic nuclear factor ICH International Council on Harmonization IOMS Islamic Organization for Medical Science IVRT Isovolumetric relaxation time		· ·
ventricle and left atrium pressure E'lat Peak early diastolic tissue velocity at lateral mitral annulus; E'sep Peak early diastolic tissue velocity at medial mitral annulus EF Ejection fraction ER Endoplasmic reticulum ESC/EASD European Society of Cardiology/European Association for Study Diabetes) guidelines Fiasp Faster acting insulin aspart FMASU REC Research Committee of Faculty of Medicine, Ain Shams University FPG Fasting plasma glucose GCK Glucokinase HbA1c Hemoglobin A1c HF Heart failure HFrEF Heart failure with preserved ejection fraction HHS Hyperglycemic hyperosmolar state HNF Hepatic nuclear factor ICH International Council on Harmonization IOMS Islamic Organization for Medical Science IVRT Isovolumetric relaxation time		· · · · · · · · · · · · · · · · · · ·
E'lat	E/E lat latio	
lateral mitral annulus; E'sep Peak early diastolic tissue velocity at medial mitral annulus EF Ejection fraction ER Endoplasmic reticulum ESC/EASD European Society of Cardiology/European Association for Study Diabetes) guidelines Fiasp Faster acting insulin aspart FMASU REC Research Committee of Faculty of Medicine, Ain Shams University FPG Fasting plasma glucose GCK Glucokinase HbA1c Hemoglobin A1c HF Heart failure HFrEF Heart failure with preserved ejection fraction HHS Hyperglycemic hyperosmolar state HNF Hepatic nuclear factor ICH International Council on Harmonization IOMS Islamic Organization for Medical Science IVRT Isovolumetric relaxation time	F/lot	
E'sep	12 lat	
medial mitral annulus EF	F'gon	,
EF	E sep	· · · · · · · · · · · · · · · · · · ·
ER	यय	
ESC/EASD European Society of Cardiology/European Association for Study Diabetes) guidelines Fiasp Faster acting insulin aspart FMASU REC Research Committee of Faculty of Medicine, Ain Shams University FPG Fasting plasma glucose GCK Glucokinase HbA1c Hemoglobin A1c HF Heart failure HFrEF Heart failure with preserved ejection fraction HHS Hyperglycemic hyperosmolar state HNF Hepatic nuclear factor ICH International Council on Harmonization IOMS Islamic Organization for Medical Science IVRT Isovolumetric relaxation time		· ·
Association for Study Diabetes) guidelines Fiasp		<u>-</u>
Fiasp		2 0 2
FMASU REC		·
Medicine, Ain Shams University FPG Fasting plasma glucose GCK Glucokinase HbA1c Hemoglobin A1c HF Heart failure HFrEF Heart failure with preserved ejection fraction HHS Hyperglycemic hyperosmolar state HNF Hepatic nuclear factor ICH International Council on Harmonization IOMS Islamic Organization for Medical Science IVRT Isovolumetric relaxation time	_	
FPG		· · · · · · · · · · · · · · · · · · ·
GCK		,
HbA1c Hemoglobin A1c HF Heart failure HFrEF Heart failure with preserved ejection fraction HHS Hyperglycemic hyperosmolar state HNF Hepatic nuclear factor ICH International Council on Harmonization IOMS Islamic Organization for Medical Science IVRT Isovolumetric relaxation time		
HF		
HFrEF Heart failure with preserved ejection fraction HHS Hyperglycemic hyperosmolar state HNF Hepatic nuclear factor ICH International Council on Harmonization IOMS Islamic Organization for Medical Science IVRT Isovolumetric relaxation time		
fraction HHS		
HHSHyperglycemic hyperosmolar state HNFHepatic nuclear factor ICHInternational Council on Harmonization IOMSIslamic Organization for Medical Science IVRTIsovolumetric relaxation time	111 1121	
HNFHepatic nuclear factor ICHInternational Council on Harmonization IOMSIslamic Organization for Medical Science IVRTIsovolumetric relaxation time	HHS	
ICHInternational Council on Harmonization IOMSIslamic Organization for Medical Science IVRTIsovolumetric relaxation time		
IOMSIslamic Organization for Medical Science IVRTIsovolumetric relaxation time		
IVRTIsovolumetric relaxation time		
		_
2 / 2		
KgKilograms		
LL-37The only human cathelicidin antimicrobial	_	
peptide		· ·