

EFFECTS OF CHILDHOOD BRONCHIECTASIS ON CARDIAC FUNCTIONS

Thesis

Submitted For Fulfillment Of Master Degree In Pediatrics

By

Marwa Aly Mahmoud Aly

(M.B, B.Ch)

Supervised by

Dr. Amal Mahmoud El Sisi

Professor of Pediatrics

Faculty of Medicine- Cairo University

Dr. Reem Ibrahim Ismaiel

Assistant Professor of Pediatrics

Faculty of Medicine- Cairo University

Dr. Noussa Ragab Mohamed

Assistant Professor of Pediatrics

Faculty of Medicine- Cairo University

Faculty of Medicine

Cairo University

2015



بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ
قَالُوا سُبْحَانَكَ لَا عِلْمَ لَنَا
إِلَّا مَا عَلَّمْتَنَا إِنَّكَ أَنْتَ الْعَلِيمُ الْحَكِيمُ

صدق الله العظيم
سورة البقرة الآية (32)



Acknowledgement

First of all thanks to **“Allah”** the kind and the merciful, who gave me the power to perform and complete this work. I would like to express my sincere and deepest gratitude to **Dr. Amal Mahmoud El Sisi** Professor of Pediatrics, Faculty of Medicine, Cairo University, for her supervision, and valuable guidance.

I wish to thank **Dr. Reem Ibrahim Ismaiel** Assistant Professor of Pediatrics, Faculty of Medicine, Cairo University for her generous help in performing the echocardiography of this study, her gracious supervision, and valuable guidance through the whole research

I am grateful to **Dr. Noussa Ragab Mohamed** Assistant Professor of Pediatrics, Faculty of Medicine, Cairo University, for her continuous encouragement, valuable advice, and guidance.

I wish to express my sincere thanks and appreciation to **Dr. Mona Mostafa El Falaki** Professor of Pediatrics, Faculty of Medicine, Cairo University, for her help in diagnosis of patients in this study.

Special thanks to **Dr. Nahla Atia Atia Said** Fellow colleague of Pediatrics, Faculty of Medicine, Cairo University, for performing pulmonary function tests and interpretation.

My deep thanks to my family and my husband for their constant support, patience, and encouragement.

Finally, my sincere gratitude goes to all the examined group of this study for their cooperation.

Marwa Aly Mahmoud

Abstract

Bronchiectasis is a common structural end-point of many chronic respiratory diseases. Chronic hypoxia in these patients eventually may lead to pulmonary hypertension and consequently cor pulmonale. We enrolled thirty one patients with bronchiectasis as well as fourteen healthy control subjects were studied using echocardiography. Trans-thoracic two dimensional (2D) guided (Mmode) and Doppler echocardiography were performed for all patients. Right ventricular systolic and diastolic functions were impaired in most of our patients. Left ventricular diastolic function was impaired while left ventricular systolic function was preserved. The clinical score correlated significantly with most of parameters measured for the right ventricle and also correlated with R5.

Key words: Bronchiectasis; Echocardiography; Ventricular dysfunction.

List of Content

	Page
List of Abbreviations	I
List of Tables	V I
List of Figures	VIII
Introduction and Aim of the Work	XI
Review of Literature	
Chapter (1): <ul style="list-style-type: none">• Bronchiectasis	1
Chapter (2): <ul style="list-style-type: none">• Bronchiectasis Associated Disorders And Predispositions	45
Chapter (3): <ul style="list-style-type: none">• Management Of Bronchiectasis	76
Chapter (4): <ul style="list-style-type: none">• Pulmonary Hypertension	91
Chapter (5): <ul style="list-style-type: none">• Echocardiography	138
Patients and Methods	186
Results	196
Discussion	223
Conclusion	245
Recommendations	246
Summary	247
References	250
Appendix	
Arabic Summary	

Abbreviations

3D	three-dimensional
6MWT	6 minute walk test
A. Fumigates	Aspergillus fumigatus
ABPA	Allergic bronchopulmonary aspergillosis
AIHA	Autoimmune haemolytic anaemia
Am	Late diastolic mitral annular velocity
ANOVA	Analysis of variance
Ao	Aorta
AOMV	Aorta maximum velocity
ASE	American society of echocardiography
ASL	Airway surface liquid
AT	acceleration time
At	late diastolic tricuspid annular velocity
ATD	α 1-antitrypsin deficiency
ATS/ERS	American Thoracic Society/ European Respiratory Society
AV	Atrioventricular
AVV	Atrioventricular valve
BAL	bronchoalveolar lavage
BDR	bronchodilator response
BMI	body mass index
BMPR	bone morphogenic protein receptor type II
CAV1	caveolin-1
CBAVD	congenital bilateral absence of the vas deferens
CCBs	calcium channel blockers
CF	cystic fibrosis
CFRD	cystic fibrosis–related diabetes mellitus
CFTR	cystic fibrosis transmembrane conductance regulator
cGMP	cyclic GMP
CHD	congenital heart disease
c-HRCT	Chest high-resolution computed tomography
CNS	central nervous system
CO	cardiac output
COPD	Chronic obstructive pulmonary disease
CPA	chronic pulmonary aspiration
CPET	cycle ergometry cardiopulmonary exercise testing
CPT	Chest physiotherapy

CTEPH	Chronic thromboembolic pulmonary hypertension
DecT	deceleration time
DHF	diastolic heart failure
DIOS	distal intestinal obstruction syndrome
DLCO	Diffusing capacity of the lungs for carbon monoxide test
Dnase	human deoxyribonuclease
EDV	end-diastolic volume
EF	ejection fraction
Em	early diastolic mitral annular velocity
ENG	endoglin
ET	ejection time
Et	early diastolic tricuspid annular velocity
ET-1	Endothelin-1
ETA	endothelin receptors type A
ETB	endothelin receptors type B
FB	Foreign body
FDA	Food and Drug Administration
FEES	fiberoptic-endoscopic evaluation of swallowing
FEV₁	forced expiratory volume in 1 second
FVC	forced vital capacity
HIV	human immunodeficiency virus.
HPOA	hypertrophic osteoarthritis
HR	heart rate
HRCT	high-resolution computed tomography
HS	Hypertonic saline
IBAs	Inhaled β-agonists
ICS	inhaled corticosteroids
ICT	isovolumic contraction time
Ig	Immunoglobulins
IgA	Immunoglobulin A
IL	Interleukin
IL-8	interleukin-8
ILD	interstitial lung disease
IOS	Impulse oscillometry
IRT	immunoreactive trypsinogen
IRT	isovolumic relaxation time
ITP	idiopathic thrombocytopenia
IVIg	intravenous immunoglobulin treatment
IVRT	Isovolumic relaxation time

IVSd	interventricular septal thickness
JVP	Jugular venous pressure
LA	left atrium
LABA	Long acting β -agonist
LTB4	leukotriene B4
LTOT	Long term oxygen therapy
LV	left ventricle
LVDd	left ventricular diastolic diameter
LVPWd	Left ventricular posterior wall
LVRS	Lung volume reduction surgery
MAE	mitral annulus excursion
MAPSE	Mitral annular plane systolic excursion
MBL	mannose binding lectin
mPAP	Mean pulmonary artery pressure
MPI	myocardial performance index
MRI	magnetic resonance imaging
NAC	N-Acetylcysteine
NBS	Newborn Screening
NCFB	non cystic fibrosis bronchiectasis
NK	natural killer
NO	nitric oxide
NP	nasopharyngeal
NPD	Nasal potential difference
NSAIDs	Non steroidal anti-inflammatory drugs
NTHi	Nontypeable Haemophilus influenzae
NYHA	New York Heart Association
NZ	New Zealand
P. aeruginosa	pseudomonous aeruginosa
PA	pulmonary artery
PA	Posteroanterior
PAD	primary antibody deficiency
PAH	Pulmonary arterial hypertension
PAMPs	pathogen associated molecular patterns
PAP	pulmonary artery pressure
PC	pulmonary circulation
PCD	Primary ciliary dyskinesia
PCR	Polymerase chain reaction
PCWP	pulmonary capillary wedge pressure
PDE 5 inhibitor	phosphodiesterase 5 inhibitor

Peak A	peak flow velocity during atrial contraction
Peak E	Peak velocity at early diastole
PEF	peak expiratory flow
PH	pulmonary hypertension
PMNs	polymorphonuclear neutrophils
PPHN	persistent pulmonary hypertension of the newborn
PRMC	Pulmonary radioaerosol mucociliary clearance
PRRs	pattern recognition receptors
PVR	pulmonary vascular resistance
PVRi	pulmonary vascular resistance indexed for body surface area
QS	quorum sensing
R	resistance
RA	right atrium
RHC	Right heart catheterization
RV	residual volume
RV	right ventricle
RV-ASI	Right ventricular automated systolic index
RVDD	Right ventricular diastolic diameter
RVFAC	Right ventricular fractional area change
RVMPI	right index of myocardial performance
SF	shortening fraction
SIL	Sildenafil
SLPI	secretory leukocyte proteinase inhibitor
SP-A	surfactant protein-D
SPSS	statistical program for social science
SR	Strain rate
SV	stroke volume
SVR	systemic vascular resistance
TAPSE	Tricuspid annular plane systolic excursion
TAPSE	Tricuspid annular plane systolic excursion
TBM	tracheobronchomegaly
TDI	tissue Doppler imaging
TEF	tracheoesophageal fistula
TGF	transforming growth factor
TLC	total lung capacity
TMP-SMX	Trimethoprim sulphamethoxazole
TNF	tumour necrosis factor
TPG	transpulmonary gradient

TR	tricuspid regurgit gradient
TR	peak tricuspid regurgitation gradient
TTE	Transthoracic doppler-echocardiography
V/Q	ventilation perfusion
VSS	Video fluoroscopic swallowing studies
VTI	velocity time integral
WU	Wood Units
X	reactance
XLA	X-linked agammaglobulinemia
α 1-PI	α 1-protease inhibitor

List of Tables

Table number	Title	Page
Table (1)	List of causes of localized Bronchiectasis	6
Table (2)	Categories and causes of non-cystic fibrosis bronchiectasis	10
Table (3)	Host pulmonary defenses	17
Table (4)	Time frame of appearance of symptoms of CF	51
Table (5)	Key features of primary antibody deficiencies	59
Table (6)	Common acute infections in primary antibody deficiency	60
Table (7)	Summary of organ-specific complications of primary antibody deficiency	61
Table (8)	Updated Classification of Pulmonary Hypertension	93
Table (9)	World Health Organization Functional Classification of pulmonary arterial hypertension	94
Table (10)	The European Society of Cardiology Consensus Criteria for Diastolic Heart Failure (DHF)	174
Table (11)	Principal and General Objectives in Treatment of Diastolic Heart Failure	177
Table (12)	The clinical scoring system for patients with bronchiectasis	189
Table (13)	World Health Organization Functional Classification of pulmonary arterial hypertension	190
Table (14)	Age of both cases and controls	196
Table (15)	Underlying etiology of bronchiectasis in the studied group	197
Table (16)	Clinical manifestations encountered in bronchiectasis patients	199
Table (17)	WHO functional classification of PH of the study group	201
Table (18)	Anthropometric measurements of the patients with bronchiectasis and controls	202
Table (19)	Lobar involvement in bronchoiectasis patients	203
Table (20)	Spirometry results of bronchiectasis patients	204
Table (21)	Results of spirometry among patients with bronchiectasis	204
Table (22)	Severity classification of the FEV1 of among patients with bronchiectasis	205
Table (23)	IOS parameters in bronchiectasis patients	206
Table (24)	Pulmonary function tests results among patients with bronchiectasis	206

Table (25)	M-mode echocardiographic measurement results for patients with bronchiectasis and the control group	208
Table (26)	Pulsed wave Doppler ultrasound recordings of diastolic function of the RV among patients with bronchiectasis	210
Table (27)	Pulsed wave Doppler ultrasound recordings of the RV valve outflow among patients with bronchiectasis	211
Table (28)	Pulsed wave Doppler ultrasound recordings of mitral valve Inflow for patients with bronchiectasis	212
Table (29)	Pulsed wave Doppler ultrasound recordings of mitral valve diastolic functions among patients with bronchiectasis	213
Table (30)	Correlations of the clinical score with echocardiographic variables for patients with bronchiectasis	215
Table (31)	Correlations of RVMPI and LVMPI with patients' variables	216
Table (32)	M-mode echocardiographic measurement results among patients with bronchiectasis	218
Table (33)	Pulsed wave Doppler ultrasound recordings of diastolic function of RV among patients with bronchiectasis	219
Table (34)	Pulsed wave Doppler ultrasound recordings of the LV outflow	220
Table (35)	Pulsed wave Doppler ultrasound recordings of LV Inflow among patients with bronchiectasis	221
Table (36)	Pulsed wave Doppler ultrasound recordings of mitral valve diastolic functions among patients with bronchiectasis	222

List of Figures

Figure number	Title	Page
Figure(1)	Cross-section of normal and bronchiectatic airways	2
Figure(2)	Obstructive bronchiectasis	8
Figure(3)	Bronchogram and Pulmonary angiogram	13
Figure(4)	The vicious cycle' hypothesis of bronchiectasis	14
Figure(5)	Proposed pathway of tissue injury in a microenvironment of inflammatory cells	20
Figure(6)	Reserve cell hyperplasia, a dense mononuclear inflammatory infiltrate, and fibrosis	23
Figure(7)	The fibrotic area is stained in red, surrounding a bronchus with mononuclear infiltrate.	24
Figure(8)	Saccular bronchiectasis	24
Figure(9)	Finger clubbing in 4-year-old girl with an inhaled foreign body and right lower lobe bronchiectasis presenting with 6 months of wet cough	30
Figure(10)	Posteroanterior (PA) chest radiograph of a child with bronchiectasis due to chronic aspiration	31
Figure(11)	Bronchogram of a patient with extensive saccular bronchiectasis, primarily in right upper lobe	32
Figure(12)	Graphs of IOS in patients with normal, obstructive, and restrictive lung disease	40
Figure(13)	Cystic fibrosis transmembrane conductance regulator (CFTR) gene mutations	47
Figure(14)	Section of lung from autopsy of a patient with CF demonstrating remarkable dilation of large airways and preservation of intervening pulmonary parenchyma	50
Figure(15)	Typical progression of radiographic changes in cystic fibrosis.	53
Figure(16)	Lung injury caused by chronic aspiration	64
Figure(17)	Distribution of ciliated organs.	65
Figure(18)	CT (virtual) bronchoscopy images of the middle lobe during inspiration and expiration	75
Figure(19)	Therapeutic scheme for bronchiectasis	76
Figure(20)	A) PEP mouth piece B) PEP mask	78
Figure(21)	High frequency chest wall oscillation Jacket	79
Figure(22)	The basis for the classification of pulmonary hypertension (PH) according to the World Health Organization	97

Figure(23)	Pulmonary arteries of the muscular type displaying obstructive arteriopathy in lungs of patients with PAH.	101
Figure(24)	The sick lung circulation—right heart failure axis. RVF: right ventricle failure; LV: left ventricle	107
Figure(25)	Pathophysiology of RV Dysfunction in PAH	108
Figure(26)	A chest radiograph from a patient with PAH	113
Figure(27)	An ECG of a patient with pulmonary hypertension (PH).	114
Figure(28)	TR gradient in child with severe PH seen as downward contour	117
Figure(29)	Measurement of TAPSE using the four-chamber view	119
Figure(30)	Treatment algorithm proposed in the management of pediatric patients with idiopathic or heritable pulmonary arterial hypertension.	135
Figure(31)	Assessment of left ventricular fractional shortening	140
Figure(32)	Assessment of right ventricular function.	141
Figure(33)	Measurement of the right ventricular ejection fraction	142
Figure(34)	Measurement of TAPSE using the four-chamber view	143
Figure(35)	Assessment of the right ventricular automated systolic index	144
Figure(36)	Left ventricular ejection fraction	146
Figure(37)	Examples of normal and reduced septal mitral annular plane systolic excursion (MAPSE) by M-mode images	148
Figure(38)	Measurement of the rate of pressure rise in the ventricles (dp/dt) of tricuspid regurgitation in the four chamber view in pulmonary artery hypertension individual	150
Figure(39)	Doppler echocardiographic determination of systolic pulmonary artery pressure (sPAP)	151
Figure(40)	Pulmonary artery systolic pressure by the continuous-wave Doppler method.	152
Figure(41)	Typical pulsed-wave-derived myocardial velocity profile in the basal septal segment.	153
Figure(42)	Pulsed Doppler recordings of velocities in right ventricular inflow	156
Figure(43)	Typical mitral inflow Doppler during childhood.	157
Figure(44)	Pulmonary venous inflow Doppler.	158
Figure(45)	Transmitral inflow velocity, pulmonary vein flow velocity, mitral annular velocity, and color M-mode imaging in stages of diastolic dysfunction.	159
Figure(46)	MPI calculation	160
Figure(47)	Measurement of right ventricular myocardial performance index (RVMPI) by pulsed wave Doppler of tricuspid regurgitation and tissue Doppler	161