

Body Composition Changes, Bone Density and Bone Turnover Markers in Obese Children

Thesis
Submitted for the fulfillment of Ph. D. in Medical Childhood Studies
(Child Health and Nutrition)

By Fatma Abdel-Rahman El-Zaree

M.B.B.Ch., M.Sc. Pediatrics Ain Shams University Assistant Researcher of Child Health National Research Center

Under supervision of

Dr.Ghada Farag El Dorry

Professor of Pediatrics
Department of Medical studies
Institute of Postgraduate Childhood
Studies. Ain Shams University

Dr.Hala Hussien El-Ashry

Professor of Child Health Department of Child Health National Research Center

Dr.Hanaa Wafai ElSherif

Professor of Biochemistry Department of Biochemistry National Research Center

Dr. Tarek M. Salah El- Din

Professor of Child Health Department of Child Health National Research Center

Abstract

Background: Osteoporosis is a major health problem. It is a disease of progressive bone loss associated with increased risk of fractures. A dramatic increase in prevalence of pediatric obesity has occurred in most countries over the past few decades. Understanding the relationship between pediatric obesity and bone health is relevant for health professionals, because childhood and adolescence are two critical periods in the prevention and development of diseases in adulthood.

Aim: This study aimed to study the relation between obesity, body composition and bone density by using dual energy x-ray absorptiometry (DEXA) and some bone turnover markers as Osteocalcin (OC) and Deoxypyridinoline (DPD) in obese children.

Design: Case-control study.

Methods: a case-control sample of 80 pre-pubertal, Egyptian children aged 6-10 years were divided into 40 cases with simple obesity (BMI ≥ 95th percentile) and 40 controls (non-obese). Physical examination that included weight, height, hip circumference and waist circumference were performed. Body mass index (BMI) and waist-hip ratio were calculated. Blood and urine samples were collected. Serum was separated and assayed for Osteocalcin, calcium, phosphorus, alkaline phosphatase and lipid profile. Urine was collected, centrifuged and assayed for deoxypyridinoline.

Results: All anthropometric parameters were increased (except for height) in obese children. All DEXA parameters for the whole body, hip and lumbar areas were greater in obese children. All DEXA parameters for the whole body were positively correlated with BMI, weight and height. Lipid profile was positively correlated with most of DEXA parameters as area, BMD, total body fat, lean, lean + BMC and total mass but they were negatively correlated with high density lipoprotein (HDL). Calcium showed significant increase in obese children, while alkaline phosphatase showed significant decrease in the same group. Osteocalcin was found to be negatively correlated with most of DEXA results in obese children in comparison to non-obese children. While the urinary DPD, showed no significant difference between obese and non-obese groups.

Conclusion: obese children have increased anthropometric and DEXA parameters which were positively correlated with BMI, weight, height and lipid profile except for HDL. Obese children also showed significant increase in serum calcium and significant decrease in alkaline phosphatase. Osteocalcin was found to be negatively correlated with most of DEXA results in obese children in comparison to non-obese children. While the urinary DPD, showed no significant difference between obese and non-obese groups.

Recommendations: we recommend the childcare providers to supply the children with healthy balanced diet to avoid obesity throughout their life with the use of DEXA and Osteocalcin as

early predictors of osteoporosis in obese children to avoid continuation of the problem of osteoporosis in the adulthood, while for the urinary DPD, as it did not give us any significant data either in obese or non-obese children in addition to its high price, so we do not recommend its use in this early age.

Keywords: Osteoporosis, obese children, bone markers, dual energy x-ray absorptiometry (DEXA).

ACKNOWLEDGMENT

First of all, thanks to *ALLAH*, the most kind and most merciful, for completing this work and for the chance I had to go through this work with the supervision of my dear professors.

My deepest thanks are to be presented to *Or. GhadaFarag El-Dorry;* Professor of Pediatrics, Department of Medical studies, Institute of Postgraduate Childhood Studies. Ain Shams University, for her supervision, helpful discussion and suggestions. Words are not enough to express what I feel towards her.

I can't fully express my deepest thanks and gratitude to **Dr. HalaHussien El-Ashry**; Professor of Child Health, National Research Center, who was my wise mind during the whole work. In fact, few words never suffice to do justice in thanking her for her extraordinary contribution of time, effort and valuable experience.

I would like to thank *Dr. Tarek Salah El-Din,* Professor of Child Health, National Research Center, for his patience, time and effort he gave to me during this work.

I would like also to thank *Dr. Hanaa El-Sherif*, Professor of Biochemistry, National Research Center for her advice and support. Special thanks and gratitude to *Dr. Tahany Ramzy Elias*, Professor of Medical Biochemistry, National



Research Center for her time, special effort and generous advice during preparation of this work.

My heart is grateful to my parents, my husband and my children for their encouragement and support given throughout the work. My special thanks to all my patients and their parents who agreed to participate in this study. I'm thankful to them for their effort, time and cooperation.

Fatma El- Zaree Cairo, 2014.



Contents

	Page
Abstract	i
List of Abbreviations	iv
List of Tables	ix
List of Figures	xi
Introduction	3
Aim of the Study	7
Review of Literature	11
Chapter 1: Obesity	11
Chapter 2: Bone Minerals and Metabolism	51
Chapter 3: Assessment of bone status in children	114
Chapter 4: Osteoporosis	145
Subjects and Methods	173
Results	201
Discussion	261
Summary	279
Conclusions	285

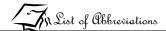


	Page
Recommendations	289
References	293
Arabic Summary	١

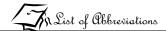


List of Abbreviations

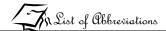
AR	adiposity rebound
AP	Anteroposterior
BIA	Bioelectric Impedance Analyzer
BMC	bone mineral content
BMD	Bone mineral density
BMI	Body mass index
BMP	bone morphogenic protein
BMU	Basic multicellular units
BSP	Bone sialoprotein
Ca	Calcium
CaR	calcium-sensing receptor
CDC	the Centers for Disease Control
CRP	C-reactive protein
CT	computerized tomography
CTX	Urinary or serum collagen type 1 cross-
	linked C-telopeptide
DEXA	Dual energy X-ray absorptiometry
DPD	Urinary deoxypyridinoline
DXR	Digital X-ray Radiogrammetry
ECM	extracellular matrix
ELISA	Enzyme linked immunosorbent assay
EPR1,2,3,4	E-prostanoid receptors, 1,2,3,4
ERα or ERβ	estrogen receptor-α or-β
FDA	Food and Drug Administration
FM	Fat mass



	T	
FFM	fat free mass	
FGFs	fibroblast growth factors	
GC	Glucocorticoids	
GH	Growth Hormone	
GHD	GH deficiency	
GIO	glucocorticoid induced osteoporosis	
HDL	high density lipoprotein	
HRP	horseradish peroxidase	
Ht.	height	
IGF-1	Insulin growth factor-1	
Ihh	Indian hedge hog	
ISCD	International Society for Clinical	
	Densitometry	
IU	International unit	
LBM	Lean body mass	
LDL	low density lipoproteins	
LPL	lipoprotein lipase	
LRP5	Low density lipoprotein receptor	
LST	lean soft tissue	
MAbs	monoclonal antibodies	
MCP-1	monocyte chemo attractant protein-1	
M-CSF	macrophage colony stimulating factor	
MMP	matrix metallo-proteinases	
MRI	Magnetic Resonance Imaging	
NTX	Urinary collagen type 1 cross - linked N	
	- telopeptide	
OC	Osteocalcin	



OCPs	Osteoclast precursors
OD	Optical density
OPG	osteoprotegerin
OST	serum human osteocalcin
PBM	Peak Bone Mass
PCOS	Poly cystic ovary syndrome
PGFF2	prostaglandin factor 2
Pi	Inorganic phosphorus
PTH	Parathyroid Hormone
PTHrp	Parathyroid hormone related protein
PYD	Urinary total pyridinoline
QCT	Quantitative Computed Tomography
QUS	Quantitative ultra sonography
RANKL	receptor activator of nuclear factor
	kappa B ligand
r.b.m	Round per minute
RER	rough endoplasmic reticulum
rhPTH	recombinant human parathyroid
	hormone
ROI	Region of interest
Runx2	Runt-related protein2
SAS	sleep apnea syndrome
SCFE	Slipped Capital Femoral Epiphysis
SD	standard deviations
SIBLING	small integrin-binding ligand
SOX	sry-related high-mobility-group box
TBW	Total body water



TFM	total fat mass
TGF-B	tumor growth factor-beta
TNF	tumor necrosis factor
TSH	Thyroid Stimulating Hormone
UVB	ultraviolet B
VBMD	volumetric BMD
VDBP	Vitamin D binding protein
VDRs	Vitamin D receptors
VEGF	vascular endothelial growth factors
VLDL	very low density lipoproteins
VOI	Volume of interest
WHO	World Health Organization
WHR	Waist-hip ratio or waist-to-hip ratio
Wt.	weight
Zn	zinc



List of Tables

	Title	Page
Table (1):	The International Classification of adult underweight, overweight and obesity according to BMI	15
Table (2):	Strength and limitations of laboratory methods for assessing body fatness among children and adolescents.	17
Table (3):	Comparison between idiopathic and endogenous obesity	21
Table (4):	Summary of important growth factors and signalling molecules with relevant impact for the regulation of proliferation and differentiation of growth plate chondrocytes	76
Table (5):	Recommended daily Calcium intake	93
Table (6):	Adequate intake (AI) for vitamin D	98
Table (7):	Methods of measuring BMD	127
Table (8):	Definition of terms relating to Bone Mineral Density	130
Table (9):	Common terms seen in DEXA report	131
Table (10):	Shows the causes of primary and secondary osteoporosis.	150
Table (11):	Distribution of the studied sample according to sex.	201
Table (12):	Distribution of the studied sample according to family history of obesity	202
Table (13):	Age and anthropometric measurements of the studied sample	203
Table (14):	Comparison between obese and non-obese	205



	Title	Page
	children in DEXA results for the whole body	
Table (15):	Comparison between obese and non-obese children in DEXA results for hip	208
Table (16):	Comparison between obese and non-obese children in DEXA results for Lumber Spine	210
Table (17):	Correlation between DEXA parameters and (BMI, weight and height) for the whole body	212
Table (18):	Correlation between DEXA parameters and (BMI, weight and height) for the hip	225
Table (19):	Correlation between DEXA parameters and (BMI, weight and height) for the lumber Spine	229
Table (20):	comparison between obese and non-obese in laboratory parameters	235
Table (21):	Correlation between DEXA parameters for whole body and lipid profile	237
Table (22):	Correlation between DEXA parameters for hip and lipid profile	247
Table (23):	Correlation between DEXA parameters for lumber spine and lipid profile	248
Table (24):	Correlation between DEXA parameters for the whole body and Ca., Ph., Alkaline phosphatase, OC & DPD	249
Table (25):	Correlation between DEXA parameters for Hip and Ca., Ph., Alkaline phosphatase, OC & DPD	256
Table (26):	Correlation between DEXA parameters for Lumber Spine and Ca, Ph, Alkaline phosphatase, OC & DPD	260



List of Figures

	Title	Page
Fig. (1):	Factors which may cause obesity	24
Fig. (2):	Childhood obesity complications	29
Fig. (3):	The Food pyramid	44
Fig. (4):	Compact bone & spongy (cancelluos) bone	52
Fig. (5):	Osteclast cell	61
Fig. (6):	Osteocyte cells	63
Fig. (7):	Zones epiphyseal growth plate	68
Fig. (8):	Endochondral ossification	69
Fig. (0):	Hormonal factors influencing bone density	72
Fig. (9):	in obese adolescents	12
Fig. (10):	Effects of GH and IGF-I on bone	73
Fig. (11):	Phases of bone remodeling	86
	Synthesis and metabolism of vitamin D	
Fig. (12):	and its role in the regulation of calcium,	101
	and phosphorus, and bone metabolism	
Fig. (13):	The parathyroid axis	103
Fig. (14):	Deoxypyridinoline. Deoxypyridinoline	109
116. (14).	cross-linking in bone collagen	10)
Fig. (15):	Comparison between bone mineral density	118
_	in men and women	
Fig. (16):	DXA images	124
Fig. (17):	Dual Energy X-ray Absorptiometry	125
8' (')'	(DEXA)	_
Fig. (18):	DEXA (Dual Energy X-ray	127
- 25* (20)*	Absorptiometry)127	
Fig. (19):	Vertebral compression fractures in	1.40
	lumbar spine of a child with juvenile	149
	idiopathic osteoporosis	1 7 0
Fig. (20):	Normal bone and osteoporotic bone	150
Fig. (21):	measurement of waist hip ratio	176