Institute of Postgraduate Childhood Studies

Medical Studies Department for Children

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

2014

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 $\geq 95^{th}$ 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 ***Dr. 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

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

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

List of Figures