Changes In Adipocyte Hormones In Relation To Body Composition And Pubertal Development In Obese Adolescents After Physical Activity And Dietary- Restriction Programs.

Thesis Submitted For Fulfillment Of Ph.D In Childhood Studies
(Child Health And Nutrition)
Medical Studies Department

By

Maysa Samir Mahmoud Nassar

M.Sc Pediartics - Cairo University
Assistant Researcher - National Research Centre

Under Supervision of

DR. HAYAM KAMAL NAZIF
Professor of Pediatrics
Department of Medical Studies
Institute of Postgraduate Childhood Studies

DR. ZEINAB MOHAMED MONIR
Professor of Child Health Department
of Child Health
National Research Centre

DR. AHMED NASR ELDEIN SAID
Professor of sports physiology Department of
Health Science Sports Faculty of Physical
Education for Boys in Cairo

DR. SAFAA TAHA ZAKI
Professor of Child Health
Department of Child Health
National Research Centre

DR. SOHEIR ABD ELMAWGOUD ABDELMAKSOUD
Professor of Clinical and chemical pathology
Department of Clinical and chemical Pathology
National Research Centre

Institute of Postgraduate Childhood Studies
Ain Shams University

2015

Abstract

Background: The prevalence of obesity continues to rise in both developed and developing nations. An association has been reported between plasma level of adiponectin and leptin hormones and the existence of adolescent obesity. Findings from recent reports suggest that intervention with structured exercise and diet program support to modulation of the level of these hormones and also the BMI. ***Aim of the study:*** The aim of this study was to investigate the changes in Adipocyte hormones in relation to body composition and pubertal development in obese adolescents after physical activity and dietary restriction program. ***Subjects and Methods****:* the present study was conducted on 60 adolescents aging 12-14 years old, divided into two groups. Group (A): adolescents presenting with obesity and who were subjected to exercise and diet program. Group (B): adolescents presenting with obesity and who were subjected to diet program only. Both groups (A&B) were subjected to the following before and after 6 months of the program: full medical history taking, anthropometric measurements, thorough clinical examination, body composition analysis, laboratory investigations: lipid profile and hormonal assessment. **Results:** Both groups (A&B) showed significantly elevation of the levels of adiponectin hormone, significant reduction in level of leptin hormone, BMI, WC, WHR, TG, Cholesterol ,LDL, SBP, DBP, FAT %,VF. No significant difference was found between both groups except in fat% after the program, there was significant reduction in group A than that of group B. Plasma adiponectin level correlated positively with cholesterol in group A after the intervention program but leptin correlated negatively with BMI ,DBP and adiponectin in group A after the intervention program . **Conclusion:** Results of the present study reported that the plasma level of Adiponectin hormone will increase and the plasma level of Leptin hormone will decrease through physical activity and diet programs intervention in obese adolescent**.**

Keywords: Obesity, Adiponectin and Leptin hormones, physical activity, diet restriction.

Acknowledgment

*First and above all, thanks to **GOD,** the most **Beneficial** and **Merciful** for helping me bring this work to light.*

*The sincere and honest help of many people, made it possible for this work to be accomplished. I wish to thank them all, even though I can list only a few names am much obliged and deeply indebted to Professor **Dr .Hayam Kamal Nazif**, Professor of Pediatrics, Department of Medical Studies ,Institute of Post graduate Childhood Studies, Ain Shams University, for her valuable help, competent guidance and fruitful criticism throughout the work. Production of this thesis wouldn't have been accomplished without the prodigious guidance, constant encouragement and experienced advice of Prof. Dr. **Zeinab Mohamed Monir**, Professor of ChildHealth, , National Research Center , for whom I would like to express my deep gratitude and appreciation.*

*And I would like to express my deepest and sincere thanks toProf. Dr. **Soheir Abd Elmawgoud Abdel Maksoud**, Professor of Clinical and chemical pathology National Research Center , for her faithful supervision and guidance and her overwhelming kindness that has been of great help throughout this work.*

*I Wish to express my deep everlasting gratitude to Prof. Dr .**Safaa Taha Zaki** Professor of ChildHealth, , National Research Center for her kind supervision, valuable advice, comments and remarks .I'm also so grateful to Dr. **Ahmed Nasr Eldein Said** Professor of sports physiology Department of Health Science Sports Faculty of Physical Education for Boys in Cairo , for his kind and generous cooperation in the practical part of this thesis ,This thesis is dedicated to all the children in the world, by whom and for whom this work existed, may God bless and cure them all.*

*My utmost thanks and appreciation to Professor **Dr Ayman Mohamed Nada** Assistant Professor of pediatrics Department of Medical Studies ,Institute of Post graduate Childhood Studies, Ain Shams University.*

*Special thanks to my friends **Dr.Rhab Mohamed Selim**, and **DR. Amera Said El-refaii** Researchers of Child Health, National Research Center on whose constant encouragementand help during completion of this work..Finally, you are all mentioned in my prayer of thanks to God.*

*Finally words are not enough to express my love and gratitude to my dear **Father**, **mother, my husband and my children** for their love and support throughout my life.*

List of Abbreviations

ACE	Angiotensin Converting Enzyme
Acrp30	Adipocyte Complement-Related Protein
ADIPOR 1	Adiponectin Receptor 1
ADIPOR 2	Adiponectin Receptor 2
AI	Adequate Intake
Alpha - MSH	Alpha-Melanocyte-Stimulating Hormone
apM1	Adipose Most Abundant Gene Transcript 1
BF	Breast Fed
BMI	Body Mass Index
CAD	Coronary Artery Disease
CDC	Centers For Disease Control And Prevention
CHO	Carbohydrate
CRH	Cytokine Receptor Homology
CRP	C-Reactive Protein
CT	Computed Tomography
DASH	Diatery Approaches To Stop Hypertension
DBP	Diastolic Blood Pressure
DEXA	Dual Energy X-Ray Absorptiometry
DHEAS	Dehydroepiandrosterone Sulfate
DNA	Deoxyribonucleic Acid
DRIs	Dietary Reference Intakes
DUB	Dysfunctional Uterine Bleeding
EAR	Estimated Average Requirement
EERs	Estimated Energy Requirements
ELISA	Enzyme-Linked Immunosorbent Assay
FSH	Follicle-Stimulating Hormone
GBP	Gelatin-Binding Protein Of 28
GH	Growth Hormone
GLP-1	Glucagon-Link Peptide-1
GnRH	Gonadotropin-Releasing Hormone
HDL	High-Density Lipoprotein

HEI	Health Eating Index
HEI	Healthy Eating Index
HMW	High Molecular Weight
HR	Heart Rate
HRP	Horseradish Peroxidase
IGF -1	Insulin-Like Growth Factor 1
IOTF	International Obesity Task Force
JAK STAT	Janus Kinase Signal Transduction And Translation System
LH	Follicle-Stimulating Hormone Luteinizing Hormone
LMW	Low Molecular Weight
MRI	Magnetic Resonance Imaging
MSH	Melanocytestimulating
NP Y	Neuropeptide Y
paI -1	Plasminogen Activator Inhibitor Type-1
Pal-I	Plasminogen Activator Inhibitor .I
PEL	Physical Exercise Lessons
POMC	Proopiomelanocortin
PPARα	Peroxisome Proliferator –Activated Receptor
RBS	Random Blood Sugar
RDAs	Recommended Dietary Allowances
SBP	Systolic Blood Pressure
SES	Socio Economic statues
SMR	Sexual Maturity Rating
SMR	Sexual Maturityrate
SNS	Sympathetic Nervous System
T2D	Type 2 Diabetes
TG	Tri- Glycrides
TMP	Tetra Methyl Benzedrine
TNF	Tumor Necrosis Factor
U.S.PSTF	U.S. Preventive Services Task Force
UCP -2 and 3	Uncoupling-2 And 3
WHO	World Health Organization

List of Tables

Table No.	Table of Review	Pages No.
1	Drugs Associated with Weight Gain	**33**
2	Clinical setting of adiponectin levels In some related conditions	**49**
3	Classification of sexual maturity states (Tanner stages) in girls	**69**
4	Classification of sexual maturity states (Tanner stages) in boys	**70**
5	Components of the Healthy Eating Index	**99**
Table of Results		
1	Nutritional characteristics and life style of group A before program	**145**
2	Descriptive data of Anthropometric measurements and body composition of Group A before and after the intervention program	**146**
3	Descriptive data of blood pressure of Group A before and after the intervention program	**147**
4	Laboratory findings and serum assessment of Adiponectin and Leptin of group A before and after intervention program	**148**
5	Nutritional characteristics and life style of group B before program	**149**
6	Descriptive data of Anthropometric measurements and body composition of Group B before and after the intervention program	**150**
7	Descriptive data of blood pressure of Group B before and after the intervention program	**151**

8	Laboratory findings and serum assessment of Adiponectin and Leptin of group B before and after intervention program	**152**
9	Comparison between groups of study as regards Nutritional characteristics and life style before program	**153**
10	Comparison between groups of study as regards Height for age percentile	**154**
11	Comparison between groups of study as regards Waist circumference percentile	**155**
12	Comparison between groups of study as regards Hip circumference (cm)	**156**
13	Comparison between groups of study as regards Fat percentage	**157**
14	Comparison between groups of study as regards Visceral Fat (VF)	**159**
15	Comparison between groups of study as regards Blood pressure percentiles (mmHg)	**160**
16	Comparison between groups of study as regards Triglycerides (mg/dl)	**162**
17	Comparison between groups of study as regards Cholesterol (mg/dl)	**163**
18	Comparison between groups of study as regards Leptin hormone (ng/ml)	**165**
19	Comparison between groups of study as regards Adiponectin hormone (µg/ml)	**166**
20	Comparison between study groups regarding abnormal lab levels before and after intervention	**168**
21	Comparison between males and females as regards changes in the studied parameters in group A after intervention program	**169**

22	Comparison between males and females as regards changes in the studied parameters in group B after intervention program	**170**
23	Correlation between HEI and different studied factors before intervention in study groups	**172**
24	Correlation between Leptin and different studied factors before intervention in study groups	**174**
25	Correlation between Adiponectin and different studied factors before intervention in study groups	**175**
26	Correlation between Leptin and different studied factors after intervention in study groups	**176**
27	Correlation between Adiponectin and different studied factors after intervention in study groups	**178**
28	Correlation between change in Leptin and change in different studied factors after intervention in study groups	**179**
29	Correlation between change in adiponectin and change in different studied factors after intervention in study groups	**181**
30	Correlation between pubertal stage and change in different studied factors after intervention in study groups	**182**
31	Comparison between breakfast status regarding RBS, BP and BMI	**183**

List of Figures

Fig. No.	Figures of review	Page No.
1	Prevalence of overweight/obesity in boys and girls aged 6–18 years in developing countries	**10**
2	AdipokinesSecretedbyAdipocytes	**14**
3	Life-Course Approach to besity	**30**
4	Adiponectin can activate AMPK and PPARα in the liver and skeletal muscle	**54**
5	Major steps in the pathogenesis of atherosclerosis in relation to adiponectin	**55**
6	Adiponectin levels and inflammatory state	**58**
7	Anthrpometric measuring tape	**123**
8	Body composition analyzer TANITA model BC-418 Segmental Body Composition Analyzer (competitive edge, 2009).	**126**
Figures of Results		
1	Demographic characteristics(age&sex) of the studied groups (A&B)	**143**
2	Demographic characteristics (pubertal staging) of the studied groups(A&B)	**144**
3	Comparison between groups of study as regards Weight percentile ≥90	**154**
4	Comparison between groups of study as regards BMI percentile ≥90	**155**
5	Comparison between groups of study as regards Waist-hip ratio	**156**
6	Comparison between groups of study as regards Fat percentage	**157**

7	Comparison between groups of study as regards Free Fat Mass (FFM)	**158**
8	Comparison between groups of study as regards Muscle Mass (MM)	**158**
9	Comparison between groups of study as regards Systolic blood pressure (mmHg)	**159**
10	Comparison between groups of study as regards Diastolic blood pressure (mmHg)	**160**
11	Comparison between groups of study as regards Random blood sugar (mg/dl)	**161**
12	Comparison between groups of study as regards HDL (mg/dl)	**164**
13	Comparison between groups of study as regards LDL (mg/dl)	**164**
14	Comparison between groups of study as regards Leptin hormone (ng/ml)	**166**
15	Comparison between groups of study as regards Adiponectin hormone (µg/ml) Adiponectin hormone (µg/mL) of the studied groups	**167**
16	Comparison between males and females as regards to changes in BMI	**171**
17	Comparison between males and females as regards to changes in adiponectin	**171**
18	Correlation between HEI and age in group	**173**
19	Correlation between Leptin and BMI after intervention in study groups	**177**
20	Correlation between Leptin and BMI after intervention in study groups	**177**
21	Correlation between Adiponectin and cholesterol in group A	**178**

22	Correlation between changes in Adiponectin and leptin in study groups	**180**
23	Correlation between changes in Adiponectin and cholesterol in group A	**182**

Introduction

Nutrition in childhood has a significant impact on lifelong health. Obesity considered as a common nutritional disorder worldwide ***(Chilton et al., 2015)***.

Obesity, a disease defined by an excess accumulation of body fat to the extent that health is adversely affected has become a global public health concern ***(Schwarz, 2010).***

Obesity is diagnosed by body mass index equal to or greater than 95th percentile for age and sex in a given population where BMI is calculated by dividing the weight in kilograms by the height in meters squared *BMI = Weight (kg) / Ht (m2)* ***(Gortmaker et al ., 2015)***.

According to **U.S.PSTF., 2010** figures have indicated that about 12% to 18% of 2 to 19 years old children and adolescents are obese. In the United States the prevalence of pediatric overweight, and obesity was tripled during the past four decades. 16.3% of children and adolescents are now overweight, 11.3% are obese. ***(Ogden et al., 2010).***

In Egypt, **Aboul Ella et al., 2011** reported in a sample of preparatory and secondary school students (4251 students) through the school year 2004 to 2006 in seven Egyptian governorates, the overall prevalence of overweight and obesity among this age group ranged between 19 to 23% with higher

prevalence rates among females (22.9 to 29.6%)compared to males (14.7 to 20.7%).

Adipocyte differentiation (adipogenesis) plays an important role in obesity and energy homeostasis. It is well known that adipose tissue secretes multiple proteins that mediate various biological functions. These proteins are known as adipocytokine which include: tumor necrosis factor, **leptin, adiponectin**, plasminogen activator inhibitor type-1(paI-1) and resistin ***(Xu et al., 2014)***.

Several studies have demonstrated that there is a relation between plasma Adiponectin and plasma leptin concentrations with increase of visceral fat ***(Xu et al., 2014).***

There are several reports that argued about the effect of exercise and dietary - restriction on plasma level of Adiponectin and leptin hormones release ***(Thompson et al., 2014).***

Aim of the Study

The objectives of the present study were to investigate the changes in Adipocyte hormones in relation to body composition and pubertal development in obese adolescents after physical activity and dietary restriction program.

.

CHAPTER I

OBESITY

Obesity in children and adolescents has become an increasing clinical and public health concern**.** Its prevalence has increased significantly worldwide with an alarming rise of its co-morbidities which includes: hyperinsulinism, hypertension, hyperlipidemia, diabetes mellitus, and an increased risk of atherosclerotic cardiovascular disease in adults .Obese children and adolescents may experience more mental health and psychological issues as depression and low self-esteem compared with non obese children**.** ***(Windham et al., 2012)***

Obese children are more likely of becoming obese adults in the future ***(Nebal et al., 2010).***

The prevalence of obesity in some developing countries has reached even higher levels than in many industrialized nations. This growing rate represents a pandemic that needs urgent attention if its potential mortality and economic tolls are to be avoided ***(WHO, 2010).***

Definition

Overweight and obesity are defined as an abnormal or excessive fat accumulation that may impair health. Obesity increases the child's risk of numerous health problems, and it also