RELATION BETWEEN HOMOCYSTEINE LEVEL IN BLOOD AND CAROTID INTIMA-MEDIA THICKNESS IN OBESE EGYPTIAN CHILDREN

THESIS

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ABSTRACT

Elevated homocysteine level is widely seen as an independent risk factor of cardiovascular disease in adults. In order to investigate the role of homocysteine in pediatric population at risk for early atherosclerosis, we studied serum homocysteine in obese children and non-obese controls. Case control study was conducted on 41 obese children comparing them with 41 healthy weight sex and age matched control group in The New Pediatric Hospital, Cairo University. Serum homocysteine level determined by ELIZA and related to carotid intima media thickness (CIMT) measured by a non invasive high resolution ultrasound and relation to other anthropometric parameters. Serum homocysteine and CIMT were all significantly elevated in obese children P value was <0.01 in both in comparison with controls. No correlation between homocysteine with CIMT and lipid profile and homocysteine correlates with BMI. There were positive significant correlation between CIMT and the anthropometric measurements including: weight, weight SDS, BMI, BMI SDS, waist circumference, hip circumference, W/H ratio, triceps SFT, triceps SFT SDS, subscapular SFT ,subscapular SFT SDS, SBP and DBP while there was no correlation between CIMT and the height . There were negative significant correlation between the CIMT and the HDL-c, but there were no significant correlation between the CIMT and total cholesterol, triglycerides and LDL-c. We concluded that serum homocysteine is elevated in obese children. Serum homocysteine level might be a characteristic for early atherosclerosis in obese children independent of other classic risk factors such as hypercholesterolemia, arterial hypertension and diabetes mellitus.

Obese children are at increased risk of having thickened CIMT, especially in relation to weight, skin fold thickness (SFT), waist circumference, hip circumference, BP and HDL-c.

Key Words: serum homocysteine - carotid intima media thickness - obesity – anthropometric measurements

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Eman Ali Moustafa

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List of Abbreviations

ARIC	Atherosclerosis Risk in Communities study
ATP	Adult Treatment Panel
BMI	Body mass index
BMI SDS	body mass index standard deviation score
BP	Blood pressure
BW	Body weight
CbI	Cobalamin
CBS	Cystathionine B synthase
CCA	Common carotid artery
CCR	Creatinine clrearance
CDC	Centers for Disease Control and Prevention
CHD	Coronary heart diseases
CIMT	Carotid intima-media thickness
CRP	C-reactive protein
CT	Computed tomography
CV	Cardiovascular
CVD	Cardiovascular disease
Cysc.c	Cystatin c
DEMPU	Diabetes Endocrine and Metabolism Paediatric Unit
DEXA	Dual energy X-ray absorptiometry
DM	Diabetes mellitus
ELISA	European Lacidipine Study on Atherosclerosis
FDA	Food and drug administration
FFAs	Free fatty acids
FMD	Flow-mediated dilatation
GFR	Glomerular filteration rate
Hcy	Homocysteine
HDL	High density lipoprotein
HDL-c	High density lipoprotein cholesterol
HHcy	Hyperhomocysteinemia
HTN	Hypertension

ICA	Internal carotid artery
IL-6	interleukin-6
IOTF	International Obesity Task Force
LDL	Low density lipoprotein
MCP	Macrophage chemo attractant protein
MRI	Magnetic resonance imaging
MS	Metabolic syndrome
MTHFR	methylenetetrahydrofolate reductase
NAFLD	Non-alcholic fatty liver disease
NASH	Non-alcholic steatohepatitis
NCEP	National Cholesterol Education Program
NCHS	National Centre for Health Statistics
NHANES	National Health and Nutrition Examination Survey
NO	Nitric oxide
NTDS	Neural tube defects
OSA	Obstructive sleep apnea
PBF	Percentage body fat
PCOS	Polycystic ovary syndrome
PKC	Protein kinase c
SAH	S-adenosyl-homocysteine
SAM	S-adenosyl-methionine
SFT	Skin fold thickness
T2DM	Type 2 diabetes mellitus
TC	Total cholesterol
TG	Triglycerides
tHcy	Total homocysteine
TNF	Tumor necrotic factor
TSH	thyroid stimulating hormone
US	United States
WHO	World Health Organization

List of Errata

Page	Line	Wrong	Correct
29	25	learns	lean
37	7	inhabit	inhibit
40	2	need need	need
43	1	homocystein	homocysteine
44	23	midly	mildly
45	13	absirotion	absorption
48	17	avid	acid
49	17	diseas	aisease
92	3	Umol/ml	Umol/l

Introduction & Aim of the work

INTRODUCTION

Over the past 20 years, obesity has become a worldwide concern of frightening proportion. The World Health Organization (WHO) estimates that there are over 400 million obese and over 1.6 billion overweight adults, a figure which will be projected to almost double by 2015. This is not a disease restricted to adults, at least 20 million children under the age of 5 years were overweight in 2005 **(Drew et al., 2007).**

Overweight and obesity in children are associated with complex metabolic changes and a low-grade inflammatory response, and thus might not only accelerate cardiovascular disease later on but may be also associated with the initiation of atherosclerosis in early life **(Nagel et al., 2008).**

Hyperhomocysteinemia is now regarded as an independent risk factor for atherothrombotic and thromboembolic vascular disease **(Shai et al, .2004)**.Elevated homocysteine (tHcy) levels occur in a large proportion of patients with coronary artery disease **,**the exact mechanism by which higher Homocysteine levels may translate into increased coronary heart disease remains speculative, there are several plausible mechanisms including endothelial dysfunction, impaired flow mediated vasodilatation, increased proliferation of vascular smooth muscle cells, enhanced coagulability and inflammatory effects; the mechanism of Homocysteine angiotoxicity seems to involve nitric oxide system by inducing oxidant stress **(Rosario et al, .2006).**

The precursor of atherosclerosis disease is impairment of endothelial function which associated very strongly with obesity **(Phillips et al., 2008).**

Endothelial dysfunction can be estimated by measuring flow-mediated vasodilation (FMD), brachial-ankle pulse wave velocity (baPWV) and carotid intima-media thickness (CIMT) **(Tsuchiya et al., 2007).**

High resolution B-mode ultrasound measurements of the carotid intima-media thickness (IMT) is a feasible, direct and non-invasive method able to evaluate and to detect preclinical lesions of arterial wall, represented by the American Heart Association (AHA) stage Π lesions **(Cosimo et al., 2008).**

Atherosclerosis can be now evaluated routinely by CIMT **(Tsushima et al., 2008).**

Homocysteine level might be a characteristic for early atherosclerosis in obese children independent of other classic risk factors such as hypercholesterolemia, arterial hypertension and diabetes mellitus **(Atabek et al., 2007).**

Early atherosclerotic changes may still be reversible, as suggested by a reduction in carotid IMT observed in obese children over a 6-week period of diet and physical exercise **(Weihua et al., 2005).**

AIM OF THE WORK

To assess the fasting serum homocysteine level and carotid intima-media thickness in obese children and analyze the relation between intima-media thickness and serum homocysteine level and other anthropometric parameters and to know if homocysteine could be a predictor factor for cardiovascular complications in obese children.