Relationship of obesity and visceral adiposity with serum concentrations of CRP, and IL-6 in Adults

Thesis

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LIST OF ABBREVIATIONS

AF	Atrial fibrillation
AgRP	Agouti-related peptide
Ala	Alanine
AMP	Adenosine monophosphate
AMPK	AMP-activated protein kinase
ARC	Arcuate nucleus
Asp	Aspartate
ATMs	Adipose tissue macrophages
BMI	Body mass index
CAD	Coronary artery disease
CART	Cocaine- and Amphetamine-regulated transcript
CCR2	CC Chemokine receptor2
CD	Cluster of differentiation
CLA	Conjugated linoleic acid
CNS	Central nervous system
CNTF	Ciliary neurotrophic factor
CR	Concentric remodeling
CRP	C-reactive protein
CVD	Cardiovascular disease
Da	Dalton
DHEA	Dehydroepiandrosterone
EIA	Enzyme immunoassay
ELISA	Enzyme-linked immunosorbent assay
EO	Extremely obese
ER	Estrogen receptor
ESR	Erythrocyte sedimentation rate
GLUT	Glucose transporter
gp130	Glycoprotein 130
HDL-C	High-density lipoprotein-cholesterol

HER2	Human epidermal growth factor 2
HF	Heart failure
HMG-COA	3-hydroxy-3-methyl-glutaryl-CoA
HMW	High molecular weight
HR	Heart rate
HRP	horseradish peroxidase
HS	Highly significant
hs-CRP	High-sensitivity C-reactive protein
ICAM-1	Inter-Cellular Adhesion Molecule-1
ICV	Intracerebroventricular
IFN-γ	Interferon-gamma
IGF	Insulin like growth factor
IL	Interleukin
IL-6R α	Interleukin 6 receptor α
IL-1RI	Interleukin 1 type I receptor
IL-1Ra	Interleukin 1 receptor antagonist
IRS	Insulin receptor substrate
ISPs	Inflammation-sensitive plasma proteins
JAKs	Janus kinases
KDa	kilodalton
LA	Left atrium
Lepr	Leptin receptor
LH	Lateral hypothalamus
LHA	Lateral hypothalamus area
LIF	Leukemia inhibitory factor
LMW	Low molecular weight
LV	Left ventricular
LVH	Left ventricular hypertrophy
MCP-1	Monocyte chemoattractant protein-1
MCSF	Macrophage colony stimulating factor
MI	Myocardial infarction
MIF-β	Macrophage migration inhibitory factor-β

mRNA	Messenger Ribonucleic acid
MSR	Macrophage scavenger receptor
N	Number
NAC	N-acetyl cysteine
NF	Nuclear factor
NGF	Nerve growth factor
NPY	Neuropeptide Y
NS	Non significant
NW	Normal weight
OD	Optical density
OW/OB	Overweigt/Obese
PAI-1	Plasminogen activator inhibitor-1
PAMPs	Pathogen associated molecular patterns
PBEF	Previously known as B cell colony enhancing factor
PD-1	Programmed cell death 1
PDL	Programmed cell death ligand 1
POMC	Pro-opiomelanocortin
PVN	Paraventricular nucleus
RV	Right ventricular
S	Significant
SAA	Serum amyloid A
SC	Subcutaneous
SD	Standard deviation
SOCS	Suppression of cytokine signalling
STATs	Signal transducers and activators of transcription
Std	Standard
TGF-β	Tumor growth factor-beta
TNF-α	Tumor necrosis factor-alfa
TMB	Tetramethylbenzidine
TLRs	Toll-like receptors
VCAM-1	Vascular cell adhesion molecule-1

VEGF	Vascular endothelial growth factor
VMH	Ventromedial hypothalamus
WAT	White adipose tissue

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INTRODUCTION

Obesity is a steady increasing health problem that is defined as increased mass of adipose tissue. It causes complications such as, diabetes mellitus, hypertension, stroke, coronary heart disease, cardiomyopathy, non-alcoholic steatohepatitis, osteoarthritis, reproductive problems, sleep apnea, gall bladder disease and some cancers as endometrial, breast and colon **(*Al-Hazimi, 2004)***.

Adipose tissue is an important source of cytokines, and adiposity contributes to the proinflammatory milieu. Serum cytokine levels are elevated in humans and animals with excess adiposity ***(Park et al., 2004)***.

Approximately, 30% of circulating IL-6 is estimated to be from adipose tissue. Moreover, some reports have suggested that visceral adipose tissue secretes more IL-6 than subcutaneous adipose tissue ***(Park et al., 2004)***.

Obese patients demonstrate a variety of biochemical and metabolic abnormalities. Considerable interest has been raised regarding the role of interleukin-6 (IL-6) in mediating the host response to obesity and ***(Roytblat et al., 2000)*** showed that serum IL-6 concentrations were positively correlated with the level of obesity as assessed by body mass index (BMI). They hypothesized that adipose tissue may play a role in the regulation of serum IL-6 production. IL-6 released from adipose

tissue may cause low-grade systemic inflammation in persons with excess body fat ***(Chaikate et al., 2006)***.

C-reactive protein (CRP) has been used as an acute phase reactant and a marker of systemic inflammation. Moreover, CRP has been recognized as a very useful and sensitive predictor of the future risk of myocardial infarction (MI) and stroke in the past several years. It is well known that CRP levels in adult subjects elevate with aging, excess of body mass index (BMI), and smoking. It has been proven that weight loss and the improvement of insulin resistance lead to decreases of CRP levels ***(Hiura et al., 2003)***.

In additional to overall obesity, the accumulation of visceral adipose tissue is a key factor responsible for the up-regulation of low-grade chronic inflammation in obese subjects. These findings suggest that decreasing obesity and visceral adiposity may prevent the elevation of cytokine levels as well as atherosclerosis ***(Park et al., 2004)***.

AIM OF THE WORK

The objective in this study is to assess serum concentrations of CRP and the cytokine IL-6 in obese and non obese individuals in order to determine the relationship between their levels with obesity and visceral adiposity.

INTRODUCTION TO OBESITY

Obesity is one of the major medical problems in the western world. The clinical definition of obesity is a body mass index (BMI) of 30 or higher. The BMI is the body's weight in kilograms divided by the square of the body's height in meters ***("http://www.wisegeek.com/", 2011)***.

Obesity results when a person ingests more calories than he or she can burn off. If this happens regularly over a period of time, the body will store the extra calories as fat. The body is able to burn off calories as energy needed throughout the day, but if the energy is not burned away, it will be stored as fat ***("http://www.wisegeek.com/", 2011).***

Obesity is a condition that represents a serious worldwide threat to public health ***(Haslam and James, 2005)*** and it is a disease that brings several complications and increases the risk of other diseases like metabolic syndrome, diabetes mellitus type II, coronary heart disease ***(Gnacińska et al., 2010 a)***, hypertension, gallbladder disease, osteoarthritis and certain types of cancer ***(Neilson and Scleinder, 2005)***. Epidemiological studies have demonstrated that lifestyle choices, accumulated across the life course, greatly influence the risk of developing obesity ***(Brasil et al., 2007)***.

Greater consumption of high-fat and energy-dense food is generally considered to be associated with the increasing

prevalence of obesity ***(Howarth et al., 2006)***. Another contributory factor for the development of obesity is an individual's genetic background. Large differences in prevalence of obesity have been reported across different ethnic groups ***(Tanaka et al., 2003)***.

However, increases in energy expenditure through sports and other forms of physical activity have been reported as important lifestyle factors that enhance overall health and prevent the development of central obesity ***(Jakicic and Otto, 2006)***.

Obesity results from the interaction of many factors, including genetic, metabolic, behavioral and environmental influences ***(Kumanyika et al., 2002)***. Likely a combination of increasing energy consumption and decreasing energy expenditure has led to a positive energy balance and a marked increase in excess weight in the society ***(Stein and Colditz, 2004)***.