Monocyte Chemoattractant Protein-١ In Morbidly Obese Patients

Thesis

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In Clinical and Chemical Pathology

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List of Abbreviations

α	: Alpha
β	: Beta
γ	: Gamma
A-FABP	: Adipocyte Fatty Acid–Binding Protein
A-II	: Angiotensin-II
AIR	: Acute Insulin Response to Glucose
ARI	: Adipose Resident Immune
ATMs	: Adipose Tissue Macrophages
AVP	: Arginine Vasopressin
BF	: Body Fat Percentage
BMI	: Body Mass Index
BP	: Blood Pressure
CAD	: Coronary Artery Disease
CCL٢	: Chemokine Ligand ٢
CD	: Cluster of Differentiation
CR	: Caloric Restriction
CRH	: Corticotropin Releasing Hormone
CRP	: C-Reactive Protein
CT	: Computed Tomography
CVD	: Cardiovascular Disease
DCs	: Dendritic Cells
DRG	: Dorsal Root Ganglia
ECAT	: European Concerted Action on Thrombosis and Disabilities
FACS	: Fluorescence Activated Cell Sorting
FFAs	: Free Fatty Acids
FPG	: Fasting Plasma Glucose
HDL	: High Density Lipoprotein
HGF	: Hepatocyte Growth Factor
HOMA	: Homeostasis Model Assessment
hs-CRP	: High Sensitivity C-Reactive Protein
ICAM-١	: Intercellular Adhesion Molecule-١
IDF	: International Diabetes Federation
IHD	: Ischemic Heart Disease

IL	: Interleukin
IVGTT	: Intravenous Glucose Tolerance Test
LAK	: Lymphokine Activated killer
LDL	: Low Density Lipoprotein Cholesterol
M-CSF	: Macrophage Colony Stimulating Factor
MCP-١	: Monocyte Chemoattractant Protein -١
MetS	: Metabolic Syndrome
MIF	: Macrophage Migration Inhibitory Factor

List of Abbreviations (Cont.)

MIP-١	: Macrophage Inflammatory Protein-١
NASH	: Non Alcoholic Steatohepatitis
NGF	: Nerve Growth Factor
NHANES III	: The Third National Health and Nutrition Examination Survey
NK	: Natural Killer Cells
NO	: Nitric Oxide
NTS	: Neurotrophins
OGTT	: Oral Glucose Tolerance Test
PAI-١	: Plasminogen activator inhibitor-١
PBEF	: Pre-B Cell Colony Enhancing Factor
PHA	: Phytohaemagglutinin
PKC	: Protein kinase C
PMNLs	: Polymorph Nuclear Leucocytes
RA	: Rheumatoid Arthritis
RANTES	: Regulated on Activation of Normal T-cell Expressed and Secreted
RBP٤	: Retinol-Binding Protein ٤
RD	: Retinal Detachment
rs	: Restriction Site
S	: Insulin Sensitivity Index
SAA٣	: Serum Amyloid A ٣
SNPs	: Single Nucleotide Polymorphisms
SSc	: Systemic Sclerosis
SVF	: Stroma Vascular Fraction
TG	: Triglyceride
TGF-β١	: Transforming growth factor beta
TNF-α	: Tumor Necrosis Factor Alpha
VAT	: Visceral Adipose Tissue
VCAM-١	: Vascular Cell adhesion Molecule-١
VEGF	: Vascular Endothelial Growth Factor
VLDL	: Very Low Density Lipoproteins
WAT	: White Adipose Tissue
WBCs	: White Blood Cells
WC	: Waist Circumference
WHO	: World Health Organization
WHR	: Waist to Hip Ratio
WHtR	: Waist to Height Ratio

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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, ٢٠٠٤).***

For a long time, white adipose tissue (WAT) has been regarded as an inert tissue for energy storage. With the rapidly rising incidence of obesity related complication such as metabolic syndrome, type ٢ diabetes and hypertension; these diseases have attracted increasing attention in research and health politics. In parallel, WAT was recognized as an active endocrine and paracrine organ that plays an important role in the metabolic syndrome ***(Matter and Handschin, ٢٠٠٧)***.

Obesity is characterized by a state of chronic mild inflammation, with raised circulating levels of inflammatory markers and the expression and release of inflammatory-related adipokines such as monocyte chemoattractant protein ١ (MCP−١). The elevated production of inflammation-related adipokines is increasingly considered to be important in the development of diseases linked to obesity, particularly type II diabetes and the metabolic syndrome. WAT is involved in extensive cross-

talk with other organs and multiple metabolic systems through the various adipokines ***(Trayhurn and Wood, ٢٠٠٥).***

Visceral adipose tissue (VAT) seems to be an active compartment in pro-inflammatory molecule secretion. Adipocytes and VAT are able to produce large amounts of MCP−١ ***(Malavazos et al., ٢٠٠٥).***

Recent findings: MCP-١ is a proinflammatory adipokine that is believed to play a role in the pathogenesis of obesity and diabetes also MCP-١ has the ability to induce insulin resistance in adipocytes and skeletal muscle cells **(*Henrike and Jurgen, ٢٠٠٧).***

MCP-١ plays also a pivotal role in the pathogenesis of atherosclerosis ***(Troseid et al., ٢٠٠٤).*** It is involved in the recruitment of monocytes into the arterial vessel wall as one of the major events leading to atherosclerotic vascular diseases, such as coronary artery disease (CAD) ***(Martinovic et al., ٢٠٠٥)***. Moreover, MCP-١ has been implicated in many inflammatory and autoimmune diseases ***(Dawson et al., ٢٠٠٣).***

AIM OF THE WORK

The aim of the present study is to assess the serum levels of MCP-١ in morbid obesity and to correlate it with the corresponding laboratory risk factors. In addition, the serum levels of MCP-١ will be assessed in a group of morbidly obese patient after significant weight loss induced by bariatric surgery.

HIGH RISK OBESITY

Introduction:

The prevalence of obesity is increasing worldwide at an alarming rate in both developed and developing countries. Obesity significantly affects the quality of life and reduces the average life expectancy ***(Vojtch et al., ٢٠٠٨).*** Obesity has significant adverse effects on public health and health-care costs. The co-morbidities associated with obesity affect virtually every physiologic system ***(O'Rourke et al., ٢٠٠٥).***

Obesity is becoming endemic, particularly because of increasing nourishment and a decrease in physical exercise. Obesity is created by a positive energy balance (when energy intake exceeds energy consumption) in which case the surplus of energy is stored as adipose tissue. Approximately ٥٠% of the inter-individual variation in body mass index [the weight of a person in kilograms divided by the square of the height in meters ($kg/m^{٢}$)] (BMI) is genetically determined via the influence on various complex neuroendocrine systems; ultimately it is the interaction between genetic predisposition and environment that finally determines the attained body weight ***(Bult et al., ٢٠٠٨).***

Definition and Types of Obesity:

Obesity is defined as an increase in total body fat. The prevalence of obesity and being overweight is commonly assessed by using the BMI. A BMI over ٢٥ $kg/m^{٢}$ is defined as

overweight and a BMI over ٣٠ kg/m^{٢} is defined as obese (Table ١) ***(Calle and Kaaks, ٢٠٠٤).***

Table (١): World Health Organization (WHO) guidelines for classification of overweight and obesity ***(Calle and Kaaks, ٢٠٠٤).***

BMI (kg/m^2)	WHO classification	Popular description
< 18.5	Underweight	Thin
18.5–24.9	Normal range	'Healthy', 'normal' or 'acceptable' weight
25.0–29.9	Grade 1 overweight	Overweight
30.0–39.9	Grade 2 overweight	Obesity
≥ 40.0	Grade 3 overweight	Morbid obesity

Relevant Parameters to Diagnose High Risk Obese Patients:

Some individuals are more predisposed than others to obesity-associated diseases, but it might be difficult to identify the 'at risk' individuals who would benefit the most from individualized monitoring and care ***(Andrew et al., ٢٠٠٦).***

A-Body Mass Index

Higher BMI increases the risk of premature atherosclerosis, cardiovascular diseases mortality and the risk is highest in morbidly obese patients (BMI above ٤٠) ***(Hanusch et al., ٢٠٠٣).*** Morbid obesity is associated with an increased risk of coronary heart disease, stroke, hypertension, type ٢ diabetes and dyslipidemia. The risk is proportional to body mass index and duration of obesity ***(Schernthaner et al., ٢٠٠٦).***

The BMI has been the gold standard to gauge obesity but healthcare providers have noted that given two overweight or obese patients with the same BMI, one patient may have few metabolic risk factors while the other may show a full spectrum of cardiac and metabolic risk. Furthermore, a description based on BMI may classify athletes and obese patients as the same; though their body composition is clearly different therefore waist circumference should be done together with BMI ***(Schaller and Dean, ٢٠٠٨).***

B-Waist Circumference and Waist Hip Ratio:

Measures of abdominal fat distribution such as waist circumference (WC) or waist to hip ratio (WHR) are encouraged. WC is measured around the narrowest point between ribs and hips when viewed from the front after exhaling. Hip circumference is measured the point where the buttocks extended the maximum, when viewed from the side both are measured to the nearest ١ cm. WHR is the WC divided by hip circumference ***(Schneider et al., ٢٠٠٦).***

Waist circumferences greater than ١٠٢ cm for men and greater than ٨٨ cm for women portend high risk for obesity related complications ***(Schaller and Dean, ٢٠٠٨)*** While WHR greater than ١.٠ for men or ٠.٨٥ for women is indicative of android obesity and increases risk of obesity related complications ***(O'Dea et al., ٢٠٠٢).***