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Original article

Relationship of serum leptin with some biochemical, anthropometric parameters and abdominal fat volumes as measured by magnetic resonance imaging

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ABSTRACTS

Aims: To measure the level of leptin in volunteers and correlate it with several anthropometric, biochemical variables and abdominal fat volumes.
Methods: The level of leptin was investigated in 167 disease-free volunteers. Serum levels of IL-6, adiponectin, and resistin, blood lipid profile (cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), and triglyceride (TG) were determined. Waist circumference (WC) was measured using tape and magnetic resonance imaging (MRI) images.
Results: All measured anthropometric (BMI, WC measured by tape and MRI) and biochemical variables (adiponectin, resistin, cholesterol, HDL, LDL and TG); and abdominal fats showed a significant ($p < 0.05$) difference between participants with abnormal serum leptin levels and those with normal leptin levels. A higher percentage of participants with abnormal serum leptin were obese males while participants with normal leptin levels were either overweight or normal weight females. A significant ($p < 0.05$) positive correlation was detected between serum leptin concentration and WC, BMI, subcutaneous fat, visceral fat, total abdominal fat, and resistin. A moderate association was found between serum leptin concentration and the inflammatory cytokine IL-6.
Conclusion: Abnormal serum leptin, was detected in obese male individuals which may be considered as an important indicator for the development of cardiovascular diseases and type 2 diabetes.

1. Introduction

Leptin is a 167-amino-acid peptide which is produced in the adipocytes of white adipose tissue (WAT), brown adipose tissue, placenta, ovaries, skeletal muscle, stomach, mammary epithelial cells, pituitary gland, bone marrow, lymphoid organs and other body tissues [1]. Leptin regulates energy balance by inhibiting hunger and in obesity, a decreased sensitivity to leptin was observed [2]. Many studies in the literature reported a clear relationship between serum leptin and adipose tissue [3–5], cytokines [5,6] and lipid profiles [7–9]. A previous study showed that circulating leptin levels are directly proportional to the amount of body fat, which reflects the status of long-term energy stores[10]. Leptin was found to be positively correlated with body mass index (BMI) and waist circumference (WC)[11]. Moreover, in a study which was conducted on Mexican Americans, the concentration of leptin was found to be significantly correlated with BMI (r = 0.741, 0.814), waist-to-hip ratio (WHR) (r = 0.567, 0.377), WC (r = 0.840, 0.718) and hips circumference (r = 0.842, 0.779) in both men and women [12].

Regarding the type of body fat, subcutaneous fat was observed to produce more leptin than visceral fat, and consequently, this may contribute to the higher leptin levels in females than in males

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[13]. In addition, obese individuals were always observed to have elevated levels of circulating leptin which indicates a high level of leptin expression in adipose tissue [14]. This high level of leptin and its failure to diminish excess adiposity is an indicator for leptin resistance [14].

Studies on the relationship between serum leptin and blood lipid profile have shown ambiguous results. Many studies did not show any direct relationship between leptin level and lipid profile [15,16]. On the other hand, some studies reported a significant positive correlation between leptin and high-density lipoprotein (HDL) [17] and triglyceride (TG) [18]. Furthermore, a new study confirmed the positive correlation between leptin and TG blood concentration but observed a weak negative correlation with HDL [19].

A previous study indicated that leptin is regarded as a negative predictor of adiponectin levels independent of body composition [20], in contrast to this, other study detected a significant association between leptin and adiponectin in men and women only when considered separately but not in the entire cohort study [21]. Moreover, a subsequent study did not detect any association between serum leptin and adiponectin levels [22]. Many studies in the literature indicated that leptin is involved in the regulation of the inflammatory response and play a major role as an inflammatory marker and in terms of structure and function, it was found that leptin resemble IL-6 and can be regarded as a member of the cytokine superfamily [23–25].

As indicated above, it is clear that most of the studies regarding leptin and its association with other biochemical parameters related to obesity and excessive weight gain are controversial and require further investigations. Therefore, the present cross-sectional study was carried out to investigate the level of leptin in a 167 apparently healthy volunteers and correlate it with several anthropometric, biochemical variables as well as abdominal fat volumes (using magnetic resonance imaging; MRI).

2. Materials and methods

2.1. Study population

A total of 167 (83 males and 84 females) apparently healthy volunteers were recruited in the present study (mean age 27.2 years; age range 18–51) from King Hussein Medical Center (KHMC) during the period of October 2014 to July 2015. Security manpower, hospital cleaners, and employees in administrative positions were asked to participate in this cross-sectional study. Inclusion criteria were being disease-free and at least 18 years old. Participants were recruited conveniently, however, the response rate for the blood sample collection and anthropometric measurements were about 90%. Pregnant and lactating women and persons suffering from eating disorders or having any disease were excluded.

Ethical approval to conduct the present study was obtained from the Royal Medical Services (RMS) and a consent form was signed individually by each participant. Furthermore, to measure the visceral fat, all participants completed the MRI safety questionnaire before participating in this study.

2.2. Biochemical analysis

Blood samples were collected separately in vacutainer plain tubes with gel to separate the serum. The samples were allowed to clot at room temperature (22–25 °C) then centrifuged at 4000 rpm for 5 min using Roto Fix 32A Centrifuge (Germany) to separate serum from other blood components. After that, the serum was decanted in two (2 ml) Eppendorf tubes and frozen at −80 °C until subsequent analysis. Serum IL-6, adiponectin, resistin, and leptin concentrations were measured using commercially available enzyme-linked immunosorbent assay (ELISA) kits for human leptin (ELISA Kit, USA, Cat# ELH-Leptin); IL-6 (RayBio® Human IL-6 ELISA Kit, USA, Cat# ELH-IL-6; RayBio® Human Acrp30 ELISA Kit USA); Adiponectin (Cat# ELH-Adiponectin; RayBio®) and Resistin (RayBio® Human Resistin ELISA Kit, USA, Cat# ELH-Resistin) which were measured using ELISA Microplate Readers-USA (ELX 800 TC models 96 well). The reproducibility of the intra- and inter-assay coefficients of variation were <10% and <12% respectively for all RayBio® ELISA kits.

The fasting blood lipid profile (total cholesterol, LDL, HDL, and TG) for all participants, was measured by Spectrophotometer (Jenway 6305 UV/Visible, USA) using commercially available kits (TECO DIAGNOSTICS, USA).

2.3. Anthropometric measurements

Body weight was measured with minimal clothes and without shoes, using a calibrated scale (Tanita, Model SC-331S, Japan) and to the nearest 0.1 kg. Height was measured in standing position without shoes, using a portable measuring rod and to the nearest 1 cm. BMI was calculated by dividing weight in kilograms to the square of height in meters [26]. WC was estimated using two methods: 1) tape at the mid-point between the costal arc and the iliac crest at the end of normal expiration in a standing position and 2) MR images at a level just below the lower costal margin. All anthropometric variables except the MR imaging were measured by trained dietitian.

2.4. Magnetic resonance imaging (MRI) measurement

Abdominal MRI was performed on a 3T Siemens Trio MR system (Siemens Medical Systems, Erlangen, Germany), equipped with 4-channel phase-array body coil. The acquired axial slices covered the region between the level above of the diaphragm and the head of the femur in the supine position and full expiration. The imaging protocol included in (IP) and out (OP) of phase, non-enhanced T1 wted sequence with the following imaging parameters; repetition time (TR = 5 ms), echo time (TE_{OP} = 1.225 ms) and (TE_{IP} = 2.45 ms), flip angle (FA = 10°), slice thickness (ST = 5 ms), 80 slices, 256 × 192 matrix size, 380 × 285 mm^2 field of view, number of signal averages (NSA = 1), acceleration factor of 2, and scan time = 18 s. The MRI scanner calculated the "fat-only" and "water-only" images from this sequence as follows:

$$\text{"}Fat\text{"}\ image = \frac{[IP - OP]}{2} \quad \text{"Water"}\ image = \frac{[IP + OP]}{2}$$

2.5. Image post processing and analysis

"Fat" MR images were imported into image analysis software (SliceOmatic, Tomovision Inc., Montreal, Canada) in their standard formats (Digital Imaging and Communications in Medicine; DICOM) to segment the subcutaneous and visceral fat tissues. Slices covering the region between the top of the diaphragm and the top of the first sacral vertebra (S1) were used to segment and analyze the subcutaneous and visceral fat tissues by an expert in image analysis. Each segmented tissue was saved as a separate "tag" and the total volumes of subcutaneous fat (SF) and visceral (VF) were calculated from all analyzed slices and saved into a separate file for further analysis. The model and method employed to segment the various tissues is fully described and illustrated elsewhere [27]. "Fat" images were also used to measure the waist circumference at a level just below the lower costal margin.

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