International Journal of Cardiology 215 (2016) 318–324

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Obesity can predict and promote systemic inflammation in healthy adults

Mohammed S. Ellulu [a,*], Huzwah Khaza'ai [b], Asmah Rahmat [c], Ismail Patimah [b], Yehia Abed [d]

[a] Department of Nutrition and Dietetics, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia (UPM), Malaysia
[b] Department of Biomedical Science, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia (UPM), Malaysia
[c] Cancer Resource and Education Centre (CARE), Faculty of Medicine and Health Sciences, Universiti Putra Malaysia (UPM), Malaysia
[d] Primary Health Care Specialist (Gaza 2020: Health Matters), Gaza, Palestine

ARTICLE INFO

Article history:
Received 8 February 2016
Accepted 11 April 2016
Available online 14 April 2016

Keywords:
Inflammation
Obesity
Blood pressure
Lipid profile
Fasting glucose
Healthy adults

ABSTRACT

Background: To find out the differences on biomedical data between obese and non-obese participants, and to identify risk factors associated with systemic inflammation in healthy Palestinian adults.
Methodology: A cross-sectional study involved 105 apparently healthy adults. Interview questionnaire was used to collect personal information. Participants were excluded if they suffered from acute or chronic inflammatory diseases, or continued using medicines, which might affect the biomedical results.
Results: In association with increased Body Mass Index (BMI), the obese group displayed significant higher markers including: interleukin 6 (IL-6), high sensitivity C reactive protein (hs-CRP), total cholesterol (TC), systolic blood pressure (SBP), and diastolic blood pressure (DBP). Obese group in association with increased waist circumference (WC) was higher significantly in inflammatory markers (IL-6, hs-CRP), lipid profile (TC) and triglyceride (TG), and blood pressure (SBP, DBP). A tertile of a feature of systemic inflammation (hs-CRP) was created, by Ordinal Logistic Regression, after adjusting for the age, gender, smoking habits, physical activity pattern, father and mother's health history; risk factors were the increased BMI [OR: 1.24] (95% CI: 1.005–1.548, P = 0.050), IL-6 [OR: 3.35] (95% CI: 1.341–8.398, P = 0.010), DBP [OR: 1.19] (95% CI: 1.034–1.367, P = 0.015), and reduced Adiponectin [OR: 0.59] (95% CI: 0.435–0.820, P = 0.001). Finally, BMI correlated with IL-6 and hs-CRP ($r = 0.326$, P = 0.005; $r = 0.347$, $P < 0.001$; respectively), and hs-CRP correlated with IL-6 ($r = 0.303$, P = 0.010), and inversely with Adiponectin ($r = -0.342$, P = 0.001).
Conclusion: The increased level of IL-6 and reduced Adiponectin, which strongly associated with obesity, indicated that having high BMI is a useful marker in association with IL-6 and further developed systemic inflammation.

1. Introduction

Obesity is a public health problem at all stages of life worldwide, in both developed and developing countries [1]. Obesity is an excessive unhealthy accumulation of body fat [2], that results in serious health complications and increases the risks of morbidity and the prevalence of several health complications, such as type-2 diabetes, hypertension, atherosclerosis, dyslipidemia, arthritis, prothrombotic state, insulin resistance, cardiovascular disease, metabolic syndrome, and various types of cancers [3,4,5]. Moreover, it has been considered as the fifth leading risk for global deaths, and it usually refers to the accumulation of abnormal or excessive fat that may interfere with the maintenance of optimal state of health [6]. The causes of obesity are attributed to a complex interaction between the environmental factors, genetic predisposition, and human behavior [1]. However, the environmental factors are most likely to be the major contributors to the obesity epidemic. It is certain that obesity develops when there is a positive imbalance between energy intake and energy expenditure [7].

Obesity has been linked strongly with metabolic abnormalities including increased blood pressure [8,9], increased blood sugar [10,11], and disturbances in lipid profile [12,13]. Furthermore, obesity has been predisposed to metabolic abnormalities via inflammatory process [14]. In the state of obesity, the pro-inflammatory adipokines derived from adipose tissue are overexpressed, among which, increased production and secretion of inflammatory mediators: interleukin 6 (IL-6) and tumor necrosis factor alpha (TNF-α), and decreased production of anti-inflammatory mediator Adiponectin or even reduced sensitivity [15]. The increased circulatory levels of inflammatory mediators particularly IL-6 have been associated with hepatocyte stimulation to synthesize and produce a low-grade systemic inflammation marker C reactive protein (CRP) [16].

The systemic inflammation represented by increased level of high sensitivity CRP (hs-CRP) has been classified as a characteristic feature and an essential cause of many illness conditions including metabolic syndrome [17], atherosclerosis and coagulation [18], coronary heart disease [19], cancers and metastases [20], and other health conditions like depression [21]. The status of hs-CRP is very sensitive; showing us that the desirable value of hs-CRP is less than 3.0 mg/L [22], where it could be elevated by pathological or non-pathological response [23]. Also, the

* Corresponding author.
E-mail address: mohdsubhilulu@gmail.com (M.S. Ellulu).

http://dx.doi.org/10.1016/j.ijcard.2016.04.089
0167-5273/

extreme high values (≥10 mg/L) tend to be acute inflammation more than chronic inflammation, while the continued high value predisposes to 2- or 3-fold increase of mortality rates [24]. Thus, the objective of this study is to clarify the independent clinical effect of obesity indices on systemic inflammation in Palestinian healthy adults.

2. Materials and methods

2.1. Participants and study design

A cross-sectional study was conducted involving 105 apparently healthy participants (out of 484 subjects screened) between 20–60 years of age and free from acute and chronic inflammatory diseases. The enrolment of participants continued for seven months from November 2013 to May 2014 at seven centers of primary health care departments of Ministry of Health in Gaza (Palestine) based on cluster random sampling. The study was ethically approved by the Ethical Committee of University Putra Malaysia (JKEUPM), Ref No.: FPSK_Mac (13)04 and Helsinki Committee for Ethical Approval of Gaza (Number: PHRC/HC/11/13). All participants had a stable weight with no fluctuations >2% of their body weight for at least two months prior to this study. Other than that, patients who suffered conditions might affect laboratory results like acute or chronic inflammatory diseases like arthritis, infections, diabetes (type 1 or 2), hypertension (systolic blood pressure ≥140 mm Hg and/or diastolic blood pressure ≥90 mm Hg), dyslipidemia (increased levels of total cholesterol, low density lipoprotein cholesterol, and triglyceride), cancers (malignancies), heart disease (coronary heart disease), liver and renal diseases, pregnancy, or regularly used medicines like non-steroidal anti-inflammatory drugs (NSAIDs) as diclofenac and COX-2 inhibitors, antibiotics, supplements like Omega-3 fatty acids (can produce anti-inflammatory 3 & 5 series eicosanoids) and antioxidants (like vitamin C) were excluded.

2.2. Interview questionnaire

Information containing participants' characteristics, lifestyle factors, and parents' health history was collected after conducting an assignment of the informed consent, in which the participants' characteristics factors included age and gender. For instance, lifestyle factors in this study involved smoking habits and physical activity pattern. The smoking habits was then assessed according to modified form of the Behavioral Risk Factor Surveillance System that was approved by the Centers for Disease Control and Prevention (CDC) Survey Data [25], and physical activity pattern was evaluated according to the Global Physical Activity Questionnaire (GPAQ) Version-2 that considers the Palestinian specialties [26]. Parents' health history depended on participants self-reporting; mother or father considered diseased if had one or more of non-communicable diseases (NCDs) like hypertension and diabetes.

2.3. Anthropometric measurements

Seca Stadiometer was used to assess Body Mass Index (BMI). Moreover, the participants' BMI was calculated by using height and weight, which was also classified internationally according to World Health Organization [27], and measured based on the formula [BMI (kg/m^2) = weight (kg) / height square (m^2)]. Other than that, BMI was classified according to the obesity status [NON-obese: <30 kg/m^2, and obese: ≥30 kg/m^2]. Seca 201 non-elastic tape was used to assess waist circumference (WC) according to National Institute for Health and Clinical Excellence [28] [high: male ≥102 cm, female ≥88 cm; normal: male <102 cm, female <88 cm].

2.4. Biomedical data

The quantitative method was used to assess fasting blood glucose (FBG), total cholesterol (TC), triglyceride (TG), and high sensitivity C reactive protein (hs-CRP) via Mindray BS-120 Chemistry Auto-analyzer. CRP turbidimetric latex 1:5 kit was used to assess hs-CRP. Enzymatic colorimetric method with glucose oxidase used to estimate FBG. Apart from that, the commercial kits were used to assess TC and TriG. Sigma-Aldrich® ELISA kits via ELISA Reader, which was used to assess IL-6 and Adiponectin. Blood pressure (BP), which was determined by validated and standard mercury sphygmomanometer. For instance, systolic blood pressure (SBP) was defined as the appearance of first sound (Korotkoff phase 1), and diastolic blood pressure (DBP) was referred as the disappearance of the sound (Korotkoff phase 5) during deflation of the cuff at a 2–3 mm Hg/s reduction rate of the mercury column. Seven milliliters of blood-into-two-tubes was drawn into a polyethylene evacuated tube. One tube was used to evaluate quantitative measures hs-CRP, FBG, TC, and TG, and the other stored at −80 °C after separation of serum to analyze IL-6 and Adiponectin via One-Run ELISA.

2.5. Statistical analyses

Data was analyzed by using the Statistical Package for Social Sciences version 21.0 software (SPSS Inc., Chicago, IL, USA). Descriptive statistics including Chi-square (χ^2) was used to compare the categorical variables. The central tendency of continuous variables was presented by mean ± standard error of mean (SEM). The independent T Test was used after dividing the participants into two groups, based on obesity factors BMI and WC. Then, a tertile of hs-CRP was created; where a One-Way ANOVA was used to detect the differences between the tertile groups, and an Ordinal Logistic Regression was used to estimate the Exp(B) [Odds Ratio (OR)] after adjusting for age, gender, smoking habits, physical activity, and parents' health history. The Bivariate analysis via Pearson's correlation coefficient explained the relationships of BMI with IL-6 and hs-CRP, and hs-CRP with IL-6 and Adiponectin. P value of ≤0.05 was considered statistically significant and level of confidence was 95%.

3. Results

A total of 105 apparently healthy adults were enrolled in the study to identify the effects of obesity indices on systemic inflammation. BMI as a measure of total obesity and WC as a measure of abdominal obesity were used as indicators of obesity indices. As shown in Table 1, the baseline characteristics of participants is described, which denotes that the study involved 74 (70.5%) women and 31 (29.5%) men. It also involved three different age groups as the following: 44 (41.9%) less than 30 years, 47 (44.8%) from 30 to less than 45 years, and 14 (13.3%) aged from 45 years and more. The smoking habits revealed the largest group of the participant was never smokers 62 (59%), while the group past smokers was the smallest one 10 (9.5%), and current smokers group was 34 (32.4%). According to the physical activity pattern, the group of low physical activity was 34 (32.4%), 42 (40.0%) were moderate, and 29 (27.6%) indicated high physical activity. Furthermore, 51 (48.6%) and 64 (61.0) of the participants indicated that their fathers and mothers had one or more NCDs, respectively. With regard to the obesity indices, majority of participants were obese; 71 (67.6%) and 68 (64.8%) were obese according to BMI and WC measures, while 34 (32.4%) and 37 (35.2%) were non-obese based on BMI and WC, respectively.

The differences of clinical characteristics in biomedical data according to change obesity indices are shown in Table 2. The biomedical data involved inflammatory indicators (hs-CRP, IL-6, and Adiponectin) and metabolic markers (FBG, TC, TG, and BP). A high consistency was observed in the differences of biomedical data between BMI and WC. In BMI comparisons, the obese participants got significant higher values as compared to non-obese on hs-CRP (3.79 ± 0.37 vs. 1.88 ± 0.43 mg/L), IL-6 (1.94 ± 0.10 vs. 1.50 ± 0.14 pg/mL), TC (202.66 ± 3.94 vs. 176.38 ± 7.31 mg/dL), SBP (121.24 ± 1.51 vs. 110.76 ±