Original Article

Association Between BMI and Inflammation Among Diabetic Polyneuropathy Patients

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Abstract

Background: Inflammation is defined as body tissues response to harmful stimuli. Obesity-related inflammation leads to increased risk chronic diseases including diabetic polyneuropathy (DPN). The present study was performed to determine association between body mass index (BMI) and inflammatory markers including erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) in DPN patients. **Methods:** In this cross-sectional study, 200 DPN patients with a mean (SD) of age 58.76 (9.53) years were selected. All patients completed the questionnaire including demographic data and chronic disease history. In addition, anthropometric measures and clinical laboratory tests were taken. Multivariate linear regression was used to detect the association between BMI, CRP, and ESR levels. **Results:** BMI was associated with increase in ESR and CRP levels (β-ESR = 4.67, $P < 0.001$ and β-CRP = 0.71, $P < 0.001$). Also, this association remained after adjustment for other different variables. **Conclusions:** These findings indicate that higher BMI is related to increase inflammatory markers including CRP and ESR in DPN patients. Therapies for DPN and reducing inflammation should target the weight loss among obese patients.

Keywords: *Body mass index, C-reactive protein, diabetes, erythrocyte sedimentation rate, polyneuropathy*

Introduction

Inflammation is defined as a physiological response to physical, chemical, and biological stimuli.[1] Inflammation is linked to obesity,[2] characterized by increased levels of C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR).[3,4] Obesity is related to different risk factors such as increased consumption of energy and reduced physical exercise.[5,6] The source of inflammation in obesity is known,[2] however, obesity-related inflammation is followed by the immune system activation.[7] Obesity is associated with chronic diseases such as diabetic polyneuropathy (DPN).[8] The pathogenesis of DPN is not completely known. Inflammation, oxidative stress, and mitochondrial dysfunction have been involved in the pathogenesis of DPN.[8] About 50% of diabetic patients are expected to observe symptoms of diabetic neuropathy.[9] Diabetic neuropathy can be attributed to disability related to foot ulceration, amputation, and walking disturbance.[10] The DPN prevalence estimated 53% in Iran.[11] The high concentrations of inflammatory markers among obese patients seem to be effective in the progression of DPN.[8]

Recently, researchers have found an increased interest in the relationship between obesity and inflammation.[12,13] No studies have been conducted to investigate the relationship between body mass index (BMI) and inflammation among DPN patients. The objective of the present article is to investigate association between BMI and inflammation in patients with DPN.

Methods

Study population

The present study was approved by the ethical committee of the Isfahan University of Medical Sciences. Baseline started in 4th March 2017 and ended in 23rd October 2017. A total of 50 patients were excluded due to missing values for BMI (n = 10), CRP (n = 20), ESR (n = 20), and other variables (n = 5). Finally, 200 patients were entered in the final analysis.

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Assessment process and data collection

Participants selected from the Khorshid and Imam Mousa Sadr clinics. Random sampling method was used. Currently smoking and education were reported by self-report. Hypertension was expressed as systolic/diastolic blood pressure ≥140/90 mm Hg or using antihypertensive medication. Diabetes was expressed as fasting blood sugar ≥7.0 mmol/L or using antidiabetic treatment. Height and weight were measured to the nearest 0.1 cm and 0.01 kg using a Seca scale and height gauge, respectively. Patients with no shoes and light clothing.

BMI was defined as body weight in kilograms divided by height squared in meters. Venous blood samples were collected on admission after a 12-h overnight fast and were immediately sent to laboratory for analysis based on the clinical routine. Two hundred patients undergoing electromyography and nerve conduction velocity (EMG–NCV) for diagnosis of DPN were selected in the present study. CRP was measured with the enzyme-linked immunosorbent assay (ELISA) method. ESR was determined using the Westergren method.

Statistical analysis

Statistical analyses were performed using the STATA, version 13 software (StataCorp). *P* values <0.05 were considered significant. Quantitative variables were expressed as mean [standard deviation (SD)] and qualitative variables were expressed as frequency (percentage). Multivariate linear regression analysis was used to evaluate the relationship between BMI and inflammatory markers including ESR and CRP.

Results

A total of 200 patients (101 men) with a mean (SD) of age 58.76 (9.53) years were included in this cross-sectional study. About 9% of the participants reported a history of smoking. The mean years of education for patients were 5.61 years. The prevalence of hypertension, coronary heart disease, hyperlipidemia, and non-proliferative diabetic retinopathy among all diabetic patients were 40%, 31.5%, 75%, and 37%, respectively. The demographic characteristics and clinical examination of the patients are demonstrated in Table 1. Type I and II of diabetes patients with DPN assessment were selected. From these participants, 75 patients with DPN treated with insulin, 85 patients in combinations of insulin and oral antidiabetic drugs, and 40 with oral antidiabetic drugs. CRP and ESR concentration among patients with diabetic neuropathy were 9.81 mg/dl and 49.02 mg/dl, respectively. Patients with higher BMIs had high level of CRP and ESR. This result is obtained from crude model.

The multivariate linear regression model indicated that CRP and ESR were positively related to BMI. After adjusting for age, education, sex, and smoking (Model 1), 1 unit increase in BMI was related to increase of 0.73 unit CRP and 4.99 unit ESR ($P < 0.001$) [Table 2]. The relationship remained significant after adjustment for other variables in Model 2 [Table 2].

Discussion

The present study demonstrates a positive association between BMI and serum levels of CRP and ESR among patients with DPN. Obese patients demonstrated significantly higher inflammation.

Table 1: Demographic and clinical characteristics diabetic polyneuropathy patients

Variables	*n* (%)	Mean (SD*)
Age (year)		58.76 (9.53)
Male	101 (50.5)	
Currently smoking (%)	18 (9)	
Education (years of school)		5.61 (3.60)
Body mass index (kg/m^2)		25.92 (5.31)
Hypertension (%)	80 (40)	
Coronary heart disease (%)	63 (31.5)	
Hyperlipidemia (%)	150 (75)	
Non-proliferative diabetic retinopathy (%)	74 (37)	
C-reactive protein (mg/L)		9.81 (5.73)
Erythrocyte sedimentation rate (mm/h)		49.02 (40.82)
HbA1C (%)		8.11 (1.34)
Fasting blood sugar (mg/dl)		172.89 (54.71)
Blood sugar (2-hpp)** (mg/dl)		259.22 (26.00)
Triglycerides (mg/dl)		148.68 (44.24)
Total cholesterol (mg/dl)		208.33 (39.52)
HDL-cholesterol*** (mg/dl)		45.07 (9.15)
LDL-cholesterol**** (mg/dl)		150.19 (19.88)
Albumin (g/dl)		4.02 (0.42)

*SD=Standard deviation, **2-hpp= 2 h postprandial, ***HDL=High-density lipoprotein, ****LDL=Low-density lipoprotein

Table 2: Relationship between BMI, CRP, and ESR levels

Models	β (SE)†	*P*	95% CI
Crude model			
CRP	0.74 (0.05)	<0.001	0.63-0.85
ESR	5.07 (0.41)	<0.001	4.26-5.87
Model 1*			
CRP	0.73 (0.05)	<0.001	0.62-0.85
ESR	4.99 (0.44)	<0.001	4.11-5.86
Model 2**			
CRP	0.71 (0.06)	<0.001	0.59-0.83
ESR	4.67 (0.52)	<0.001	3.63-5.71

*Model 1: Adjusted for age, education, sex, and smoking,**Model 2: Model 1 + HbA1C, fasting blood sugar, blood sugar (2 h postprandial), triglycerides, high-density lipoprotein-cholesterol, low-density lipoprotein-cholesterol, cholesterol, albumin, and chronic disease such as coronary heart disease, hyperlipidemia, hypertension, and non-proliferative diabetic retinopathy. $^{\dagger\beta}$Coefficient was interpreted as change of CRP and ESR for each kg/m^2 increase in BMI. ***CRP=C-reactive protein, ****ESR=Erythrocyte sedimentation rate, SE=Standard error, CI=Confidence interval

The finding is consistent with findings of other studies.[12,14-16] The relationship might be confounded using covariate variable such as chronic diseases. Therefore chronic diseases such as coronary heart disease, hypertension, hyperlipidemia, non-proliferative diabetic retinopathy, and other related factors were controlled in Model 2. Also, the existence of medical features related to inflammation was excluded.

Increased serum levels of inflammatory markers play an important role among diabetic patients with higher BMI.[17] However, the mechanism of relationship between CRP and blood sugar remains unclear.[17] In fact, adipose tissue as a producer tissue of inflammatory markers indicates the positive association between higher BMI and inflammation.[18] Adipose tissue as inflammatory markers can increase lipogenesis[19,20] and response of the systemic inflammatory phase.[18]

The sources of inflammation activated by hyperglycemia and metabolic disease are immune cells such as increased macrophage, mast cells, and natural killer T cells that contribute for expression of tissue cytokine.[17,21] Obesity increases metabolic stress related to the immune system activation and inflammation,[22] as a risk factor for cardiovascular disease, colon cancer, breast cancer, dementia, and depression.[23] Also, inflammation is related to increased intake of calorie and other nutrients such as intake of high fat and carbohydrate.[24] Increased of proinflammatory macrophages are inversely related to sensitivity insulin.[24]

Studies have demonstrated that weight loss is related to decrease inflammatory markers.[18,25] Also, weight loss among people with gastric bypass indicate decreased levels of inflammatory markers.[2]

These findings about association between BMI and increased CRP and ESR levels highlight susceptible to various outcomes of inflammation such as chronic diseases.[15]

The present study has several strengths. Our study is the first cross-sectional study about the association between BMI and inflammation among DPN patients in Iran, Isfahan. Second, the results of present study have been controlled for covariate variables. Besides, this study has several limitations. First, design of present study is cross-sectional and could not determine causal relationship for these factors. Second, two inflammatory markers were considered in this study for assessment of inflammation.

In conclusion, increased BMI was related to increased levels of CRP and ESR among DPN.

Conclusions

These findings indicate that higher BMI is related to increase inflammatory markers including CRP and ESR in DPN patients. Therapies for DPN and reducing inflammation should target the weight loss among obese patients.

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Conflicts of interest

There are no conflicts of interest.

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