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Uncontrolled Glycemia and High Percentage of Truncal Fat Elevate Levels of CRP and IL-6 Among Patients with Type 2 Diabetes

Hiba Bawadi[1], Rami Katkhouda[2]

[1]Qatar University, Dept of Health Sciences, QA
[2]University of Jordan, JO

Email: hbawadi@qu.edu.qa

Background

Systemic inflammation is the continuous phenomenon of inflammatory response which can promote tissue damage. Systemic inflammation is characterized by circulatory elevation of many inflammatory mediators such as (CRP, IL-6 and TNF-α). This state plays a pivotal role in all stages of type 2 diabetes. Stages include pathogenicity and progression and chronic complication development. This study aimed at investigating the risk of systemic inflammation among type 2 diabetic patients according to glycemic control.

Objectives

This work aimed to investigate the risk of systemic inflammation among type 2 diabetic patients in relation to body fat accumulation and distribution among patients with controlled glycaemia versus poorly controlled patients.

Subjects/Methods

Study protocol and tools were approved by the research ethics committee; Institutional Review Board (IRB) at Jordan University of Science and Technology (JUST). Patients were recruited from out-patient endocrinology unit at King Abdullah University Hospital (KAUH), Jordan University of Science and Technology Health Center and major private endocrinology clinics in North of Jordan. Initial screening included 1500 patients diagnosed with type 2 diabetes. Due to the multiple co-variation nature of the relationship of interest, about 75% of the initially screened patients were excluded from the study. A total of 198 male and female patients diagnosed with type 2 diabetes

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participated in this cross-sectional. Patients' weight, height, waist circumference, total body fat and truncal fat percent were measured. Venous blood specimen were collected and levels of HbA1c, serum hs-CRP, serum IL-6 were determined. A 10-ml sample of venous blood was collected from each patient by a registered nurse. HbA1c blood samples collected in Ethylene-Diamine-Tetra-Acetic acid (EDTA) tubes and measured in whole blood using the Immuno-inhibition test for the quantitative determination of glycosylated hemoglobin (Beckman Coulter AU analyzers). Blood samples of hs-CRP and IL-6 collected in Z-Clot activator tubes. Samples were allowed to clot before centrifugation for 15 minutes at 1000×g. Aliquot of serum stored at ≤ –22°C in a sterile small tubes prior to biochemical assay. Immuno-turbidimetric test was used to determine hs-CRP levels (Beckman Coulter AU analyzers). IL-6 was measured using a human immunoassay kit from R&D SYSTEMS through sandwich-type enzyme-linked immunosorbent assay (ELISA). Absorbance Microplate reader was used to measure the optical density of IL-6 (BioTek ELx800). Anthropometrics (weight, height) were measured following World Health Organization procedures. 18 Body weight was measured with the individuals wearing no shoes and light clothing. Height was measured using measuring rod (Seca, Germany). Body Mass Index (BMI) was calculated using the ratio of weight (kilograms) to the square of height (meters) kg/m^2. Waist circumference (WC) was measured to the nearest centimeter using non-stretchable circumference measuring tape (SECA 203, Germany). The site of tape placing was determined according to World Health Organization (WHO) description of middle way between the iliac crest and lower rib border. The WHO BMI cutoff points were used to classify patients based on their BMI and WC. Patients' total body fat and truncal fat percent were determined using bioelectrical impedence technique (TANITA, BC-418). The Segmental body composition analyzer (TANITA, BC-418) used in this study was previously validated against hydro-densitometry in the assessment of body composition in healthy young adults. Body fat and percentage cut-off points used were gender and age specific based on which patients were classified into healthy, over-fat, and obese. Cut-off points for truncal fat % were gender specific based according to which patients were classified into three levels of truncal fat: low, average, and high. A P-value of < 0.05 was considered the cut-off level for statistical significance. Multivariate analysis of variance (MANOVA) was used to examine the relationship between serum levels of hs-CRP, IL-6 and glycemic control and body fatness, Least Significant Difference (LSD) post-hoc MANOVA was conducted to determine the difference between patients in different categories.

Results

Poorly controlled females had higher levels of hs-CRP as compared to poorly controlled males (P=0.004). However, no differences were noticed in the CRP serum levels in good glycemic control group. At the same time, older patients with poor glycemia had higher serum IL-6 levels as compared to younger patients. In poor glycemic control group and after adjusting for age, gender, lipid lowering drugs and diabetes duration, the (hs-CRP) serum levels of patients with high BMI (obese) was significantly higher than that observed in the normal, and overweight patients (P-value = 0.02). Body fat percentage was significantly associated with hs-CRP serum levels inpoor glycemic control group; patients with healthy body fat percentages had lower hs-CRP (6.30 ± 0.66) compared to patients with obese patients (11.89 ± 1.30). Trunk fat mean seems to be significantly associated with patients' hs-CRP serum levels regardless of the glycemic control groups (P-value= 0.05). Among patients with poor glycemic control, higher levels of serum IL-6 were detected in obese patients (6.10 ± 0.93) compared to those with normal body weight patients (4.06 ± 1.82). Similar trend is found with regard to WC where patients with poor glycemic control continue to have higher levels of IL-6 with higher WC (P= 0.018). Positive relationship was found between IL-6 serum levels and trunk fat percentage among all patients regardless of glycemic control.

Conclusion

Findings of the current study indicate that high subcutaneous intraperitoneal fat induces the risk of systemic inflammation regardless of glycemic control. General obesity is associated with systemic inflammation only among patients with poor glycemic control. This study had several strengths including the tough selection procedure of the participants to rule out any response to acute response to inflammation. Several blood measurements

were performed on the patients including HbA1c, CRP, and IL-6 which add to the validity of our hypothesis testing. Moreover, the study operationalized obesity in different ways BMI, WC, total and truncal fat%. However, findings of this study is limited due to the cross-sectional nature of the study design.