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## Inflammatory markers of cardiovascular risk among diabetic patients with neuropathic foot ulceration

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Foot ulcer increases cardiovascular disease (CVD) among individuals with diabetes that may seem logical for patients with ischemic ulcers. However, increased CVD had also been reported in patients with neuropathic foot ulceration (NFU) without clear explanation. Inflammation is thought to be one of the major processes contributing to atherosclerosis. C-reactive protein (CRP) is the final end product of various converging inflammatory pathways in atherosclerosis and high-sensitivity CRP (hsCRP) had been shown to predict future CVD in a variety of clinical settings regardless of traditional cardiovascular risk factors. The aim of this work was to study serum levels of hsCRP and determine the clinical variables that could be associated with elevated levels in diabetic patients with NFU. The study included three groups of patients: the neuropathic group (forty-one diabetic patients with NFU; 52.1±5.4 yrs; M/F 20/21), the diabetic group (twenty diabetic patients without clinical evidence of peripheral nerve dysfunction; 49±6.6 yrs; M/F 9/11) and the control group (twenty healthy subjects of matched age and sex; 49.6±5.2 yrs; M/F 10/10). Subjects with PAD, smoking, obvious inflammatory or infectious conditions were excluded. Serum hsCRP concentrations were measured using immunoenzymometric assay (Monobind Inc., Lake forest, CA 92630, USA). Subjects with serum CRP levels greater than10 µg/ml were excluded from the analysis in order to exclude possible exogenous acute-phase stimuli. Results: serum hsCRP levels were significantly higher in the neuropathic group (5.1±2.4 µg/ml) in comparison to the diabetic or the control group (3.9±1.6 and 2.4±1.6 µg/ml respectively). hsCRP correlated with known duration of diabetes (r=0.466, P 0.002) and body mass index (r=0.362, P 0.02) but not with age, ulcer size or duration, systolic or diastolic blood pressure. Nearly two-thirds of patients with NFU (65.9%) were considered as high risk for CVD using 3 µg/ml cut-off values of hsCRP. Patients with hsCRP >3 µg/ml were more obese (BMI 39.9±7.5) with female predominance (F/M 18/9) in comparison to the rest of the patients (BMI 33.2±5.4 and F/M 3/11). It is concluded that hsCRP is elevated in diabetic patients with uncomplicated NFU especially in obese women with long duration of diabetes. About two-thirds of diabetic patients with NFU had elevated hsCRP levels to the degree that will categorize them as high risk for CVD. We suggest that identification of nontraditional risk factors for CVD should be an integral part of the multidisciplinary foot care for diabetic patients with NFU in order to save not only limbs but also lives.