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Single nucleotide polymorphisms in cytokine/chemokine genes are associated with severe infection, ulcer grade and amputation in diabetic foot ulcer.

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Compared to other complications the genetics of diabetic foot ulcer is poorly studied.

The Interleukin (IL)-6 (-174G > C/rs1800795), Tumor Necrosis Factor (TNF)- $\alpha$  (-308G > A/rs1800629) and (-238G > A/rs361525) and Stromal cell Derived Factor (SDF)-1 (+801G > A/rs1801157) are well characterized single nucleotide polymorphisms (SNPs) which were previously shown to be associated with Diabetic Foot Ulcer (DFU).

In the present study, we looked at the association of these SNPs

with foot microbial infection, Wagner's ulcer grade and treatment procedure, along with serum levels of these cytokines (intermediate phenotype) and other serum biomarkers

(adiponectin, leptin, CRP and HOMA-IR) in subjects with DFU. Subjects with DFU

(n = 270) were genotyped by PCR-RFLP and the serum levels of IL-6, TNF- $\alpha$  and SDF-1 were determined by ELISA. Microbial infections were determined by standard

microbiological methods. Ulcer grade and treatment procedures were recorded. IL-6 (-

174G > C), TNF- $\alpha$  (-308G > A) and SDF-1 (+801G > A) SNPs were associated with

severe microbial infections. TNF- $\alpha$  (-308G > A) and (-238G > A) SNPs were associated

with severe ulcer grades. SDF-1 (+801G > A) SNP was associated with major

amputation even after adjusting for confounding variables. Identification of these SNPs

in DFU subjects would help in identifying high risk individuals who need better treatment care.