GENETIC INFLAMMATORY RISK: IL-4 VNTR POLYMORPHISM AND SMOKING IN ELDERLY PATIENTS WITH CHRONIC KIDNEY DISEASE

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Abstract

Background: The interaction between smoking and interleukin-4 (IL-4) expression carries important clinical implications, particularly in individuals with chronic inflammatory diseases such as chronic kidney disease (CKD). IL-4 is an anti-inflammatory cytokine involved in regulating the immune response, whose expression can be modulated by genetic polymorphisms, directly influencing the susceptibility to and progression of inflammatory conditions. Smoking, in turn, is associated with increased oxidative stress, endothelial dysfunction, and systemic inflammation, and is recognized as an aggravating factor in patients with CKD. Evidence indicates that smokers with CKD have a significantly higher risk of all-cause mortality and cardiovascular events, especially when combined with factors like proteinuria, diabetes mellitus, and male sex. In a cohort of 1,306 patients with stage III to V kidney disease, active smokers had nearly double the risk of death compared to nonsmokers. Although smoking's isolated impact on renal function progression is not always statistically significant, its role as a risk modulator justifies targeted cessation strategies, especially in patients genetically predisposed to IL-4-associated immunoinflammatory alterations. **Purpose:** This study aimed to investigate the possible association between the IL-4 gene's VNTR intron 3 polymorphism and smoking in older adults diagnosed with CKD. **Methods:** This descriptive study included 51 older adults (mean age 67 ± 10 years), all diagnosed with CKD and receiving care at a private clinic in the Federal District. Venous blood samples were collected for DNA extraction using the PureLink® Genomic DNA Mini Kit (Invitrogen), and concentrations were measured by spectrophotometry (NanoDrop®, Thermo Fisher Scientific Inc.). Genotyping was performed via polymerase chain reaction (PCR) with IL-4 intron 3-specific primers. Amplified products were separated by 3% agarose gel electrophoresis and visualized under UV light (L-PIX Touch). The RP1 allele appeared at 183 bp and the RP2 allele at 253 bp. Genotypic frequencies were determined by direct amplicon counting, and the association between the RP2 allele and smoking was analyzed using Fisher's exact test ($\alpha = 0.05$). **Results:** Among the six participants who reported being smokers, five (83.3%) carried the RP2 allele, and one

(16.7%) did not. Among the 45 nonsmokers, 33 (73.3%) had the RP2 allele and 12 (26.7%) did not. Despite the higher relative frequency of the RP2 allele among smokers, the association was not statistically significant (p = 0.516; two-tailed). **Conclusion:** No statistically significant association was observed between the IL-4 VNTR polymorphism and smoking status in older patients (≥50 years) with CKD. The RP2 allele distribution did not differ meaningfully between smokers and nonsmokers. **Implications:** Although a direct association was not established, the exploration of immunogenetic biomarkers such as the IL-4 gene remains important for advancing the knowledge about the inflammatory mechanisms underlying CKD. Identifying genetic variants linked to modifiable risk behaviors may support more targeted and individualized prevention strategies. Future studies with larger, more diverse population samples and multifactorial approaches are needed to clarify gene–environment interactions in complex chronic conditions like CKD.

Keywords: Polymorphism; Interleukin-4; Chronic Kidney Disease; Smoking.