

Circulating Levels of Tumor Necrosis Factor-Related Apoptosis-Inducing Ligand (TRAIL) and C-Reactive Protein (CRP) in Patients with Chronic Kidney Disease of Uncertain Etiology (CKDu), A Pilot Study

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Background: TRAIL, a leukocyte-derived transmembrane protein, selectively induces apoptosis in transformed cells, including abnormal inflammatory cells and myofibroblasts, while CRP, an acute-phase reactant, increases the systemic proinflammatory response. Thus, both have potential roles in CKDu, a progressive tubulointerstitial disease characterized by cellular apoptosis, inflammation, and fibrosis.

Objective: This study aims to assess the circulating TRAIL and CRP levels in CKDu patients and its relationship with disease severity.

Methods: A cross-sectional study was conducted among 47 diagnosed CKDu patients in different severity stages; 2(n=7,14.8%), 3A(n=10,21.3%), 3B(n=10,21.3%), 4(n=10,21.3%), and 5(10,21.3%) and apparently healthy age and sex matched group (control). Serum creatinine, TRAIL, and CRP were quantified. Comparisons were made with Kruskal-Wallis and Mann-Whitney tests ($p < 0.05$).

Results: The patient group (mean age 55.9 ± 10.55 years; 87.2% males (n=41)) had significantly high median TRAIL (232.3 pg/mL, $p=0.0065$), and CRP (1.3 mg/L, $p=0.0182$) levels than the controls (n=10, 144.9 pg/mL, 0.6 mg/L). Stage 3A patients had the highest median TRAIL concentration (362.3 pg/mL) and were significantly higher than controls ($p=0.0101$). A similar observation was made in CRP levels with a significant peak at 3A (2.85 mg/L, $p=0.0057$). Although not significant, the median TRAIL and CRP levels in all CKDu stages were higher than the controls.

Conclusion: Elevated circulating TRAIL and CRP levels in CKDu, with a significant peak at stage 3A, may reflect a critical window with the most pronounced apoptotic and inflammatory activity. Further studies with large cohorts and in vitro mechanistic studies are recommended to explore their exact role in CKDu pathogenesis.

Keywords: CKDu, CRP, TRAIL