Title: Reduced Serum Soluble L-Selectin Levels but Not PCSK9 May Be Associated With Generalized Anxiety Disorder: A Case-Control Study

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Abastact: **Background:** Generalized anxiety disorder (GAD) is a complex psychiatric disorder characterized by constant, unconstrained worrying. This investigation aimed to explore the potential role of soluble L-selectin (sL-selectin) and proprotein convertase subtilisin/kexin type 9 (PCSK9) in the pathogenesis of GAD.

Methods: The study included 88 patients and 88 healthy controls (HCs) matched with age and sex. A psychiatrist confirmed the GAD diagnosis, assessed symptom severity using the GAD-7 scale, and evaluated controls based on the DSM-5 criteria. Serum levels of sL-selectin and PCSK9 were quantified using commercially available ELISA kits.

Results: Serum sL-selectin concentrations were notably lower in GAD patients than HCs (0.51 ± 0.07 µg/mL vs. 1.52 ± 0.18 µg/mL). Additionally, there was a significant inverse association between sL-selectin levels and GAD-7 scores ($r = -0.359$, $p = 0.001$). This sL-selectin also demonstrated strong predictive ability in the ROC investigation, with an area under the curve (AUC) of 0.718 ($p < 0.001$), indicating 64.3% sensitivity and 76.5% specificity at a threshold of 0.60 µg/mL. In contrast, no notable difference was observed for serum PCSK9 levels between GAD patients and HCs.

Conclusion: This study provides a better understanding of the relationship between inflammatory cytokines and GAD pathogenesis. The results indicate that sL-selectin, rather than PCSK9, may be associated with the pathophysiology of GAD. Still, more advanced investigations with greater sample sizes and extensive studies are essential to verify the probable diagnostic utility of serum sL-selectin levels.

Keywords: cytokines; diagnosis; generalized anxiety disorder; pathophysiology; pcsk9; sl-selectin.

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