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CCN5/WISP2 Serum Levels in Patients with Coronary Artery Disease and Type 2 Diabetes and Its Correlation With Inflammation and Insulin Resistance: A Case-Control Study

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ABSTRACT

Introduction: CCN5/WISP2 is a member of the CCN family, which plays a crucial role in various cellular processes. Studies have shown various effects of CCN5/WISP2 on metabolic pathways, yet no prior Investigation has established a link between its serum levels and coronary artery disease (CAD) and/or Type 2 Diabetes Mellitus (T2DM). Therefore, this study was designed to explore the relationship between CCN5/WISP2 and the susceptibility to CAD and/or T2DM, in comparison to individuals with good health, marking a pioneering endeavor in this field.

Methods and Materials: This study was conducted at Shariati Hospital using a randomized case-control approach to investigate the levels of CCN5/WISP2, TNF-α, IL-6, adiponectin, and fasting insulin in the serum of 160 participants. The participants were divided into four groups: those with type 2 siabetes mellitus (T2DM), those with CAD, those with both CAD and T2DM, and 40 healthy individuals. CAD was diagnosed by a cardiologist based on angiogram results. T2DM was identified according to the American Diabetes Association criteria. The control group consisted of healthy individuals with less than 30% narrowing in all coronary arteries. The study excluded individuals with various health issue. Anthropometric measurements, blood pressure, and various biomarkers were assessed, and serum levels were measured using ELISA. Statistical analysis included the Chi-square test, ANOVA, Spearman correlation, binary logistic regression, and ROC curve analysis.

Results: The age (62.11 ± 8.34 years; $p = 0.151$) and BMI (26.12 ± 8.54; $p = 0.461$) were found to be similar among the four groups, indicating no significant differences. Higher CCN5 concentrations were notably observed in the CAD, T2DM, and CAD-T2DM (336.87 ± 107.36, 367.46 ± 102.15, and 404.68 ± 108.15 ng/mL, respectively) groups when compared to the control Group (205.62 ± 63.34 ng/mL; $p = 0.001$), with no significant gender differences ($p = 0.05$). Serum levels of IL-6 and TNF-α were significantly higher in all three patient groups compared to healthy subjects ($p = 0.001$), while adiponectin levels were notably lower in patients than in control participants ($p = 0.05$). Additionally, a positive and significant correlation was observed between CCN5/WISP2 and cytokines (IL-6 and TNF-α) in all patient groups ($p = 0.05$). The results suggested a significant association between CCN5/WISP2 and T2DM-CAD (OR = 1.030; 95% CI: 1.020 -1.042; $p = 0.001$), T2DM (OR = 1.027; 95% CI: 1.016-1.037; $p = 0.001$), and CAD (OR = 1.024; 95% CI: 1.014-1.034; $p = 0.001$) conditions according to multinomial logistic regression analysis ($p = 0.001$). Furthermore, this relationship remained significant even after adjusting for gender, BMI, and age ($p = 0.001$).

Conclusion and Discussion: Our study has revealed, for the first time, a positive connection between CCN5/WISP2 serum levels and the risk of developing T2DM and CAD. Nonetheless, more research is needed to ascertain whether CCN5/WISP2 can serve as a predictive marker for diagnosing CAD or T2DM.

Keywords: Adipokines, Atherosclerosis, Cytokines, Coronary artery disease, Inflammation

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