



Article

Evaluating Serum RBP4 as an Auxiliary Biomarker for CKDu Diagnosis

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Abstract: Background: A chronic interstitial disease, chronic kidney disease of uncertain etiology (CKDu), has emerged as a notable contributor to the CKD burden in rural Sri Lanka. Most therapeutic and diagnostic approaches to CKD focus on glomerular diseases, and thus are not fully applicable to CKDu. Serum proteins, specifically those with the profile of markers representing different facets of a disease, are beneficial for a comprehensive evaluation of diseases, and hence in CKD. Our aim was to identify the role of serum-retinol-binding protein 4 (RBP4), a marker of the proximal tubule, in the diagnosis of CKDu. Methods: Definite CKDu cases were recruited from the renal clinic in Girandurukotte and Wilgamuwa (endemic regions). Healthy controls were recruited from Mandaramnuwara (nonendemic area). The levels of RBP4 and creatinine in serum were measured. An immunoassay (ELISA) was performed on the serum samples. The stages of CKD/ CKDu were classified according to eGFR. Results: Serum RBP4 was significantly increased in CKDu patients compared to CKD patients and healthy controls. The results show that the ratio of normalized serum RBP4 to serum creatine (S.cr) acts as a better competitive marker for CKDu (AUC 0.762, sensitivity 0.733) than CKD (AUC 0.584, sensitivity 0.733) when compared against healthy controls. Furthermore, the RBP4:S.cr ratio showed higher discriminating power (AUC 0.743) between CKDu and CKD, suggesting that the RBP4: S.cr ratio has potential as a serum marker to differentiate CKDu from CKD. Conclusion: The RBP4: S.cr ratio was identified as a plausible indicator for differentiating CKDu from CKD with >70% sensitivity and specificity. Therefore, it could be used in the evaluation of the tubular interstitial involvement of CKD.

Keywords: chronic kidney disease; chronic kidney disease of uncertain etiology; retinol-binding protein 4; estimated glomerular filtration rate; serum protein; creatinine



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1. Introduction

Chronic kidney disease of uncertain etiology (CKDu) is a term coined to describe endemic chronic kidney disease (CKD) that has not been found or associated with its conventional predominant risk factors such as hypertension and diabetes [1,2]. This novel form of CKD is a major health issue that has gained public attention due to its high mortality [3,4] in several tropical regions, including Sri Lanka, India, Latin America and Egypt [5–8]. As this health condition mainly afflicts young and middle-aged males from low-socioeconomic-status agricultural communities [1,9], hypotheses regarding the etiologies of CKDu have focused on occupational triggers, including environmental toxins that