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The role of clinicopathological factors on the adoption of Lipocalin 2 (*LCN2*) gene as a renal biomarker for chronic kidney disease

S. Saseevan[1,2], W.A.A.G.N. Nishanthi[3], S. Rajapakse[4], D.N. Magana-Arachchi[1*]

[1]*National Institute of Fundamental Studies, Kandy, Sri Lanka*
[2]*Faculty of Allied Health Sciences, University of Jaffna, Sri Lanka*
[3]*District General Hospital, Vavuniya, Sri Lanka*
[4]*Faculty of Science, University of Peradeniya, Peradeniya, Sri Lanka*

[*]*dhammika.ma@nifs.ac.lk*

The Lipocalin 2 (*LCN2)* gene has been identified as a tubular injury-related renal biomarker in chronic kidney disease (CKD). However, the findings remain equivocal as its regulations could be influenced by clinicopathological factors associated with CKD. Therefore, this study aims to elucidate the association of clinicopathological factors on adopting the *LCN2* gene expression as a diagnostic marker for CKD. The study cohort included 115 study participants, including healthy volunteers (HC) (n = 20) and CKD patients (n=95). Total RNA extraction was done from centrifuged urine pellet using the phenol-chloroform RNA extraction method. RNA was reverse transcribed and used for quantitative PCR reactions. The biochemical parameters, including serum creatinine, blood haemoglobin level, and serum potassium, were tested during the clinic visit. Socio-demographic and therapeutic data were obtained. The results showed that 67.4% of CKD patients had *LCN2* gene expression, while the diabetic nephropathy (DN) study group (n = 25) showed a significant upregulation (Log2 fold-change = 3.28 ± 0.58; p = 0.009) compared to other CKD groups. Moreover, gender variation did not influence the *LCN2* gene dysregulation in CKD (p = 0.213) and HC (p = 0.103). The *LCN2* gene expression showed a consistent increase with the duration of CKD within the DN study groups (Log2 fold-change: <1 year = 1.42 ± 1.19; 1-5 years = 2.89 ± 0.91; >5 years = 4.79 ± 1.24). This trend did not reach statistical significance (p = 0.219). The erythropoietic activity was not influenced by *Lcn2* dysregulation in CKD patients of both genders (Male: R^2=0.004, p = 0.742; Female: R^2 = 0.174, p = 0.019). The antidiabetic treatments and erythropoietin administration did not alter the *LCN2* gene regulation in the CKD group compared to CKD patients without receiving the above therapeutic agents (p >0.05). From this study, *LCN2* gene dysregulation is unaffected by gender, duration of CKD, anti-diabetic treatments, and erythropoietin administration. Therefore, *LCN2* mRNA levels could serve as a more effective predictive biomarker for the diagnosis of DN.

Keywords: *Chronic kidney disease, clinicopathological factors, gene expression, urinary lipocalin 2, diabetic nephropathy*