

## Editorial

# Proteinuria as a Marker for Cardiovascular Disease

 Swarnalatha Guditi<sup>1</sup> Karthik Karidindi<sup>1</sup>
<sup>1</sup>Department of Nephrology, Nizam's Institute of Medical Sciences (NIMS), Punjagutta, Hyderabad, Telangana, India

Indian J Cardiovasc Dis Women-WINCARS 2018;3:215–216

Chronic kidney disease (CKD) poses a major noncommunicable health problem in India and worldwide and is associated with significant morbidity and mortality. In CKD patients, premature mortality occurs due to cardiovascular disease (CVD).<sup>1,2</sup> A variety of pathophysiologic mechanisms have been proposed to explain the relationship between renal and cardiovascular disease.<sup>3</sup> Proteinuria is not only a marker of renal injury but is also an independent risk factor for cardiovascular morbidity and mortality. There is substantial evidence that proteinuria can be used as a therapeutic target for cardiovascular risk reduction.

Proteinuria is classified into microalbuminuria, albuminuria, and proteinuria.<sup>4</sup> Dipstick-positive proteinuria and albumin-to-creatinine ratio (ACR) are proven as predictors of CVD.<sup>5,6</sup>

Jee et al demonstrated that fasting sugar along with blood pressure and lipid abnormalities were found to be independent predictors for the development of proteinuria.<sup>7</sup> Farasat et al, in the Baltimore Longitudinal Study of Aging, confirmed the association between albuminuria and blood pressure.<sup>8</sup> Fort et al showed that metabolic syndrome alone had a similar effect on proteinuria.<sup>9</sup> Parving et al demonstrated the association of diabetes and proteinuria in Asian and Hispanic patients.<sup>10</sup>

The Prevention of Renal and Vascular End-stage Disease (PREVEND)<sup>11</sup> and the Heart Outcomes Prevention Evaluation (HOPE) studies<sup>12</sup> showed that cardiovascular adverse events were associated with proteinuria. Hypertensive patients with microalbuminuria had higher chances of developing coronary artery disease (CAD) than hypertensive patients without microalbuminuria.<sup>13</sup>

Accumulating evidence suggests that microalbuminuria is associated with increased mortality in patients with diabetes with or without renal dysfunction.<sup>14,15</sup>

The Strong Heart Study<sup>16</sup> and ALOFT study<sup>17</sup> confirmed an association between albuminuria and abnormal ventricular function and dimension. Association of proteinuria with clinical outcome in patients with heart failure were studied in the Candesartan in Heart Failure–Assessment of Reduction in Mortality and Morbidity (CHARM)<sup>18</sup> and the Prospective

Randomized Enalapril Study Evaluating Regression of Ventricular Enlargement (PRESERVE) study.<sup>19</sup>

Importance is given not only for the detection of proteinuria but also for the treatment with renin-angiotensin-aldosterone system (RAAS) inhibitors<sup>20</sup>. Ramipril in Heart Outcomes Prevention Evaluation (HOPE) and mini HOPE study and losartan in Losartan Intervention For Endpoint reduction in hypertension (LIFE) study resulted in significantly reduced cardiovascular risk in participants with renal impairment.<sup>21–23</sup> In the Ongoing Telmisartan Alone and combination with Ramipril Global Endpoint Trial (ONTARGET) combination of telmisartan and ramipril resulted in greater reduction in proteinuria but significant increase in adverse events.<sup>24</sup>

In this issue, Kodali et al reports that proteinuria is a marker for CVD in patients with stage 5 CKD. The major limitation of this study is that they have taken already known cases of CAD, rather than following these patients for the development of CAD. However, the most important aspect of this study is that the study populations are only females for whom there are limited studies. This study by Kodali et al will add more information to the existing literature.<sup>25</sup>

## Conflict of Interest

None declared.

## References

1. Matsushita K, van der Velde M, Astor BC, et al; Chronic Kidney Disease Prognosis Consortium. Association of estimated glomerular filtration rate and albuminuria with all-cause and cardiovascular mortality in general population cohorts: a collaborative meta-analysis. *Lancet* 2010;375(9731):2073–2081
2. Tonelli M, Wiebe N, Culleton B, et al. Chronic kidney disease and mortality risk: a systematic review. *J Am Soc Nephrol* 2006;17(7):2034–2047
3. Sarnak MJ, Levey AS, Schoolwerth AC, et al; American Heart Association Councils on Kidney in Cardiovascular Disease, High Blood Pressure Research, Clinical Cardiology, and Epidemiology and Prevention. Kidney disease as a risk factor for development of cardiovascular disease: a statement from the American Heart Association Councils on Kidney in

**Address for correspondence**  
Swarnalatha Guditi, MD, DM  
(Nephrology), FISN, Department  
of Nephrology, Nizam's  
Institute of Medical Sciences  
(NIMS), Punjagutta, Hyderabad  
500082, Telangana, India  
(e-mail: swarnamalli@hotmail.com).

**DOI** <https://doi.org/10.1055/s-0039-1683950>

©2018 Women in Cardiology and  
Related Sciences

## License terms



- Cardiovascular Disease, High Blood Pressure Research, Clinical Cardiology, and Epidemiology and Prevention. *Circulation* 2003;108(17):2154–2169
4. K/DOGI clinical practice guidelines on hypertension and hypertensive agents in CKD. Available at: [https://www.kidney.org/professionals/kdoqi/guidelines\\_bp/background.htm](https://www.kidney.org/professionals/kdoqi/guidelines_bp/background.htm). Accessed February 2018
  5. Bello AK, Hemmelgarn B, Lloyd A, et al; Alberta Kidney Disease Network. Associations among estimated glomerular filtration rate, proteinuria, and adverse cardiovascular outcomes. *Clin J Am Soc Nephrol* 2011;6(6):1418–1426
  6. Perkovic V, Verdon C, Ninomiya T, et al. The relationship between proteinuria and coronary risk: a systematic review and meta-analysis. *PLoS Med* 2008;5(10):e207
  7. Jee SH, Boulware LE, Guallar E, Suh I, Appel LJ, Miller ER III. Direct, progressive association of cardiovascular risk factors with incident proteinuria: results from the Korea Medical Insurance Corporation (KMIC) study. *Arch Intern Med* 2005;165(19):2299–2304
  8. Farasat SM, Valdes C, Shetty V, et al. Is longitudinal pulse pressure a better predictor of 24-hour urinary albumin excretion than other indices of blood pressure? *Hypertension* 2010;55(2):415–421
  9. Fort J. Chronic renal failure: a cardiovascular risk factor. *Kidney Int Suppl* 2005 Dec;(99):S25–S29
  10. Parving HH, Lewis JB, Ravid M, Remuzzi G, Hunsicker LG; DEMAND investigators. Prevalence and risk factors for microalbuminuria in a referred cohort of type II diabetic patients: a global perspective. *Kidney Int* 2006;69(11):2057–2063
  11. Hillege HL, Fidler V, Diercks GF, et al; Prevention of Renal and Vascular End Stage Disease (PREVEND) Study Group. Urinary albumin excretion predicts cardiovascular and non-cardiovascular mortality in general population. *Circulation* 2002;106(14):1777–1782
  12. Gerstein HC, Mann JF, Yi Q, et al; HOPE Study Investigators. Albuminuria and risk of cardiovascular events, death, and heart failure in diabetic and nondiabetic individuals. *JAMA* 2001;286(4):421–426
  13. Jensen JS, Feldt-Rasmussen B, Strandgaard S, Schroll M, Borch-Johnsen K. Arterial hypertension, microalbuminuria, and risk of ischemic heart disease. *Hypertension* 2000;35(4):898–903
  14. Stadler M, Auinger M, Anderwald C, et al. Long-term mortality and incidence of renal dialysis and transplantation in type 1 diabetes mellitus. *J Clin Endocrinol Metab* 2006;91(10):3814–3820
  15. de Zeeuw D, Remuzzi G, Parving HH, et al. Albuminuria, a therapeutic target for cardiovascular protection in type 2 diabetic patients with nephropathy. *Circulation* 2004;110(8):921–927
  16. Liu JE, Robbins DC, Palmieri V, et al. Association of albuminuria with systolic and diastolic left ventricular dysfunction in type 2 diabetes: the Strong Heart Study. *J Am Coll Cardiol* 2003;41(11):2022–2028
  17. Jackson CE, MacDonald MR, Petrie MC, et al; ALiskiren Observation of heart Failure Treatment (ALOFT) investigators. Associations of albuminuria in patients with chronic heart failure: findings in the ALiskiren Observation of heart Failure Treatment study. *Eur J Heart Fail* 2011;13(7):746–754
  18. Jackson CE, Solomon SD, Gerstein HC, et al; CHARM Investigators and Committees. Albuminuria in chronic heart failure: prevalence and prognostic importance. *Lancet* 2009;374(9689):543–550
  19. Smith DH, Thorp ML, Gurwitz JH, et al. Chronic kidney disease and outcomes in heart failure with preserved versus reduced ejection fraction: the Cardiovascular Research Network PRESERVE Study. *Circ Cardiovasc Qual Outcomes* 2013;6(3):333–342
  20. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. *Kidney Int Suppl* 2013;3(1):1–150
  21. Mann JF, Gerstein HC, Pogue J, Bosch J, Yusuf S. Renal insufficiency as a predictor of cardiovascular outcomes and the impact of ramipril: the HOPE randomized trial. *Ann Intern Med* 2001;134(8):629–636
  22. Heart Outcomes Prevention Evaluation Study Investigators. Effects of ramipril on cardiovascular and microvascular outcomes in people with diabetes mellitus: results of the HOPE study and MICRO-HOPE substudy. *Lancet* 2000;355(9200):253–259
  23. Lindholm LH, Ibsen H, Dahlöf B, et al; LIFE Study Group. Cardiovascular morbidity and mortality in patients with diabetes in the Losartan Intervention For Endpoint reduction in hypertension study (LIFE): a randomised trial against atenolol. *Lancet* 2002;359(9311):1004–1010
  24. Mann JF, Schmieder RE, McQueen M, et al; ONTARGET investigators. Renal outcomes with telmisartan, ramipril, or both, in people at high vascular risk (the ONTARGET study): a multicentre, randomised, double-blind, controlled trial. *Lancet* 2008;372(9638):547–553
  25. Kodali M, Sarada CV, Bhanuja Rani B, et al. Proteinuria as a marker for cardiovascular disease in renal (chronic kidney disease) patients. *Ind J Car Dis Wom* 2018