Available online at http://www.journalcra.com

International Journal of Current Research
Vol. 7, Issue, 07, pp.18065-18067, July, 2015

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

ISSN: 0975-833X

RESEARCH ARTICLE

AN OVERVIEW AND CYTOLOGICAL APPROACH OF CHRONIC KIDNEY DISEASE

***Pavani, S. and Sudhakar, G.**

Department of Human Genetics, Andhra University, Visakhapatnam, India

ARTICLE INFO

Article History:
Received 23rd April, 2015
Received in revised form
08th May, 2015
Accepted 19th June, 2015
Published online 28th July, 2015

Key words:

Chronic kidney disease(CKD),
Candidate gene markers,
Autoantibodies.

ABSTRACT

The burden of Chronic kidney disease (CKD), in terms of human suffering and economic costs, is unravelling its effect as we move through the early years of the 21st century, making it as a major public health issue. The attention paid globally to CKD is attributable to the following factors: the sudden increase in its prevalence, the enormous cost of treatment, recognition of its major role in increasing the risk of cardiovascular disease, and the discovery of effective measures to prevent its progression. The study of molecular markers identification in CKD is challenging because of high degree of cellular heterogeneity of the kidney and the paucity of human tissue availability for molecular studies. This review summarizes on protein markers discussed in context of CKD, the immunological data related to Th1 and Th17 cells that contribute to kidney injury in renal inflammatory diseases like glomerulonephritis, recent studies of oxidative stress, inflammatory markers that identify disease progression in advance CKD cases and the importance of chemokine receptors CCR and CX3CR1.

***Citation*:** Pavani, S. and Sudhakar, G. 2015. "An overview and cytological approach of chronic kidney disease", *International Journal of Current Research,* 7, (7), 18065-18067.

INTRODUCTION

Chronic kidney disease (CKD) remains a major confront in nephrology for public health care, affecting 14-15% of the adult U.S and more than 10% of the Indian population. Chronic Kidney Disease (CKD) also known as Chronic Renal Disease (CRD), is a progressive loss in renal function for ≥3 months with structural or functional abnormalities of kidney, with or without decreased glomerular filtration rate (GFR) (*National Kidney Foundation*). In principle, severity of CKD is categorised based on GFR into 5 stages and treatment is applied based on the stage of patients (refer Table 1). A number of co morbidities are associated with CKD. The major outcomes, regardless of cause, include progression to kidney failure, complications of decreased kidney function and cardiovascular disease (CVD). In view of poor prognosis, by recognizing the factors associated with CKD progression, it enables high-risk patients to be identified and render more intensive treatment if necessary. Linkage analysis, candidate gene analysis, admixture linkage disequilibrium and genome-wide association studies (GWAS) contribute in the discovery of over 26 candidate loci associated with CKD (O'Seaghdha *et al*., 2011). Indeed, candidate gene association studies and GWAS have generated novel genetic variants in previously unrecognized biological pathways, highlighting disease mechanisms with a potential role in CKD etiology, morbidity and mortality.

Corresponding author: Pavani, S.
Department of Human Genetics, Andhra University, Visakhapatnam, India

Risk factors and markers of CKD

The risk of CKD in adults increases over 65yrs. It is more likely to occur in African-Americans, American Indians, and Asian Americans. Other risk factors for CKD include: smoking, obesity, family history, diabetes both type 1 and 2, autoimmune disease, obstructive kidney disease, atherosclerosis, cirrhosis and liver failure, CVD, urological disorders, primary kidney disease, dyslipidemia, anemia, hypertension, nephrotoxins, high protein intake, kidney stones (National Kidney Foundation) (Taal *et al*., 2006).

Most commonly identified candidate markers associated with chronic kidney disease are as follows: Actin, alpha 2, smooth muscle, aorta (ACTA 2) (Badid *et al*., 2002), Matrix metalloproteinase-2 (MMP2) and Matrix metalloproteinase-9 (MMP9) (Chang *et al*., 2006), Type III collagen (COL3A1) (Souylemezoglu *et al*., 1997), Type IV collagen (COL4A1) and Fibronectin 1 (FN1) (Souylemezoglu *et al*., 1997), Resistin (RETN) (Axelsson *et al*., 2006), C reactive protein (CRP) (Tonelli *et al*., 2005), Transforming growth factor beta-1 (TGFB1) (Szeto *et al*., 2005), Parathyroid hormone (PTH) (Fliser *et al*., 1997; Salusky *et al*., 2004), Fatty acid binding protein 1, liver (FABP1)(Kamijo *et al*., 2005), Prostaglandin D2 synthase 21 kDa (PTGDS) (Hoffmann *et al*., 1997).

Epidemiology of Chronic Kidney Disease (CKD)

10–16% of the universal adult population in Asia, Europe, Australia, and the United States are affected (Perkovic *et al*., 2008; Wen *et al*., 2008; Chadban *et al*., 2003; Hallan *et al*., 2006; Verhave *et al*., 2005; Nitsch *et al*., 2006). As per 2010 Global Burden of Disease study there is a tragic rise in death rates, Of the entire global deaths in 1990, CKD was ranked 27th (based on age-standardised annual death rate of 15.7/100 000), but it rose to 18th in 2010 (based on age-standardised annual death rate 16.3/100 000) (Lozano *et al*., 2010).

act as powerful predictors of mortality. 30 and 50% of prevalent patients who are on haemodialysis (HD) have elevated serum levels of inflammatory markers such as C-reactive protein and IL-6 (Jofr´e *et al*., 2006; Spittle *et al*., 2001). Recent studies showed oxidative stress and its constant inflammation are major mediators of CKD progression and the associated complications. Borkar *et al.* highlighted the importance of the chemokine receptors CCR and CX3CR1 genotyping in relation to progression to end-stage renal disease.

Table 1. Classification of CKD

Stage	Description	GFR mL/min/1.73 m²	Action	Classification by treatment
-	At Increased risk	≥60 (with CKD risk factors)	Screening, CKD risk reduction.	T if kidney transplant recipient
1	Kidney damage with normal or ↑ GFR	≥90	Diagnosis & treatment, Treatment of comorbid conditions, halting progression, risk reduction.	
2	Kidney damage with mild ↓GFR	60-89	Estimating progression	
3	Moderate ↓ GFR	30-59	Evaluating & Treating complication	
4	Severe ↓ GFR	15-29	Preparation for kidney replacement therapy	
5	Kidney failure	<15	Replacement (if uremia present)	D if dialysis (hemodialysis, peritoneal dialysis)

Clusters of cases of chronic kidney disease have been reported in some areas of Sri Lanka and India (Jha *et al*., 2009) The affected individuals are mainly young male farmers. In addition to the well-documented relationships linking poverty with hypertension, diabetes, and cardiovascular disease, low socioeconomic status is also related with CKD. The pervasiveness of CKD increases strikingly with age. From the recent studies it has been shown that CKD is associated with an increased risk for concurrent complications (eg, anemia, acidosis) and adverse outcomes including mortality and CVD among people greater than or equal to 80 years old.

Immunology of CKD

Kidneys are repeatedly targeted by local manifestation of systemic autoimmunity or pathogenic immune responses such as renal autoantigens. Human studies have recently unravelled several underlying mechanisms that might be used to explain the previously enigmatic immunopathology of many renal diseases. These mechanism include a crosstalk between renal dendritic cells and T cells by kidney-specific damage-associated molecular patterns, development of kidney-targeting autoantibodies, sterile inflammation, and molecular mimicry with microbial pathogens. It is estimated that more than 15% of the adult subjects have some degree of CKD, and that dialysis which is applied on about 0.1% of the population consumes about 2% of total health expenditure in most developed countries (De Vechhi *et al*., 1999). T cells act as “helpers” for B cells which produce autoantibodies against kidneys. Incorporation of either ovalbumin-specific Th1 or Th17 polarized cells will induce proliferative glomerulonephritis (Summers *et al*., 2009; Turner *et al*., 2010; Ooi *et al*., 2010).

Anti-GBM glomerulonephritis has been suggested to be Th1 mediated due to the predominance of the Th1-associated IgG antibody subclasses (IgG1 and/or IgG3) and the presence of delayed-type hypersensitivity (DTH) effectors deposited in the kidney (Ooi *et al*., 2010). Besides this, inflammatory markers

They confirmed that early genotyping of CCR5 G59029A and CX3CR1 T280M and V249I polymorphism help to identify the subjects with disease progression in advanced CKD cases among the residents of North Indians (Borkar *et al*., 2011).

DISCUSSION

Chronic kidney disease is a worldwide public health issue with diverse features to be take into account in different parts of the world. The burden of chronic kidney disease is increasing worldwide, attributed to its mortality, incidence and prevalence of end-stage kidney disease. Integration of screening and management strategies for CKD into national programmes for non-communicable diseases can reduce the burden and cost of care of chronic kidney disease. The potential of candidate gene markers not only addresses early stage monitoring of CKD, but may also trigger a deeper understanding of the molecular processes causing the disease and followed by the potentially novel therapy approaches.

REFERENCES

Axelsson, J., Bergsten, A., Qureshi, A.R, Heimburger, O., Barany, P., Lonnqvist, F., *et al.* 2006. Elevated resistin levels in chronic kidney disease are associated with decreased glomerular filtration rate and inflammation, but not with insulin resistance. *Kidney Int*., 69: 596–604.

Badid, C., Desmouliere, A., Babici, D., Hadj-Aissa, A., McGregor, B., Lefrancois, N., *et al.* 2002. Interstitial expression of alpha-SMA: an early marker of chronic renal allograft dysfunction. *Nephrol Dial Transplant*., 17: 1993–8.

Borkar, M., Tripathi, G., Sharma, R. K., Sankhwar, S. N., and Agrawal, S. 2011. “Chemokine (CCR) and fractalkine (CX3CR) receptors and end stage renal disease.” *Inflammation Research*., 60(4): 399–407.

Chadban, S.J., Briganti, E.M., Kerr, P.G., Dunstan, D.W., Welborn, T.A., Zimmet, P.Z., *et al*. 2003. Prevalence of

kidney damage in Australian adults: The AusDiab kidney study. *J Am Soc Nephrol*., 14(7 suppl 2): S131-8.

Chang, H.R., Yang, S.F., Li, M.L., Lin, C.C., Hsieh, Y.S., Lian, J.D. 2006. Relationships between circulating matrix metalloproteinase-2 and -9 and renal function in patients with chronic kidney disease. *Clin Chim Acta*., 366: 243–8.

De Vecchi, A.F., Dratwa, M., Wiedemann, M.E. 1999. Healthcare systems and end-stage renal disease (ESRD) therapies--an international review: costs and reimbursement/funding of ESRD therapies. *Nephrol Dial Transplant*., 14 Suppl 6: 31-41.

Fliser, D., Franek, E., Joest, M., Block, S., Mutschler, E., Ritz, E. 1997. Renal function in the elderly: impact of hypertension and cardiac function. *Kidney Int*., 51: 1196–204.

Hallan, S.I., Dahl, K., Oien, C.M., Grootendorst, D.C., Aasberg, A., Holmen, J., *et al*. 2006. Screening strategies for chronic kidney disease in the general population: follow-up of cross sectional health survey. *BMJ*., 333: 1047.

Hoffmann, A., Nimtz, M., Conradt, H.S. 1997. Molecular characterization of beta-trace protein in human serum and urine: a potential diagnostic marker for renal diseases. Glycobiology., **7**: 499–506.

Jha, V. 2009. Current status of chronic kidney disease care in southeast Asia. Semin Nephrol., 29**:** 487–96.

Jofr´e, R., Rodriguez-Benitez, P., L´opez-G´omez, J. M., and P´erez-Garcia, R. 2006. "Inflammatory syndrome in patients on hemodialysis," *Journal of the American Society of Nephrology.,* 17(3): S274–S280.

Kamijo, A., Sugaya, T., Hikawa, A., Yamanouchi, M., Hirata, Y., Ishimitsu, T., *et al*. 2005. Clinical evaluation of urinary excretion of liver-type fatty acid-binding protein as a marker for the monitoring of chronic kidney disease: a multicenter trial. *J Lab Clin Med*., 145: 125–33.

Lozano, R., Naghavi, M., Foreman, K, *et al*. 2013. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet*., 380**:** 2095–128.

National Kidney Foundation., 2002. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. *Am J Kidney Dis*., 39: S1-266.

Nitsch, D., Felber Dietric, D., Von Eckardstein, A., Gaspoz, J.M., Downs, S.H., Leuenberger, P., *et al*. 2006. Prevalence of renal impairment and its association with cardiovascular risk factors in a general population: results of the Swiss SAPALDIA study. *Nephrol Dial Transplant*., 21: 935-44.

O'Seaghdha, C.M., Parekh, R.S., Hwang, S.J., Li, M., Kottgen, A., Coresh, J., *et al*. 2011 Jun 15. The MYH9/APOL1 region and chronic kidney disease in European-Americans. Hum Mol Genet., 20(12): 2450–6. [PubMed: 21429915].

Ooi, J.D., Kitching, A.R,, Holdsworth, S.R. 2010. Review: T helper 17 cells: their role in glomerulonephritis. Nephrology (Carlton)., 15(5): 513-21.

Perkovic, V., Cass, A, Pate, l A.A., Suriyawongpaisal, P., Barzi, F, Chadban, S., *et al*. 2008. High prevalence of chronic kidney disease in Thailand. Kidney Int.,73: 473-9.

Salusky, I.B., Juppner, H. 2004. New PTH assays and renal osteodystrophy. *Pediatr Nephrol*., 19: 709–13.

Soylemezoglu, O., Wild, G., Dalley, A.J., MacNeil, S., Milford-Ward, A., Brown, C.B., *et al.* 1997. Urinary and serum type III collagen: markers of renal fibrosis. *Nephrol Dial Transplant*., 12: 1883–9.

Spittle, M. A., Hoenich, N. A., Handelman, G. J., Adhikarla, R., Homel, P., Levin, N.W. 2001. "Oxidative stress and inflammation in hemodialysis patients," *American Journal of Kidney Diseases*., 38(6): 1408–1413.

Summers, S.A., Steinmetz, O.M., Li, M., Kausman, J.Y., Semple, T., Edgtton, K.L, *et al.* 2009. Th1 and Th17 cells induce proliferative glomerulonephritis. *J Am Soc Nephrol*., 20(12): 2518-24.

Szeto, C.C., Chan, R.W., Lai, K.B., Szeto, C.Y., Chow, K.M., Li, P.K., *et al.* 2005. Messenger RNA expression of target genes in the urinary sediment of patients with chronic kidney diseases. *Nephrol Dial Transplant*., 20: 105–13.

Taal, M. W. & Brenner, B. M. 2006. Predicting initiation and progression of chronic kidney disease: developing renal risk scores. Kidney Int., 70: 1694–1705.

Tonelli, M., Sacks, F., Pfeffer, M., Jhangri, G.S., Curhan, G. 2005. Biomarkers of inflammation and progression of chronic kidney disease. *Kidney Int*., 68: 237–45.

Turner, J.E., Paust, H.J., Steinmetz, O.M., Panzer, U. 2010. The Th17 immune response in renal inflammation. Kidney Int., 77(12): 1070-5.

Verhave, J.C., Hillege, H.L., Burgerhof, J.G., Gansevoort, R.T., de Zeeuw, D., de Jong, P.E. 2005. The association between atherosclerotic risk factors and renal function in the general population. *Kidney Int*., 67: 1967-73.

Wen, C.P., Cheng, T.Y., Tsai, M.K., Chang, Y.C., Chan, H.T., Tsai, S.P., *et al*. 2008. All-cause mortality attributable to chronic kidney disease: a prospective cohort study based on 462 293 adults in Taiwan. *Lancet*, 371: 2173-82.

****