Evaluation of laboratory measurements for the clinical assessment of chronic kidney disease

Seema Jawalekar*

Seema Jawalekar. Evaluation of laboratory measurements for the clinical assessment of chronic kidney disease. J Kidney Treat Diagn. November-2017;1(1):1-3.

Chronic kidney disease (CKD) earlier used to called as chronic renal failure (CRF). Chronic kidney disease (CKD) is having higher rate of morbidity and mortality. CKD is a globally recognized public health problem.

It involves all degrees of decreased renal function, progressively leads from damaged–at risk through mild, moderate, and ultimately end-stage kidney failure. Most patients are asymptomatic until the disease has significantly progressed, they remain unaware of the condition. Thus, it is essential to have clinical guidelines, aimed at early detection, evaluation, diagnosis, and treatment for slowing down the progression of this condition. CKD is more common in the elderly population. Whereas in younger patients with CKD typically experience progressive loss of renal function, about 30% of patients over the age of 65 years with CKD have stable disease [1].

CKD is recognized for its association with an increased risk of cardiovascular disease and end-stage renal disease (ESRD). Major cause for chronic kidney disease may be by diabetes, high blood pressure and other disorders. Early detection and treatment can often useful to keep chronic kidney disease from getting worse. When kidney disease progresses, it may eventually lead to end-stage renal disease (ESRD), which requires dialysis or a kidney transplant to sustain life.

Chronic kidney disease (CKD) is classified according to the degree of kidney damage – measured by the level of proteinuria – and the decline in glomerular filtration rate. The most severe form is end-stage renal disease. CKD define as either presence of kidney damage or a decreased glomerular filtration rate (GFR) which is less than 60 mL/min/1.73 m^2 for at least 3 months. Whatever the underlying cause, once the loss of nephrons occurs and reduction of functional renal mass reaches to a certain point, the remaining nephrons begin a process of irreversible sclerosis which leads to a progressive decline in the GFR [2].

Based on GFR estimation, the National Kidney Foundation has classified CKD into five stages.

Table 1: Stages of Chronic Kidney Disease.

Stage	eGFR value	Clinical symptoms associated with CKD
Stage 1 – Structural or functional abnormalities of Kidney with normal kidney function	From 90-120	Hypertension, urinary tract infections, abnormal findings in Urine
Stage 2 – Structural or functional abnormalities of Kidney with mild loss of kidney function	From 60–89	Hypertension, urinary tract infections, abnormal findings in Urine
Stage 3a – Mild to moderate loss of kidney function	From 45–59	Hypertension, urinary tract infections, abnormal findings in Urine
Stage 3b – Moderate to severe loss of kidney function	From 30–44	Anemia, malnutrition, bone problems, abnormal nerve sensations, reduced mental functioning
Stage 4 – Severe loss of kidney function	From 15–29	Swelling and puffiness, anemia, decreased appetite and blood and urine abnormalities
Stage 5 – Kidney failure, also known as end stage renal disease (ESRD)	Less than 15	difficulty breathing , decreased appetite, fatigue, mental symptoms and blood and urine abnormalities

Chronic kidney disease (CKD) can be diagnosed with blood and urine tests.

In many cases, it's only picked up because a routine blood or urine test indicates that the kidneys may not be working normally. Decreased kidney function results in buildup of substances such as urea, creatinine, and certain electrolytes in the blood.

Serum Creatinine Estimation of blood creatinine level helps to estimate the glomerular filtration rate (GFR).

GFR: GFR-glomerular filtration rate is the best index to measure the kidney function and also use to determine stage of kidney disease. By using this result, the estimated glomerular filtration rate (eGFR) is calculated. This is used to screen and detect early kidney damage, and help diagnose chronic kidney disease (CKD), and also monitor kidney status [3]. It is a calculated on the results of a blood creatinine test along with other variables such as age, sex, and race, depending on the equation used.

Blood Urea Nitrogen: A blood urea nitrogen (BUN) test measures how much nitrogen from the waste product in the form of urea present in blood. BUN level rises when the kidneys are not working properly to remove urea from the blood.

Urine albumin (microalbumin) and albumin/creatinine ratio (ACR): Used for the screening of chronic conditions, such as diabetes and hypertension, that put person at an increased risk of developing kidney disease; increased excretion of albumin in the urine may indicate kidney damage.

Cystatin C: Cystatin C is an alternative agent for estimation of GFR. It is filtered by the glomeruli and is totally reabsorbed and degraded by tubules,

Department of Biochemistry, Teerthankar Mahaveer Medical college and Research centre, Moradabad, UP, India

**Correspondence: Moradabad, UP, India, E-mail: seems2april@rediffmail.com*

Received: November 08, 2017; Accepted: November 13, 2017; Published: November 18, 2017

so it could be used as a novel agent for GFR estimation [4]. Cystatin C concentration is less dependent upon muscle mass, weight or status disease and it is dependent on kidney function, age, sex, smoking and inflammation.

β-trace protein: BTP or lipocalin prostaglandin D2 synthase is a lipocalin glycoprotein. It is used for the evaluation of kidney function. Increased levels of BPT were positively associated with progression to ESRD, when compared with traditional markers of kidney function such as measured GFR [5]. BTP is not vary by age, sex, and race than creatinine and is also not affected by race than cystatin C. But BTP gives less accurate GFR estimates as compared to CKD-EPI creatinine and cystatin C equations [6].

Neutrophil Gelatinase-associated Lipocalin: NGAL may also be a good biomarker in patients with CKD. Higher urinary and serum NGAL levels are observed in various kidney diseases, which includes including nephropathy of IgA, autosomal polycystic kidney disease, and diabetic nephropathy [7]. NGAL was found to be a diagnostic biomarker for identifying CKD because of uncertain causes.

Kidney Injury Molecule-1: KIM-1 expression is recognized to promote kidney fibrosis and also provide a mechanically determined link between acute and recurrent injury with progressive CKD. A study by Sabbisetti et.al studied patients with type 1 diabetes and proteinuria, serum KIM-1 level at its minimal strongly predicted theloss of rate of estimated GFR and increasing risk of ESRD during 5-15 years of follow-up of patients, recognized KIM-1 as a marker for CKD and also predictor of CKD progression [8]. Like urinary NGAL, KIM-1 can also be used as a probable biomarker in diagnosis of CKD because of uncertain causes.

Asymmetric Dimethylarginine (ADMA): ADMA is synthesized endogenously as a methylated arginine whose action is to reversibly inhibits the enzyme nitric oxide synthase. ADMA is consistently investigated as a biomarker in CKD and its progression. In a study of early stage of CKD in type 2 diabetics, Hanai et al. found that higher plasma concentration of ADMA were found to be predictive of the development and progression of nephropathy [9]. Ravani et al. found in his prospective study in patients with CKD that plasma ADMA levels were inversely proportional with GFR and predictor of progression to ESRD [10]. ADMA therefore considered being relevant biomarker for CKD [11].

Uromodulin: Uromodulin or Tamm–Horsfall protein is a glycoprotein. It synthezised in the tubular cells of the thick ascending limb and the early distal tubule and released into the tubular lumen. Patients with CKD are distinguished by interstitial fibrosis and tubular atrophy.These patients have lower levels of uromodulin.Thus,uromodulin may be represented by intact renal mass rather than kidney function. Steubl et al. in his study found that plasma concentration of uromodulin was a robust marker for intact renal mass and it allowes for identification of early stages of CKD [12].

microRNA: There is a novel role of microRNA in the pathogenesis and progression of CKD. MicroRNA may be considered as a diagnostic marker of impaired filtration (because microRNAs are cleared renally) and also indicator of tubular function (levels change with when tubular function impaired).

Khurana et al. studied several different noncoding RNA classes, such as transfer RNAs (tRNAs), tRNA fragments (tRFs), mitochondrial tRNAs, or long intergenic noncoding RNAs (lincRNAs), and he identified nearly 30 differentially expressed noncoding RNAs in CKD patients which can be used as suitable biomarkers for early diagnosis. Among all of these, miRNA-181a found to be the most novel biomarker for CKD [13].

Sometimes other tests are also used to assess the level of damage of kidneys. These may include:

1. An ultrasound scan, magnetic resonance imaging (MRI) scan or computerised tomography (CT) scan to see what the kidneys look like and check whether there are any blockages.

2. A kidney biopsy–a small kidney tissue sample is removed using a needle so the cells can be examined under a microscope for signs of damage.

3. A kidney biopsy may use to find out the cause of chronic kidney disease. After a kidney transplant, this test is use to find out in suspicion of if the organ is being rejected by the body.

4. An ultrasound of the kidney (renal ultrasound) use to estimate length of duration one may have had chronic kidney disease. It also checks flow of urine from the kidneys is blocked. It also may help to find out causes of kidney disease, such as obstruction or polycystic kidney disease.

5. A duplex Doppler study or angiogram of the kidney advised to check for complications caused by restricted blood flow (renal artery stenosis).

References

1. O'Hare AM, Choi AI, Bertenthal D, et.al. Age affects outcomes in chronic Kidney disease. J Am Soc Nephrol. 2007;18(10):2758-65.
2. Schnaper HW. Remnant Nephron physiology and the progression of chronic kidney disease. Pediatr Nephrol. 2014;29(2):193-202.
3. National Kidney Foundation. K/DOQI Clinical practice guidelines for chronic kidney disease: Evaluation, classification, and stratification. Am J Kidney Dis. 2002;39:S1-S266.
4. Chew JS, Saleem M, Florkowski CM, et al. Cystatin C-a paradigm of evidence based laboratory medicine. Clin Biochem Rev. 2008;29:47–62.
5. Bhavsar NA, Appel LJ, Kusek JW, et.al. Comparison of measured GFR, Serum creatinine, Cystatin C and beta trace protein to predict ESRD in African Americans with hypertensive CKD. Am J Kidney Dis. 2011;58(6): 886-93.
6. Inker LA, Tighiouart H, Coresh J, et.al. GFR estimation using β-Trace Protein and β2-Microglobulin in CKD. Am J Kidney Dis. 2016;67(1):40–8.
7. Bolignano D, Coppolino G, Campo S, et.al. Neutrophil gelatinase associated lipocalin in patients with autosomal dominant polycystic kidney disease. Am J Nephrol. 2007;27(4):373-8.
8. Sabbisetti VS, Waikar SS, Antoine DJ, et.al. Blood kidney injury molecule-1 is a biomarker of acute and chronic kidney injury and predicts progression to ESRD in type I diabetes. J Am Soc Nephrol. 2014;25(10): 2177-86.
9. Hanai K , Babazono T, Nyumura I, et.al. Asymmetric dimethylarginine is closely associated with the development and progression of nephropathy in patients with type 2 diabetes. Nephrol Dial Transplant. 2009;24(6):1884-8.
10. Ravani P, Tripepi G, Malberti F, et al. Asymmetrical dimethylarginine predicts progression to dialysis and death in patients with chronic kidney disease: a competing risks modeling approach. J Am Soc Nephrol. 2005;16(8):2449-55.
11. Wasung ME, Chawla LS, Madero M. Biomarkers of renal function, which and when? Clin Chim Acta. 2015;438:350-7.
12. Steubl D, Block M, Herbst V, et al.Plasma Uromodulin Correlates With Kidney Function and Identifies Early Stages in Chronic Kidney Disease Patients. Medicine (Baltimore). 2016;95(10):e3011.
13. Khurana R, Ranches G, Schafferer S, et.al. Identification of urinary exosomal noncoding RNAs as novel biomarkers in chronic kidney disease. RNA. 2017;23(2):142-52.