

## Review Article

**Limitations of serum creatinine as a marker of renal function**Dixon Thomas<sup>1</sup>, Seeba Zachariah<sup>1</sup>, Abdelgadir Elamin Eltom Elamin<sup>2</sup>, Ahmed Luay Osman Hashim<sup>2</sup><sup>1</sup>College of Pharmacy, Gulf Medical University, Ajman, UAE.<sup>2</sup>College of Allied Health Sciences, Gulf Medical University, Ajman, UAE.**\*Corresponding author**

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**Abstract:** Serum creatinine is widely used in the assessment of renal function to detect and prognosis of conditions with impaired renal function. Serum creatinine is a convenient test, but it has several limitations to interpret renal function. Glomerular filtration rate (GFR) estimation uses serum creatinine levels along with other variables, but still it can be erroneous due to many confounding variables. Extensive efforts by scientific community improved specificity of the creatinine assays and standardized it across different laboratories. Sensitivity of serum creatinine in severe renal impairment is better in relation to poor sensitivity in detection of early damage. Diseases of the kidney will increase tubular secretion and extra-renal elimination of creatinine. Several drugs block, tubular secretion of creatinine. Changes in muscle mass and protein metabolism significantly affect serum creatinine levels. A combination of serum creatinine and serum cystatin C was found to be less erroneous as the confounding factors for both shall not be the same. Limitations of serum creatinine levels should be considered while making relevant clinical decisions in a patient with renal impairment.

**Keywords:** Creatinine, Renal function, Glomerular filtration rate, Muscle mass.

**INTRODUCTION**

Serum creatinine is used in the detection and assessment of acute kidney injury and chronic kidney disease [1]. Limitations of serum creatinine as a marker of kidney function should be considered. Estimated glomerular filtration rate (eGFR) is a better marker of kidney function than Serum creatinine alone. Serum creatinine is used as one of the variable of GFR along with age, body weight, gender, ethnicity, etc. In the presence of other variables like comorbidities; even the GFR calculated using serum creatinine is significantly erroneous. Measured GFR (mGFR) using the timed urine collection is claimed to be not affected by the changes in muscle mass as it is not based on serum creatinine [2]. Urine collection in e.g. 24 hours by the patient is inconvenient and will be erroneous [3]. None of the formulas available currently is considered to be universal due to variations in confounding factors in different patients. It is not advisable to make important drug dose changes, initiation of dialysis or dose changes of dialysis based on a single GFR measured. Serum creatinine or estimated GFR shall be inaccurate in the case of rapidly changing kidney function [4]. It is important to consider the limitations of serum creatinine as a marker of kidney function.

**Serum creatinine measurement**

Creatinine is mostly formed from creatine and phosphocreatine in skeletal muscle. Creatinine is freely excreted through kidneys makes it useful to interpret kidney function. Most common methods of measuring serum creatinine are based on Jaffé reaction. Creatinine reacts with picrate in alkaline medium and the resulting orange-red complex is measured spectrophotometrically. Some factors are found to interfere with creatinine assays; protein in serum, glucose and ketoacids in high levels (diabetic ketoacidosis). Lack of specificity is a major issue with this method that was reduced by use of kinetic assays. Automated analyzers measure the color generation typically between 20 – 80 seconds. Enzymatic methods are thought to have more specificity, but bilirubin and monoclonal IgG are found to interfere with the result. Calibration of methods is practiced to standardize and decrease variations in the creatinine measurements among laboratories. After the standardization of creatinine assays in 2010 serum creatinine levels measured by most of the laboratories reduced 0.1-0.3 mg/dL. The Modification of Diet in Renal Disease (MDRD) formula was revised for the standardized serum creatinine. Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula was made to use only with standardized serum creatinine.

The Cockcroft-Gault equation was not revised and will result in greater error if used with standardized serum creatinine [5, 6].

#### Potential limitations of serum creatinine levels

- Serum creatinine can increase with ingestion of large amounts of meat [7].
- Patient with fluid overload has a lower serum creatinine due to dilution of blood. Malnutrition and inactivity decreases muscle mass, thus decrease serum creatinine [2].
- A small fraction of serum creatinine is actively secreted thorough proximal tubule. The active secretion can increase in renal disease, giving overestimate of creatinine clearance than inulin clearance even up to 2.5 times [8].
- Being an adult, male sex and African race shall have increased production of creatinine because of increased muscle mass. Around 2% of the creatine in the body is converted to creatinine every day. Pathological conditions with increased muscle breakdown (rhabdomyolysis) could increase serum creatinine even up to 5 mg/day [9].
- Extra-renal elimination (mainly intestinal) of creatinine happens, especially in advance renal disease [10].
- Drugs such as; cimetidine, trimethoprim, corticosteroids, pyrimethamine, phenacemide, salicylates and active vitamin D metabolites can block active tubular secretion of serum creatinine and increase serum creatinine [11].
- Diseases interfere with GFR; high blood pressure, diabetes mellitus, congestive heart failure, diseases of the transplant kidney, etc. [12].
- Serum creatinine shall not increase in tubulointerstitial or vascular damage happening in the kidneys. Serum creatinine increases only when there is a significant decline in glomerular filtration. Sensitivity of serum creatinine in mild to moderate renal impairment is poor. Thus serum creatinine is an incomplete marker of kidney damage. [12].

Serum cystatin C is found to be a better marker than serum creatinine especially in the elderly. It has been a common practice now to include both serum creatinine and serum cystatin C in the formulas for GFR calculation as confounding factors for these markers shall not be the same [6].

#### CONCLUSION

The value of serum creatinine in detection of levels of kidney function is limited, especially in the earlier impairment and in patients with comorbidities. Many patient specific factors related to muscle mass

and protein metabolism alter serum creatinine levels. Estimated or measured GFRs are better measures than serum creatinine alone. The limitations should be considered while interpreting serum creatinine levels.

#### Authors' contribution

DT, SZ, AEEE and ALO discussed to conceptualize the paper. DT and AEEE conducted the literature search. DT, SZ, AEEE and ALO contributed to the organization of content. DT, AEEE, and SZ wrote and DT, SZ, AEEE and ALO reviewed the content.

#### Conflicts of interest

None to declare. The authors of this manuscript declare that they all have followed the ethical requirements for this communication.

#### Funding information

No funds received.

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