

Reference range:

0.5 – 1.0 mg/L

Methodology:

Nephelometry

Specimen required:

Serum

Background

The prevalence of chronic kidney disease and end-stage renal disease is increasing worldwide with the aging of the world population and a global epidemic of type 2 diabetes. The National Kidney Foundation estimates that over 26 million individuals have chronic kidney disease (CKD). High risk groups include those with diabetes, hypertension and family history of kidney failure. Elevated Cystatin C correlates with impaired glomerular filtration and CKD.

Cystatin C Defined

Cystatin C, a serum protein associated with vascular damage, is produced by all nucleated cells at a constant rate and is freely filtered out of the blood by the kidneys; therefore serves as a measure of kidney function. Cystatin C is produced by all nucleated cells at a reasonably constant rate. Production is minimally affected by diet, inflammatory states, lean body mass or circadian rhythm. Like creatinine, Cystatin C is freely filtered by the glomeruli. It is reabsorbed and metabolized by renal tubular cells and does not appear in the urine. Tan et al ⁽¹⁾ showed serum Cystatin C has good correlation with creatinine clearance ($R=0.74$), is superior to serum creatinine in estimating GFR, and is a leading bio-marker of renal dysfunction in diabetic patients. Because creatinine production is relatively variable, Cystatin C has been proposed as a better marker of glomerular filtration.

Correlation and Study Results

Cystatin C has been shown to be a better measure of kidney function in diabetic patients ^(1, 2). The Kidney Disease: Improving Global

Outcomes (KDIGO) committee's 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease (CKD) recommends that CKD be classified based on cause, GFR category and albuminuria. They highly recommend that Cystatin C be utilized instead of creatinine in order to calculate a more accurate eGFR.

Cystatin C has emerged as a more accurate estimator of glomerular filtrate rate than creatinine and demonstrates a linear association with cardiovascular disease. Cystatin C has proven to be not just a marker of kidney disease, but also an independent marker of cardiovascular and all-cause mortality ^(3, 4).

Recommended Testing Guidelines

Leading nephrology guidelines like KDIGO and the National Kidney Foundation have recommended the use of Cystatin C because of its increased accuracy in both patients with diabetes and kidney disease. Cystatin C is also recommended in the elderly because it is not sensitive to decreased muscle mass like creatinine; which can underestimate the reduction in kidney function in the eGFR equation.

References

- (1) Tan et al; Clinical Usefulness of Cystatin C for the Estimation of GFR in Type 1 Diabetes. *Diabetes Care*; 2002; 25: 2004—2009.
- (2) Laura Pucci, et al; Cystatin C and Estimates of Renal Function: Searching for a Better Measure of Kidney Function in Diabetic Patients. *Clinical Chemistry* 53:3: 2007
- (3) Shlipak, M et al; Cystatin C and the Risk of Death and Cardiovascular Events among Elderly Persons; *N Engl J Med* 2005; 352: 2049–60
- (4) Zethelius et al; Use of Multiple Biomarkers to Improve the Prediction of Death from Cardiovascular Causes; *N Engl J Med* 2008; 358: 2107—2116