

## Evaluation of Serum Cystatin C in Iraqi Cardiovascular Patients

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### Abstract

**Background:** Cystatin C has been reported to be a potent predictor of increased cardiovascular disease mortality. Serum Cystatin C may have a stronger association with mortality and cardiovascular disease than serum Creatinine in patients with normal or mildly reduced kidney function.

**Objectives:** The aim of this study to

- 1- Determine the prognostic value of cystatin C in patients with cardiovascular disease (CVD) and compare the observed value with that obtained for healthy controls.
- 2- Study the correlation between serum cystatin C and creatinine in cardiovascular disease patients.

**Patients and Methods:** The prospective study included thirty (30) patients admitted to hospital with cardiovascular disease (CVD) selected from Baghdad teaching hospital and twenty-one (21) healthy individuals were included in this study. Fasting serum cystatin C and creatinine were measured in all patients and controls.

**Results and Discussion:** A significant increase in the level of serum cystatin C concentration was observed in patients with (CVD) as compared with the control group.

**Conclusion:** Cystatin C is a prognostic biomarker of CVD. A graded association exists between higher serum Cystatin C and increased CVD prevalence in patients without chronic kidney disease (CKD).

**Key word:** Cystatin C, Cardiovascular disease, creatinine.

### الخلاصة

**الخلفية:** أشير إلى أن السستاتين (C) أصبح متنبئ فعال لزيادة معدل الوفيات بأمراض القلب الوعائية. يمكن ان يمتلك مستوى السستاتين (C) في مصل الدم علاقة قوية مع معدل الوفيات وأمراض القلب الوعائية أكثر من مستوى الكرياتينين للمرضى الذين تكون وظائف الكلية لديهم طبيعية أو بها اختزال خفيف.

**الأهداف:** الهدف من هذه الدراسة هو

- 1- تقدير القيمة التكهنية للسستاتين (C) لدى المرضى المصابين بأمراض القلب الوعائية ومقارنة القيم الملاحظة مع التي تم الحصول عليها من الأشخاص الأصحاء.

2- دراسة العلاقة بين مستوى السستاتين (C) والكرياتينين لدى المرضى المصابين بأمراض القلب الوعائية.

**المرضى وطرق العمل:** الدراسة الحالية تتضمن (30) مريض أدخل المستشفى لإصابتهم بأمراض القلب الوعائية تم اختيارهم من مستشفى بغداد التعليمي و (21) فرد من الأصحاء تضمنوا في هذه الدراسة.

تم قياس مستوى السستاتين (C) ومستوى الكرياتينين في مصل المرضى والأشخاص الأصحاء في حالة الصيام.

**النتائج:** وجد ارتفاع معنوي في مستوى السستاتين (C) للمرضى المصابين بأمراض القلب الوعائية مقارنة مع المجموعة الضابطة.

**الاستنتاج:** السستاتين (C) هو واسمة تكهنية لأمراض القلب الوعائية. وهناك ارتباط مدرج بين ارتفاع مستوى السستاتين (C) وزيادة انتشار أمراض القلب الوعائية لدى المرضى الغير مصابين بأمراض الكلية المزمنة.

## Introduction

CVD is the class of disease that involve the heart or blood vessels (arteries and veins) <sup>(1)</sup>. Most countries face high and increasing rates of cardiovascular disease. Each year, CVD kills more Americans than cancer. In recent years, cardiovascular risk in women has been increasing and has killed more women than breast cancer <sup>(2)</sup>. Cystatin C is a protein inhibitor of cysteine protease that is synthesized at a stable rate by all nucleated cells <sup>(3)</sup>. It is mainly used as a biomarker of kidney function. Recently, it has been studied for its role in predicting new-onset or deteriorating CVD <sup>(4, 5)</sup>. Cystatin C appears to be a marker of cardiovascular risk, and high concentrations of circulating cystatin C have been shown to be consistently and strongly associated with CVD <sup>(6)</sup>.

## Patients and Methods

Fifty-one subjects were involved in this study: thirty (30) patients with an age range between (38-56) and mean  $\pm$  SD ( $47 \pm 5.5$ ) were diagnosed as cardiovascular disease. The remaining 21 subjects were normal healthy persons with an age range (33-55) and mean ( $45 \pm 6.2$ ).

**Table 1: Basal characteristics of control and patient CVD patients.**

Parameters	Control	CVD
Cystatin C (mg/l)	0.366 $\pm$ 0.06	1.182 $\pm$ 0.624*
Creatinine (mg/dl)	0.786 $\pm$ 0.106	1.093 $\pm$ 0.246*

Values are expressed as a mean  $\pm$ SD, \*P<0.01.

This table show a significant increase of serum Cystatin C level in CVD patients when compared with controls (P<0.01).

Five millilitres of venous blood from fasting subjects were withdrawn by utilizing disposable plastic syringes and transferred into a sterile test tube. The blood was allowed to clot and centrifuged at 3000 rpm for 10 minutes. Sera were then separated and stored at 20C until analysis. Enzyme linked immune sorbant assay (ELISA) was used for the measurement of serum cystatin C level <sup>(7)</sup>. Colorimetric method was used in the determination of serum creatinine level. Data was expressed as mean  $\pm$  SD results. Statistical comparison among patients and controls. Statistical significance was defined as P<0.01.

## Results

The characteristics of control and patients with CVD are shown in table 1. This table show a significant increase of serum Cystatin C level in CVD patients when compared with controls (P<0.01).

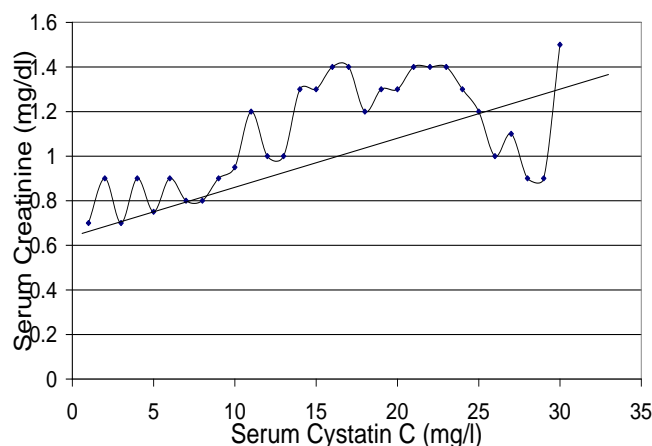
The level of serum creatinine was significantly higher among CVD patients in comparison to the controls (P<0.01).

By simple linear regression analysis it was found that the level of serum Cystatin C to be positively associated with serum creatinine (Fig 1).

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**Fig 1: Correlation between serum Cystatin C level and serum Creatinine level in CVD patients with  $r=0.714$ ,  $*P<0.01$ .**

**Table 2: Cut-off values of Cystatin C in controls and CVD patients.**

Cut-off values (mean $\pm$ SD) mg/dl	controls	CVD patients
		0.486

## Discussion

The results of the present study indicate that elevated cystatin C values predict the development of cardiovascular disease.

Several studies have found that increased levels of cystatin C are associated with the risk of death, cardiovascular disease and healthy aging<sup>(8, 9)</sup>. Cystatin c has a low molecular weight (approximately 13.3 kilo Daltons) and high isoelectric point; it can be eliminated almost exclusively from blood stream by glomerular filtration in the kidney<sup>(3)</sup>.

If kidney function and glomerular filtration rate decline, the blood levels of cystatin C rise<sup>(10)</sup>. Kidney dysfunction increases the risk of cardiovascular disease and death. Serum levels of cystatin C are more precise test of kidney function and cardiovascular risk than serum creatinine levels<sup>(11, 12)</sup>. Cystatin C

concentrations are not influenced by age, sex, muscle mass, physical activity, diet and medication as creatinine<sup>(13)</sup>. Decreased kidney function is associated with adverse cardiovascular outcomes<sup>(14)</sup>. The positive relationship between serum cystatin C and serum creatinine concentration values that was observed in the present study is in agreement with that shown by Tomas et al<sup>(15)</sup> who found a positive correlation between serum cystatin C and serum creatinine in patient with CVD. Despite the increased cardiovascular risk association with cystatin C elevation but the mechanism is unknown

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