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# Glomerular Filtration Rate by CKD-EPI Creatinine Cystatin C Equation for Diagnosis of Chronic Kidney Disease in Adults Compared with 99Tc-DTPA Scan

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## ARTICLE INFO

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## ABSTRACT

**Introduction:** Kidney disease patients can have varying degrees of clinical presentation. Not all patients with kidney diseases show traditional symptoms, thus it is necessary to test renal functions to assess how well the kidneys are working. The utilization of CKD-EPI equations provides an easy and reproducible method to determine eGFR. According to the literature, CKD-EPI Cr-Cys C equations seem to be superior to all other equations, hence we evaluated the diagnostic accuracy of the aforementioned equation, and compared it with measured GFR by 99Tc-DTPA scan. **Material and method:** A cross-sectional study was conducted at two centers. The samples were collected at Atomic Energy Medical Center, Jinnah Postgraduate Medical Centre, Karachi, and then analyzed at the department of chemical pathology, PNS SHIFA Hospital Karachi. 122 patients were enrolled during a period of 9 months. The eGFR was calculated using the 2012 CKD-EPI Cr-Cys C equation. Serum Creatinine was measured by kinetic colorimetric assay whereas Serum Cystatin C was measured by Particle enhanced immunoturbidimetric assay (PENIA) method. GFR was measured by the Gates method using the 99Tc-DTPA renal scan method. **Result:** The CKD EPI Cr-CysC equation was found to have a sensitivity of 80%, specificity of 93.5%, a positive predictive value of 92%, a negative predictive value of 83%, and diagnostic accuracy of 87%. Effect modifiers like age, gender, and duration of disease were stratified. **Conclusion:** The diagnostic accuracy of the CKD EPI Cr-Cys C equation showed high comparability with measured GFR in the general population for the diagnosis of CKD. Thus, The CKD EPI Cr-Cys C equation is a good alternative marker to mGFR in patients being screened for CKD.

## INTRODUCTION

Chronic kidney disease (CKD) is a condition characterized by the gradual loss of kidney function over a period. The diagnoses and management of CKD have a significant burden on the healthcare system; therefore, investigation procedures that are less cumbersome to both patients and laboratories are coveted. [1] CKD remains asymptomatic for a long period thus early diagnosis or prevention is difficult, and patients usually have progressed to a much later stage. [2,3] In modern diagnostics, markers of kidney function such as serum or plasma Cystatin C are sought to diagnose kidney functions. [1,4] The measured or estimated glomerular filtration rate (GFR) has been the most reliable method for the diagnosis of chronic kidney disease. [5] For measured GFR, 24 hours urine creatinine clearance is still commonly used in Pakistan but it has its short comings. One of the biggest difficulty is the requirement of 24-hour collection, which is not just time-consuming but troublesome to patients. Also, the method is liable to daily variations, is affected by changes in diet, and requires stable kidney functions. Its use is also limited to pregnant women, malnourished, and amputees. In all these situations, the estimation of GFR by Cystatin C has a significant edge. [6, 7] Moreover, the CKD EPI Cr-CysC equation has been evaluated for its accuracy in the prediction of different stages of CKD by the corresponding BMI intervals. It was found that for the BMI75 interval, excellent accuracy was shown by the eGFREPI_Cr_-CysC_2012 equation. It was also consistent to identify various CKD stage, and had the strongest ability for the prediction of renal insufficiency. In the BMI75 interval, eGFRFAS_Cr_CysC and eGFREPI_Cr_- CysC_2012 both had

similar accuracy and ability to predict renal insufficiency. However, it was found that eGFR FAS_Cr_CysC did not perform as well as the GFREPI_Cr_CysC_2012 equation in identifying CKD stages. It was found that SCr-CysC-based eGFR equations were superior in performance to SCr-based formulas in overweight or obese people in evaluating eGFR. [8] The rationale of our study is to find out the benefits of estimated Glomerular Filtration Rate (eGFR) by Chronic Kidney Disease Epidemiology creatinine cystatin C (CKD-EPI Cr-Cys C) equation over measured Glomerular Filtration Rate (mGFR) by 99TC – diethylene triamine penta acetic acid scan (99Tc-DTPA scan) to find a more easily performed test which is also more beneficial for the patient, reproducible and less hazardous than a test that involves a radioactive substance. If the diagnostic accuracy of eGFR CKD-EPI 2012 creatinine cystatin c is satisfactory to substitute other methods, its use of it can be proposed in their place.

## MATERIALS AND METHODS

**Setting and Duration of Study:** The study was conducted at 2 centers, with the samples being collected at Atomic Energy Medical Centre, Jinnah Postgraduate Medical Centre, Karachi, and analyzed at the Department of Chemical Pathology, PNS Shifa hospital, Karachi. The duration of study was of 9 months, from May 2018 to January 2019.

**Sample Size and Technique:** The sample size is calculated by an online sample size calculator with a sensitivity of 88.7%, specificity of 87.2%, prevalence of 19%, and confidence interval of 95%. The minimum sample size was 122 participants. Samples were collected by the Non-Probability Consecutive sampling technique.

**Sample selection:** The inclusion criterion was based upon (a) Adult male and female patients of the age group 18-70 years and (b). Suspected cases of chronic kidney disease. Whereas the following patients were excluded 1. Pregnant women, 2. Patients with acute renal failure, 3. Extremes in muscle mass and age and 4. Amputees, paraplegics, Malnutrition.

**Study design:** Cross-sectional study

**Data collection procedure:** The study was conducted after approval by the ethical committee of the institute. All patients fulfilling the inclusion criteria were thoroughly elaborated about the study to obtain their informed consent, and a total of 122 vitally stable patients were selected. Relevant demographics, identification number, age, and gender were entered in a specific pro forma.

**Data analysis plan:**

1. All data were entered and analyzed using SPSS version 22.
2. Quantitative variables like age, Creatinine, and Cystatin C were measured as mean & ± SD.
3. Frequency in % was calculated for gender, CKD, and 99Tc DTPA scan. A 2x2 table was used to calculate sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy.

## RESULT

The result of our study can be presented as follows. Out of 122 subjects, 57(57.38%) were female and 43 (42.62%) were male. According to the ages, the sample majorly consisted of patients aged 18-50 as shown in Table no. 1,

**Table 1**

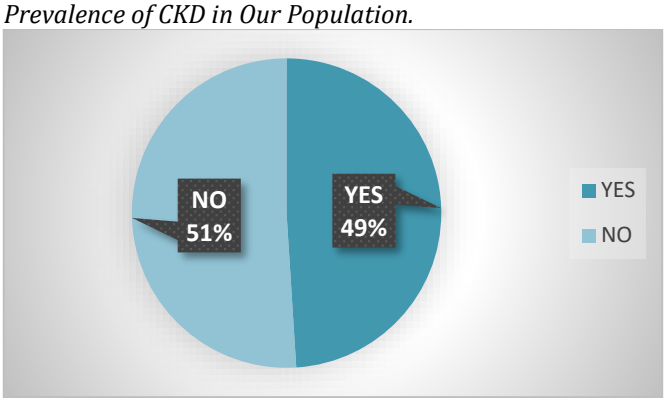
*Age Distribution of the Sample Size*

| Age (yrs.) | No. of patients | Percentages |
|---|---|---|
| 18-50 | 96 | 78.69% |
| 51-70 | 26 | 21.31% |

The prevalence of CKD as measured by the gold standard test in our population came out to be 49.18% as shown in Fig. 1.

**Figure** 1

*Prevalence of CKD in Our Population.*




The CKD-EPI creatinine Cystatin C equation was found to have the sensitivity, specificity, positive and negative predictive values, and accuracy rate as shown in the following table 3.

**Table 2**

*CKD-EPI Creatinine Cystatin C Compared to 99Tc-DTPA Scan.*

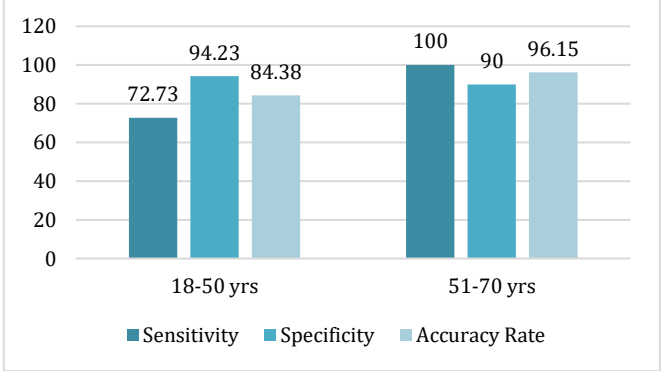
| CKD-EPI creatinine cystatin C | 99TC-DTPA SCAN | | Total |
|---|---|---|---|
| | CKD (Positive) | CKD (Negative) | |
| Positive | True positive (a) 48 | False-positive (b) 4 | a+b: 52 |
| Negative | False-positive(c)12 | True Negative (d) 58 | c+d: 70 |
| Total | a+c: 60 | b+d: 62 | 122 |

- Sensitivity = a / (a + c) x 100 =80%
- Specificity = d / (d + b) x 100 = 93.55%
- Positive predictive value = a / (a + b) x 100 = 92.31%
- Negative predictive value = d / (d + c) x 100 = 82.86%
- Accuracy rate = a + d / (a + d + b + c) x 100 = 86.89%

If we stratify according to our two major age distributions, we see that the percentages of sensitivity, specificity, and accuracy for the equation are much higher in populations above 50 years as shown in Fig. 2.

**Figure 2**

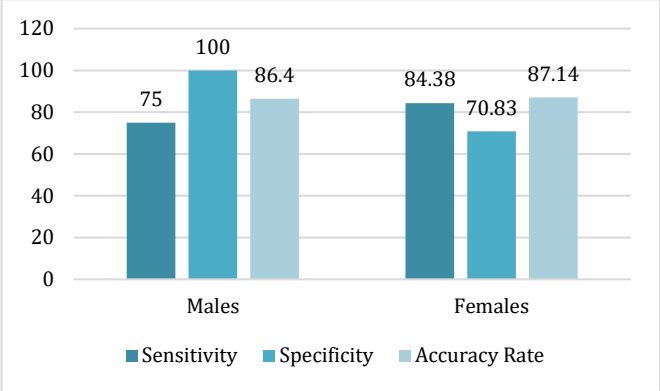
*Age Distribution of CKD Population.*



In the same way, if we stratify the given data according to gender, we see the aforementioned categories have higher values in females than males, as shown in Fig. 3.

**Figure 3**

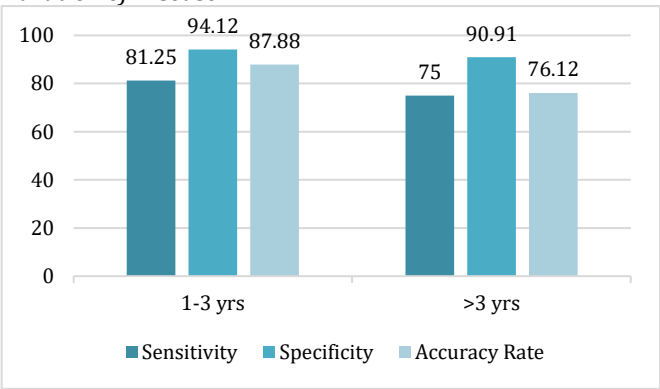
*Gender Distribution*




In the same run, if we stratify the data according to the duration of disease whilst being 1-3 years or more than 3 years, the aforementioned variables are higher in patients with a disease of fewer than 3 years, as shown in Figure 4.

**Figure 4**

*Duration of Disease*




Therefore, our study described different variables for the CKD EPI creatinine Cystatin C equation, and in comparison, with DTPA diagnostic technique validates its accuracy. It also stratifies the data according to age, gender, and duration of disease.

## DISCUSSION

Chronic kidney disease was defined as CrCl or GFR less than 60 ml/min/1.73 m or the presence of kidney damage or decrease in kidney function for at least three or more months, irrespective of the cause as per the KDIGO guidelines. [9] It is being accounted as one of the major public health problems worldwide. With the changes in its pathophysiology, glomerulonephritis being the leading etiological agent has been replaced by diabetes mellitus and hypertension as the main risk factors of the disease. CKD not only requires large resources for adequate management but it is also associated with cardiovascular diseases and all-cause mortalities. [10, 11] There are various methods for the investigation of chronic kidney disease. The low molecular weight proteins are eliminated primarily by the kidney, and thus are potential markers of renal function. [12] Cystatin C appears to be the best for this purpose as it has both a constant production rate and free glomerular filtration. [13] Cystatin C has become a part of the CKD-EPI estimation equation, which we incorporated in our study the combination equation of creatinine and Cystatin C. In the study conducted by Ying Zhu et al, it was concluded that the median mGFR was 76.35.

## CONCLUSION

In conclusion, our study has shown a better comparison between the CKD_EPI Cr-Cys C equation when compared to mGFR and thus validates its diagnostic accuracy. The equation shows greater sensitivity and diagnostic accuracy in people above 50yrs. Plus, both these variables were also higher for females for subjects with a disease duration of fewer than 3 years. Thus, the equation has been termed as a safe alternative to the 99Tc-DTPA scan when the latter is either not available or not feasible. Furthermore, the combined equation also makes up for the lacking of Cystatin C whereas it will provide an edge over the use of the Creatinine-only equation with drawbacks of serum creatinine variations. In comparison to renal dynamic imaging, the equation is easily executed with less time required for the procedure as well as the interpretation of the results. 99Tc-CTPA is invasive and involves radiation whereas the equation has neither. The strength of the study is that the notion has never been evaluated in Pakistan. Though our study encompasses adults with or without CKD, it has its limitations, for example, the sample size, the number of centers involved, etc. Plus, neither all-cause nor specific mortality could be evaluated. We recommend more large-scale studies with a greater number of patients in different centers plus collaborative research that will allow better utilization and assessment of the equation.

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