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Determination of Cystatin C and Creatinine S in Sudanese Patients with Chronic Kidney Disease

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Cystatin c is single non glycated polypeptide chains which is recently considered as markers in the renal dialysis. Our study aimed to estimate cystatin c and creatinine reduction in Sudanese patients with chronic kidney disease on dialysis. A cohort of forty patients was selected for this study creatinine and cystatin were estimated pre and post dialysis, three ml of blood were drowned by standard methods twice from each patient pre and post dialysis. 20 out of 40 patients with CKD were males while 20 were females, the most patients were more than 50years old 45.5% , 42.5% between 25-50years while 12.5% were less than 25 years. The mean and std of creatinine and cystatin c were reduced significantly in post haemodialysis than pre haemodialysis, the haemodialysis, the reduction ratio were 14.93%(pvalue 0.000) , and 58.50% (p.value0.000) for cystatin C and creatinine respectively. The pre and post haemodialysis cystatin c were not correlated with haemodialysis duration in years while pre haemodialysis creatinine level were significantly correlated with duration p.value 0.009. In conclusion cystatin C is another sensitive marker beside urea and creatinine reduction ratio further studies were required in different dialysis machine.

Keywords: CKD; Creatinine; Cystatin C; Dialysis; GFR.

The chronic kidney disease (CKD), and end-stage renal diseases (ESRD) are main health concerns affects all nation worldwide with gradual raising rates and prevalence.[1]

CKD predominately having no symptoms, and thus, a laboratory estimation of renal function is needed. the most parameter used to assess CKD were , serum creatinine as crucial indicators of glomerular filtration (GFR).[2]

Serum creatinine level have low sensitivity to early predict CKD and unable to predict half of patients in stage three CKD (GFR of 30-59 mL/min/1.73m2),[3] in which serum creatinine level may not change until approximately 50% of the kidney function has been changes .[4]In addition, creatinine production is also affected by factors like age, gender, muscle mass, physical activity and dietary intake.[5] Moreover, many factors encountered with measurements of creatinine and its use as a GFR estimate, cystatin C (CysC) has been proposed as an alternative marker of renal function. [5]

Cystatin c recently has emerged as biomarkers for assessing the renal function, especially in the context of dialysis. Moreover, cystatin C was demonstrated to estimate GFR with better adequacy than creatinine in many studies [6-7]

Beside traditional markers such as serum creatinine, cystatin C is a small, non-glycosylated protein produced at a constant rate by all nucleated cells and is freely filtered by the glomerulus. In

addition , serum levels of cystatin C is primarily determined by glomerular filtration rate (GFR), making it a reliable indicator of kidney function. [8]

In dialysis, accurate assessment of renal function is crucial for monitoring disease progression, optimizing treatment strategies, and predicting outcomes. Conventional dialysis assessment parameters such as (Serum creatinine), may be influenced by factors such as muscle mass, diet, and medications, leading to variability in the test interpretation. Cystatin C, on the other hand, is less influenced by extra-renal factors and has been shown to provide a more adequate and accurate estimation of GFR in patients with end-stage renal disease (ESRD).[9]

Many studies have been demonstrated the utility of cystatin C as a dialysis biomarker, with elevated levels correlating with reduced GFR and increased mortality risk in dialysis patients.[10-11] Furthermore, cystatin C has shown promise in identifying early renal dysfunction and predicting progression to ESRD, allowing for timely intervention and improved patient outcomes.[12]

In addition to its role in assessing renal function, cystatin C is considered as potential marker of cardiovascular risk in dialysis patients. High level of cystatin C have been associated with cardiovascular diseases , including myocardial infarction, stroke, and heart failure, independent of traditional risk factors.[13]All these make cystatin C as a biomarker, encompassing both renal and cardiovascular health in the dialysis population.

Despite this roles, several challenges remain in the clinical implementation of cystatin C as a dialysis biomarker. Standardization of assay methods, establishment of reference ranges, and consideration of patient characteristics are essential for accurate interpretation of cystatin C levels.[14]

Here in this study we estimated the cystatin level beside conventional dialysis estimator(creatinine level) pre and post haemodialysis to detect reduction ratio.

MATERIALS AND METHODS

A cohort study was done in White Nile State,Al_Dieum city Al_Dieum Dialysis Center, from 28May to 4June 2017, forty patient on dialysis was selected for this study to determine the level of cystatin C and creatinine after dialysis. Total 40 heamodialysis Patients, age ranged from (15-70) years were selected for this study while patients with severe illness were excluded , Questioner was used to obtain initial information about the Heamodialysis Patients, The study was approved from ALzaeim Alazhari University faculty of medical laboratory sciences with code (1—0017) , blood was collected after by standard methods after patient informed about the aim of the study and consented to contribute to this study. 3 ml heparinized blood samples heparin blood samples were collected from the patients and centrifuged and frozen in -20 and cystatin C was estimated within one week duration of storage in I Chroma, serum creatinine and urea was estimated by spectrophotometer , all test was performed under quality control protocol , the reduction was used with published formula reduction ratio =100*(1-(post test result/ pre test result) we used this formula for all creatinine and urea and cystatin C

Ethical approval and consents

The study approved from Alzaeim Alazhari University faculty of medical sciences with ethical committee code (1-0017)all patient signed informed consents after informed about the aim of the study and consented to contribute to this study

Data analysis

The data was entered and analyzed social package of social sciences version 20 SPSS p.value <0.050 valued as significants

RESULTS

Of 40 study participants 20 were males and 20 were females , the most patients were more than 50years old 45.5% , 42.5% between 25-50years while 12.5% were less than 25 years .The mean and STD of creatinine and cystatin c were reduced significantly in post haemodialysis than pre haemodialysis p.value 0.000. The haemodialysis reduction ratio were 14.93%(pvalue 0.000) , and 58.50% (p.value0.000) for cystatin C and creatinine respectively table(1). The higher reduction rate were achieved in females creatinine 60.29972% table (1). The pre and post haemodialysis cystatin c were not correlated with haemodialysis duration in years while pre haemodialysis creatinine level were significantly correlated with duration p.value 0.009 table(2) and figure (1).

DISCUSSION

In this study the reduction ratios of cystatin C and creatinine were measured from pre-dialysis to post-dialysis levels, which provide valuable insights into the efficiency of hemodialysis in removing these waste products from the bloodstream. Fist of all our study confirmed higher level of cystatin level in patient with CKD, as urea and creatinine impaired in CKD consequently the cystatin C was also impaired. Our study observed a significant decrease in cystatin C reduction ratio post-dialysis compared to pre-dialysis levels, whereas creatinine reduction ratio showed a substantial reduction both pre- and post-dialysis which is consistent with meta analysis that found cystatin c is reduced after hemodialysis.[15] Moreover lower reduction of cystatin C than creatinine have been proposed in many studies. [6-16] The observed decrease in cystatin C reduction ratio post-dialysis suggests a less efficient removal of this biomarker during the hemodialysis session. Cystatin C, being a low-molecular-weight protein, is freely filtered by the glomerulus and predominantly cleared through renal excretion. However, hemodialysis may not effectively remove cystatin C due to its larger size and protein-bound nature, resulting in a lower reduction ratio compared to creatinine.[10] This discrepancy highlights the limitations of cystatin C as a dialysis biomarker and underscores the need for alternative markers of renal function in the dialysis population.

In contrast, creatinine reduction ratio exhibited a significant reduction both pre- and post-dialysis, indicating effective removal of this small molecule during hemodialysis. Creatinine, a byproduct of muscle metabolism, is readily filtered by the glomerulus and efficiently removed by hemodialysis, making it a standard marker for assessing dialysis adequacy.[17] The observed decrease in creatinine reduction ratio post-dialysis reflects the successful clearance of creatinine from the bloodstream during the dialysis session.

Interestingly, our findings are consistent with those of other studies that have reported a reduction in cystatin C levels post-hemodialysis compared to pre-hemodialysis levels. For example, Huang et.al [18] observed a significant decrease in cystatin C levels following hemodialysis sessions in a cohort of nephrotic patients. Similarly, another study reported a decrease in cystatin C levels post-hemodialysis in patients on dialysis with high flux haemodialysis.[19] The differences between cystatin C reduction ratio and traditional markers such as

Table 1. Show statistics and mean differences of Cystatin C and Creatinine in pre and post dialysis with reduction ratio

Item	Parameter	Pre	Post	Reduction ratio%	P.value
Overall	Cystatin C	6.6028±.87383	5.6164±1.04928	14.93912	0.000
Overall	Creatinine	8.4900±2.18278	3.5230±1.17077	58.50412	0.000
Males	Cystatin C	6.3965±.84368	5.4130±1.15678	15.3756	0.000
	Creatinine	8.5524±1.89806	3.6857±.85105	56.90449	0.000
Females	Cystatin C	6.7726±.88353	5.8305±.90414	13.91046	0.000
	Creatinine	8.4211±2.51210	3.3432±1.44916	60.29972	0.000

Table 2. Correlation of duration in cystatin c and creatinine pre/post heamodialysis

		Cystatin C pre	Cystatin C post	Creatinine pre	Creatinine post
Duration (Year)	R value	.004	.231	.408	-.188
	P value	.982	.157	.009	.246

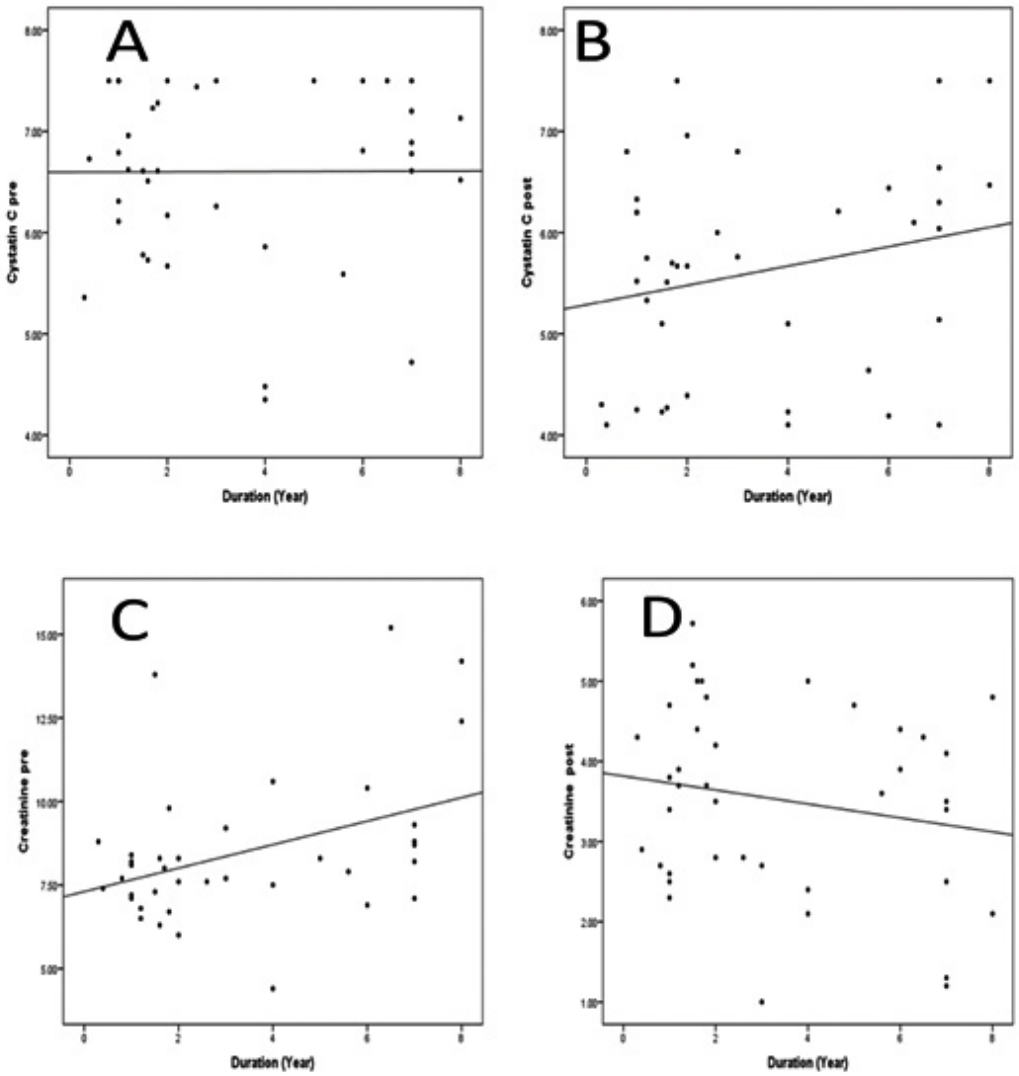

Fig. 1. Showed the association between pre and post level of the tests A) showed cystatin level pre-dialysis and duration in years B)post dialysis cystatin C and duration in years C) pre-dialysis creatinine and duration and final D) post dialysis creatinine level against duration in years

creatinine which is estimated here highlights the need for alternative markers of renal function in hemodialysis patients. While urea and creatinine are small molecules that are readily cleared by dialysis, cystatin C may exhibit different clearance kinetics and removal efficiency due to its unique properties.[11] Physicians should interpret cystatin C reduction ratio in conjunction with other markers and clinical parameters to assess dialysis adequacy and monitor renal function in hemodialysis patients until adjust their reference range and other factors affect cystatin reduction ratio.

The discrepancy between cystatin C and creatinine reduction ratios underscores the complex dynamics of solute removal during hemodialysis. While creatinine serves as a reliable marker of dialysis adequacy, cystatin C may not accurately reflect changes in renal function or dialysis

clearance due to its unique properties and clearance mechanisms.

CONCLUSION

In conclusion, our findings highlight the differences in reduction ratios of cystatin C and creatinine pre- and post-dialysis, reflecting variations in their clearance kinetics and removal efficiency during hemodialysis. More research is needed for assessing dialysis adequacy and monitoring renal function in dialysis patients.

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The author(s) do not have any conflict of interest.

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Ethics Statement

This research did not involve human participants, animal subjects, or any material that requires ethical approval.

Informed Consent Statement

This study did not involve human participants, and therefore, informed consent was not required.

Clinical Trial Registration

This research does not involve any clinical trials.

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Not Applicable

Author contributions

Ibtihal Ahmed- Conceptualization, data collection, laboratory procedures, data analysis, write original draft, and approved final draft; Amna Osman- Conceptualization, supervision, reviewing , editing of the final draft, and approved final draft.

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