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Serum Cystatin C and Creatinine level among Chronic Kidney Disease Patients Undergoing Hemodialysis

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Original Research Article

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Abstract: Chronic kidney disease (CKD) is one among the slowly progressive diseases of kidney function characterized generally by low glomerular filtration rate (GFR). The replacement therapy of renal failure by hemodialysis involves the removal of excessive toxic fluids and toxic metabolic end products from the body. The present study aimed to assess serum Cystatin c and creatinine (pre and post) in CKD patients undergoing hemodialysis. The study included 50 patients with CKD who undergo dialysis. Serum creatinine and urea measured in pre and post-dialysis by colorimetric method, cystatin c was measured by using metric immunoassay. The data were analyzed using SPSS version 21. The results revealed that the mean of serum creatinine level in post-hemodialysis patients (3.05±1.12) were lower significant compared to pre-hemodialysis (8.76±2.26) p-value 0.000, also serum urea level in post-hemodialysis patients (90.30±17.11) were lower significantly compared to pre-hemodialysis (176.58±26.72) p-value 0.000, serum Cystatin c level in post-hemodialysis patients (6.91±0.93) were higher significantly compared to pre-hemodialysis (6.34±1.51) p-value 0.007. There was a significant difference in the levels of serum urea and creatinine observed Pre and Post hemodialysis with respect to different age groups P-value 0.002 and 0.021while no significant difference in serum Cystatin c level observed Pre and Post hemodialysis with respect to different age groups P-value 0.119. The findings of this study, hemodialysis leads to decreased serum urea and creatinine level in patients with CKD under hemodialysis and decreased the increased cystatin c level.

Keywords: CKDs, Creatinine, urea, Cystatin c.

INTRODUCTION

Chronic kidney disease in particular is major health problems worldwide with dramatically rising incidence and prevalence [1]. Hemodialysis is one of the renal replacement therapy [2]. The technique plays a vital role in the process for the extracorporeal removal of waste products such as creatinine, urea and free water from the blood when the kidneys are impaired. The principle behind hemodialysis is the diffusion of solutes through a semi-permeable membrane. Hemodialysis is usually performed with uremic patientsfor two to three times a week and the required times for dialysis vary from two to four hours [3]. CKD patients are often asymptomatic, and thus, a laboratory measurement of kidney function is required. In practice, serum and plasma creatinine are the most widely used endogenous markers of GFR [4]. The sensitivity of serum creatinine in the detection of CKD is poor and it will fail to identify half of the patients with crucial stage 3 CKD (GFR of 30-59 mL/min/1.73m2) [5-7] as serum creatinine concentration may not change until approximately 50% of the kidney function has been lost [8]. Furthermore, creatinine production is also influenced by factors such as age, gender, muscle mass, physical activity and diet [9]. Urea is an organic compound and plays a vital role in the metabolism of nitrogen-containing compounds. It is a waste product from dietary protein and is also filtered into urine by the kidneys [10, 11]. Urea nitrogen is a normal waste nitrogen product found in the blood that comes from the breakdown of protein from foods. Healthy kidneys remove urea nitrogen from blood, but the level of urea in the blood rises with kidney failure occurs [12]. An attempt has been made to evaluate the increase of creatinine and urea in patient's serum of various age groups with renal failure during pre and post-hemodialysis. Due to the many problems encountered with measurements of creatinine and its use as a GFR estimate, cystatin c has been proposed as an alternative marker of renal function. Cystatin c is a 13-kDa, non-glycosylated basic protein belonging to the cystatin superfamily of cysteine proteinase inhibitors. Studies have shown that cystatin c may be more sensitive in identifying mild reductions in kidney function than serum creatinine [13, 14]. Cystatin c has several properties that make it a good candidate marker of

GFR, including a constant production rate regulated by a "housekeeping" gene expressed in all nucleated cells, free filtration at the glomerulus, complete reabsorption and catabolism by the proximal tubules with no reabsorption into the bloodstream, and no renal tubular secretion. Cystatin c is a better marker of GFR than serum creatinine because of its independence from age and gender [15] serum cystatin c levels are influenced by the method and intensity of dialysis received [16]. Dialysis efficiency greatly influences the well-being, outcome, and survival of patients with chronic renal disease. Presently, the efficacy of dialysis is assessed by estimating serum creatinine and cystatin c [17].

MATERIALS AND METHODS

This was a Cross-sectional study which conducted on patientswith CKD submitted to dialysis centers in Alshaheed Arif Renal disease Centre for pre and posts dialysis analysis of CKD. This study included all patients with CKD under and excluded the CKD patients not under dialysis. Five milliter of the blood was obtained from each patient before and after dialysis and then placed in plain tubes. The blood was centrifuged to separate serum that was used for the estimation of creatinine, urea and cystatin c.

The study was approved by the faculty of Medical Laboratory Sciences, Al-Neelain University, and informed consent was obtained from each participant before sample collection.

Serum creatinine and urea were estimated by the Jaffe's reaction, and Berthelot method, respectively.

Cystatin c Estimation

Cystatin c was measured in serum samples with latex particle-enhanced turbid metric immunoassay from gentian (Gentian AS, Moss, Norway) performed on an Olympus AU 460 (Olympus Optical, Tokyo, Japan) as per the application note provided by the manufacturer.

Statistical analysis

Data were analyzed using (SPSS 21) program. The results were expressed as percentages, mean and SD. The paired t-test was obtained to compare the change in study parameters in pre and post dialysis. Pearson correlation was applied for the relationship between parameters and study variables. Value of < 0.05 was taken as significant.

RESULTS

The study included 50 patients with CKD who undergo dialysis. Figure-1 shows the distribution of hemodialysis patients according to gender, out of 50 patients 60% was male and 40% was female. Figure-2 distribution of hemodialysis patients according to gender, age and cause, Out of 50 patients 60% were male and 40% were female. 34% were less than 45 years while 66% were more than 45 years. 94 % had HTN and 6% had HTN and DM. Table-1 shows the mean±SD of ages of hemodialysis patients (50.22±14.5 years). Table-2 shows mean concentration comparison of study parameters in pre-hemodialysis patients versus post-hemodialysis patients, The mean of serum Creatinine level in post-hemodialysis patients (3.05±1.12) were lower significant compared to pre-hemodialysis (8.76±2.26) p-value 0.000, also serum urea level in post-hemodialysis patients (90.30±17.11) were significantly lower compared to pre-hemodialysis (176.58±26.72) p-value 0.000, serum cystatin c level in post-hemodialysis patients(6.91±0.93) were higher significant compared to pre-hemodialysis (6.34±1.51)p-value 0.007. Table-3 shows the comparison of study parameters in pre-hemodialysis patientsand post-hemodialysis patients across age group. There was a significant difference in the levels of serum urea and creatinine observed Pre and Post hemodialysis with respect to different age groups P-value 0.002 and 0.021while no significant difference in serum cystatin c level observed Pre and Post hemodialysis with respect to different age groups P-value 0.119 and 0.779. Table mean concentration comparison of study parameters in Pre-hemodialysis patients and post-hemodialysis patientsacross the gender. There was a significant difference in the levels of serum creatinine in male compared to female among post-hemodialysis p-value. While Serum Urea and cystatin c level show no significant difference. Figure-4 shows a correlation between age and change in study parameters. Positively correlation between change in urea and creatinine level with age and no correlation was observed between age and change in Cystatin c level.

DISCUSSION

The present study showed that CKD is more common in males than females and most affected subjects are more than 45 years. This finding was agreed with the previous study done Noor ul Amin who observed that CKD is more common in males than in females and people between 40 to 60 years are more affected with CKD [18]. Chronic renal failure is a gradual, progressive and irreversible loss of normal functioning of kidneys. As the excretory function of the kidney is impaired, urea and Creatinine excretion is hampered leading to its increased levels in blood, so significant elevation in blood urea and serum creatinine levels are observed in CRF patients before hemodialysis HD [19].

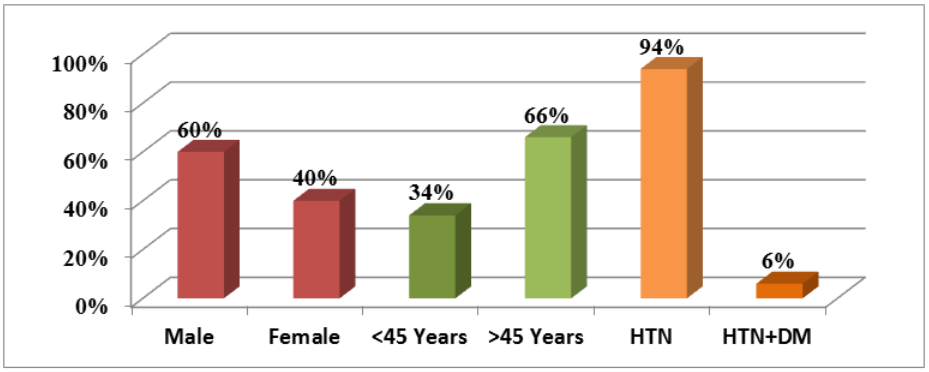

Fig-1: Distribution of hemodialysis patientsaccording to Gender, age, and Cause

Table-1: Mean age of hemodialysis patients

Variable	Minimum	Maximum	Mean±SD
Age	25.00	79.00	50.22±14.53

Table-2: Mean concentration comparison of study parameters (creatinine mg/dl, urea mg/dl, cystatin c mg/l) in Pre-hemodialysis patientsversus post-hemodialysis patients

Parameter	Pre-hemodialysis patients	post-hemodialysis patients	*P-value*
Creatinine	8.76±2.26	3.05±1.12	0.000
Urea	176.58±26.72	90.30±17.11	0.000
Cystatin	6.34±1.51	6.91±0.93	0.007

Table-3: Mean concentration comparison of study parameters in Pre-hemodialysis patientsand post-hemodialysis patientsacross age group

Age group	Pre hemodialysis		Post hemodialysis	
	Mean±SD	*P-value*	Mean±SD	*P-value*
Creatinine				
<45 Years	10.10±2.28	0.002	3.55±1.19	0.021
>45 Years	8.07±1.95		2.78±1.01	
Urea				
<45 Years	187.6±27.23	0.034	93.88±20.98	0.042
>45 Years	170.87±24.97		88.45±14.75	
Cystatin c				
<45 Years	6.73±1.01	0.119	6.86±0.82	0.776
>45 Years	6.13±1.68		6.93±0.99	

Table-4: Mean concentration comparison of study parameters in Pre-hemodialysis patientsand post-hemodialysis patientsacross the gender

Sex group	Pre hemodialysis		Post hemodialysis	
	Mean±SD	*P-value*	Mean±SD	*P-value*
Creatinine				
Male	9.21±2.46	0.070	3.36±1.26	0.007
Female	8.09±1.78		2.58±0.68	
Urea				
Male	181.03±29.04	0.129	93.73±16.91	0.082
Female	169.90±21.80		85.15±16.49	
Cystatin c				
Male	6.12±1.72	0.173	6.91±1.07	0.970
Female	6.66±1.08		6.92±0.69	

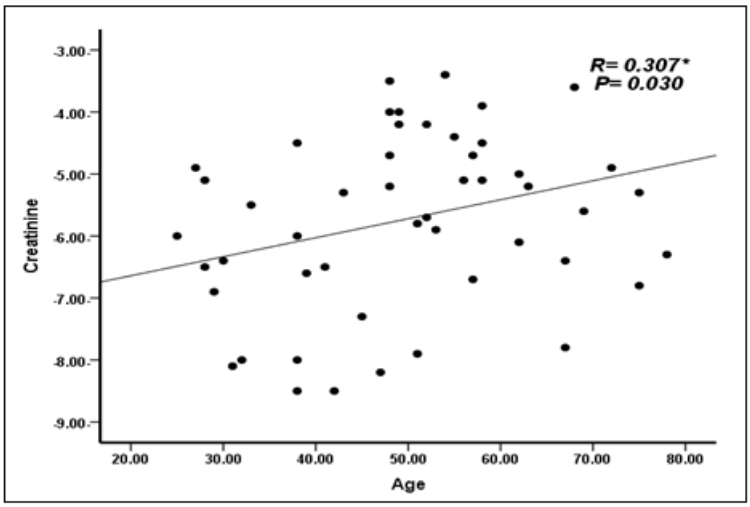

Fig-2: Correlation between age/years and Creatinine mg/dl

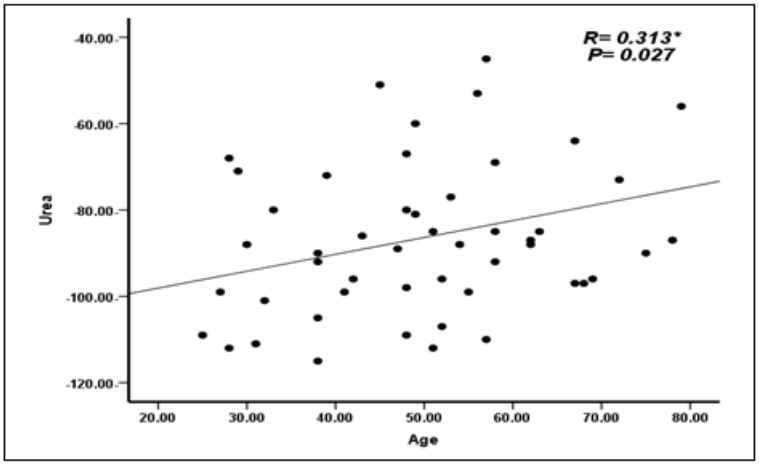

Fig-3: Correlation between age/years and Urea mg/dl levels

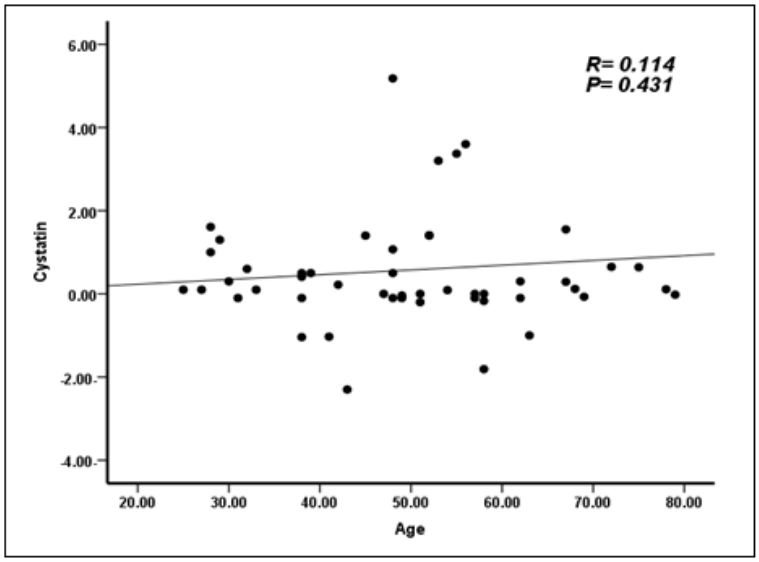

Fig-4: Correlation between age/years and cystatin c mg/l levels

In the present study, the serum urea and creatinine levels both were reduced significantly after HD. These findings are compatibles with the past studies [15, 20, 21] which explained that the continued decreased in renal clearance or GFR, leads to the gathering of urea, creatinine and other chemicals in the blood. In CRF, the increase of serum urea is proportional to the progression of the disease, but it is highly influenced by catabolic state or excessive protein ingestion, leading to a higher production of other waste substances of protein catabolism [20]. These reductions in mean levels of creatinine and urea are observed in the post-hemodialysis treatment revealing significance decreased difference, p.values (0.000, 0.000), respectively. The observation is suggestive of clearance of Creatinine and urea from blood during HD [19]. The fall in serum creatinine in post-dialysis patientsis because of the magnitude of reduction of this metabolite during dialysis [22, 23].

Also, the findings were agreed with the previous study done by Nisha R who reported that the incidence of serum creatinine and serum urea was significantly high before hemodialysis and reduced significantly after hemodialysis [3]. Serum cystatin c is eligible as a predictor of renal dysfunction and as an indicator of dialysis patients. The serum cystatin c level in post-hemodialysis patients was significantly higher in comparison to pre-hemodialysis. value (0.007). Its elevation in the serum after dialysis may be attributed to the components of dialyzing fluid and the nature of dialyzing membrane [24, 25], moreover cystatin c is cation or highly positive charged and this might hindering its filtration or considered as electro-static interaction between micro-proteins and other plasma proteins adsorbed onto the dialyzer membranes [15, 26]. When dialysis is carried out using a low flux membrane, the pore size is smaller than 1.5 nm which does not permit the removal of low molecular weight proteins such as cystatin c [27]. Some researchers observed that low flux LF hemodialysis did not reduce cystatin c [28], meanwhile high flux HF hemodialysis decreases cystatin c post-hemodialysis [29]. The present study revealed increased in serum creatinine and urea with a significant difference observed before and after hemodialysis in respect to different age groups. While cystatin c level does not change with respect to different age groups. The earlier findings of Nisha R *et al*., was similar to our results findings who reported that serum creatinine and urea levels showed significant difference before and after hemodialysis across different age group [3]. In fact that generally, urea accumulation in blood serum of kidney failure patients arises from the degradation of food and tissues such as muscle. The high level of urea in the blood leads the body very sick unless remove it from the blood streams by kidneys [30]. In this study, there was a significant difference in the levels of serum creatinine and urea observed before and after hemodialysis with respect to different-sex groups, during hemodialysis, excess urea from the patient's blood is slightly removed in order to prevent accumulation [31]. As depicted in figure-2 & 3 a significant correlation was found between age and (creatinine, urea) levels, (R= 0.307, 0.313), (p.value= 0.030, 0.027), respectively but there is no significant correlation observed between age and cystatin c.

CONCLUSION

This study concludes that hemodialysis led to decrease serum urea and creatinine level in patients with CKD under hemodialysis and increased in cystatin c level. Both serum creatinine and serum urea are widely accepted biomarkers to assess the renal functions. Hemodialysis forms an effective process as an efficient and indispensable process for the filtration.

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