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# Evaluating Urea and Creatinine Levels in Chronic Renal Failure Pre and Post Dialysis: A Prospective Study

Noor ul Amin, Raja Tahir Mahmood\*, M. Javaid Asad, Mudassar Zafar, and Asad Mehmood Raja

#### Abstract

Chronic renal failure is the progressive loss of function of kidney and patient requires a long treatment in the form of renal replacement therapy. Haemodialysis is one of the renal replacement therapy, during which body's waste products, including creatinine, urea and excess water, are removed. The current study was designed to investigate the impact of haemodialysis on the removal of excess body waste and hemoglobin level of patients. Seventy patients were randomly analyzed. 53% of patients had serum urea level above 200 mg/dl but after dialysis and 66% of patients had urea level below 200 mg/dl. Concerning serum creatinine, 57% of patients had values between 7-12 mg/dl before dialysis, whereas after dialysis in 58% of patients the values were reduced below 7 mg/dl.

Key Words - Chronic renal failure, Haemodialysis, Creatinine, Urea.

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# I. INTRODUCTION

Chronic kidney disease (CKD) is one of the major public health problems [1]. In the United States there are approximately twenty six million adults having non-dialysis dependent kidney disease [2] and over four million adults have chronic renal disease, reaching over thirteen percent of the US population [3]. It is estimated that in the next years, the weight of CKD will increase, and over two million persons are expected to be receiving renal replacement therapy (dialysis or kidney transplant) by 2030. In Pakistan the integer of patients with chronic renal failure is escalating incessantly. More than hundred new cases per million have been recently reported [4, 5].

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From the Department of Biochemistry, PMAS-Arid Agriculture University Rawalpindi, PK. Conflict of interest: none declared.

Corresponding Author: Raja Tahir Mahmood: rajatahir87@gmail.com

Chronic renal failure induces a slow and progressive decline of kidney function. It is usually a result of complications from another serious medical condition. Unlike acute renal failure, which happens quickly and suddenly, chronic renal failure happens gradually - over a period of weeks, months, or years as the kidneys slowly stop working, leading to end-stage renal disease (ESRD).

In chronic renal failure there is a steady and continued decrease in renal clearance or glomerular filtration rate (GFR), which leads to the gathering of urea, creatinine and other chemicals in the blood. According to the Kidney Disease Improving Global Outcomes (KDIGO) declaration GFR of less than 60 mL/minute/1.73 m<sup>2</sup> is the indication of CKD. KDIGO additional classified the CKD in different stages which are: GFR 30 to 60 mL/minute as stage three; GFR 15 to 30 mL/minute as stage four; and GFR less than 15 mL/minute as stage five of CKD [6]. In stage five level of serum creatinine is greater than 5.0 mg/dl in men, and greater than 4.0 mg/dl in women [7].

High blood pressure is one of the leading causes of kidney failure. Hypertension may damage the blood vessels in the kidney and effect the secretion of waste product. Waste may secrete in extra cellular fluid and further rise the blood pressure eventually leading to ESRD. G-protein coupled and  $Ca^{2+}$  dependent kinases are responsible for the control of blood pressure. Mutations may cause changes in receptors, which in turn raise blood pressure [8, 9].

Haemodialysis is one of the renal replacement therapy. In this technique body waste product like urea, creatinine and free water are removed from the blood, when the kidneys are impaired. The principle of hemodialysis is the diffusion of solutes through a semi permeable membrane. In relationship with dialysis the cost of renal transplant is very high and there are many probability of rejection. So it is very difficult for an average patient to bear the expenses of dialysis [10, 11].

The procedure of haemodialysis is performed two to three times in a week and the time of dialysis is from two to four hours. The time of dialysis depends on various factors, including kidney function, amount of waste in body, level of salts and body weight. Mortality rate with haemodialysis remains high (approximately eighteen to twenty percent per year). Improvements in the technology for dialysis, the development of new pharmaceutical agents, and experience



over the course of more than forty years since maintenance dialysis became available. The main complications of haemodialysis are sleeping sickness, exhaustion low blood pressure, chest pain, nausea, leg cramp, anemia and headache [12]. Anemia is an ordinary complication of CKD because erythropoietin, involved in the process of erythropoiesis, is normally produced by the kidney. Due to the damage or loss of the function of kidney in chronic renal failure, there is a reduction in the number of RBC count [13]. Hypoxia stimulates the renin- angiotensin-aldosterone system and contributes to renal vasoconstriction [14].

Creatinine is produced in the muscles by the non-enzymatic changes of creatine and phosphocreatinine. The liver has a momentous role in the assembly of creatinine through methylation of guanidine aminoacetic acid. The normal serum creatinine level is 0.5 to 1.0 mg/dL according to diurnal and menstrual variations, pursuit, and diet [15].

Urea is an organic compound, playing a vital role in the metabolism of nitrogen-containing compounds [16]. It was also artificially synthesized by Friedrich Wohler in 1828 as of an inorganic forerunner. The objectives of the current study were to evaluate the impacts of haemodialysis on chronic renal failure patients, removal of creatinine and urea. Also to observe various complications arising during dialysis, prevalence of anemia in chronic renal failure patients of Rawalpindi and Islamabad.

## **II. MATERIALS AND METHODS**

For pre and post dialysis analysis of CKD, blood of 70 patients was collected from dialysis centers of Pakistan Institute of Medical Science Islamabad and Bilal Hospital Rawalpindi. 5 ml of the blood was obtained from each patient before and after dialysis. Half of the blood was placed in tubes containing anticoagulant (K<sub>3</sub>/EDTA) and half in clot activator tubes. Clotted blood was centrifuge to separate serum and was used for the estimation of creatinine and urea. Non-clotted blood was used for complete blood count and hemoglobin in blood analyzer Sysmax KX-21 [17]. All the chemicals used were obtained from Sigma Aldrich and Merk.

#### A. Creatinine estimation

Creatinine was estimated by the Jaffe reaction, a calorimetric procedure in which creatinine forms a yellow orange complex in alkaline solution with picric acid. This colored complex is determined photometrically. The intensity of produced colored is directly proportional to the amount of creatinine in the sample.

#### **B.** Urea estimation

Urea was measured by diacetyl monoxime colorimetric method and Berthelot reaction. In this method the urea is converted to ammonia by an enzyme called urease. The ammonia produced is combined with 2-oxoglutarate and NADH in the presence of glutamate dehydrogenase (GDH), which yields L- Glutamate and NAD. The decrease in NADH absorbance is proportional to the urea concentration.

#### III. RESULTS

A total of 70 patients were analyzed (Fig. 1). These patients were randomly selected and their serum urea level, serum creatinine level and haemoglobin level were checked. Age and gender wise distribution was not to find the association between dialysis and gender and age, this is to show random selection of patients.

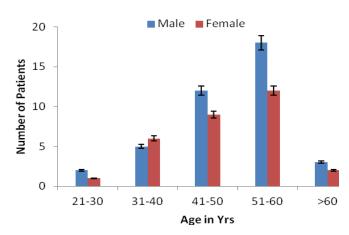


Fig. 1: Age and gender wise distribution of CKD patients.

#### A. Effect of Dialysis on Serum Urea Level

In CKD patients, pre-dialysis serum urea level was significantly higher than normal range (20-40 mg/dl). Most of the patients (53 %) had serum urea level between 200-300 mg/dl (Fig. 2). After dialysis there was a clear reduction in serum urea level; in most of the patients it was reduced to 1-100 mg/dl (26 %) and 101-200 mg/dl (40 %) (Fig. 3).

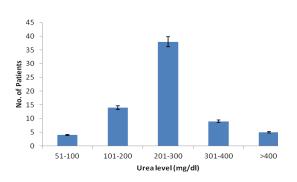


Fig. 2: Pre-dialysis serum urea level in CKD patients.



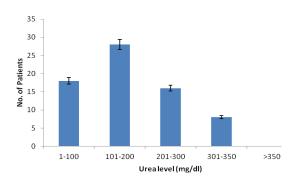


Fig. 3: Post-dialysis serum urea level in CKD patients.

#### B. Effect of Dialysis on Serum Creatinine Level

Serum creatinine level was higher than normal range (up to 1.4 mg/dl) in CKD patients undergoing dialysis. Most of the patients have serum creatinine level between 7.6-12 mg/dl (57 %) and 12-15 mg/dl (27 %) before dialysis (Fig. 4). Dialysis has positive impact on serum creatinine level and reduced its level towards normal value. Results showed that most of the patients (58%) had serum creatinine below 7 mg/dl after dialysis (Fig. 5). Glomerular filtration rate (GFR) or creatinine clearance is the based method for the estimation of kidney functioning. Factors like age, sex and physical status of person also effect serum creatinine level [18].

## C. Hemoglobin Level in CKD patients

Hemoglobin (Hb) level was found low in CKD patients due to removal of blood during dialysis. In the current study 60 patients (75%) had Hb between 5-11 g/dl, other 10 between 11-14 g/dl. This low Hb level most of the time led to the development of anemia.

#### IV. DISCUSSION

During a survey in USA from 1988-94, it was reported that CKD lead to anemia in most of the patients [19], consistent with our results. Clotting of blood during dialysis is also responsible for low Hb level in CKD patients. During the study it was also observed that CKD is more common in male then in female. People between 40 to 60 years are more affected with CKD [20]. The reason may be attributable to hypertension, diabetes or some other age related changes.

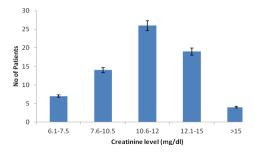


Fig. 4: Pre-dialysis serum creatinine level in CKD patients.

Removal of waste during dialysis also depends upon proper timing of dialysis, patient awareness, and appropriate dialyzer and dietary habits of patients [21]. It is usually observed that leafy green vegetables and meat might lead to increase burden on kidney and cause increase in serum urea and creatinine level [22].

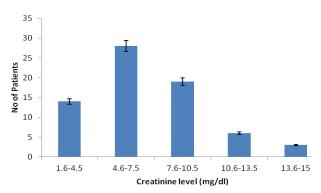


Fig. 5: Post-dialysis serum creatinine level in CKD patients.

During dialysis Hb level of patients decreased to dangerous level, which is responsible for anemia. It was also observed that middle age males are more affected to CKD disease. Molecular basis of this relationship need to be evaluated to find out possible solution [23].

#### V. CONCLUSIONS

CKD patients have higher serum urea and creatinine levels, leading to various other dangerous diseases. Haemodialysis led to decreased serum level in these patients and decreased burden on kidney.

#### References

1. Levey A S, Atkins R, Coresh J, Cohen E P, Collins A J and Eckardt K U. Chronic kidney disease as a global public health problem: Approaches and initiatives -a position statement from Kidney Disease Improving Global Outcomes. **2007**. *Kidney International*; **72**: 247-259

2. Levey A S, Coresh J, Balk E, Kausz A T, Levin A and Steffes M W. National Kidney Foundation practice guidelines for chronic kidney disease: evaluation, classification, and stratification. **2003.** *Annals of Internal Medicine;* **139(2:):** 137–47

3. Coresh J, Selvin E, Stevens L A, Manzi J, Kusek J W and Eggers P. Prevalence of chronic kidney disease in the United States. **2007** *Journal of the American Medical Association;* **298(17):** 2038–47

4. Rizvi S A and Naqvi S A. Renal replacement therapy in Pakistan. **1996.** *Saudi Journal of Kidney Disease Transplantation;* **4**: 404-8

5. Bethesda M D. USRDS 2009 annual data report: atlas of chronic kidney disease and end-stage renal disease in the United



States. **2009** .National Institute of Diabetes and Digestive and Kidney Diseases.

6. Levey A S, Eckardt U and Tsukamoto Y. Definition and classification of chronic kidney disease: a position statement from Kidney Disease. **2005.** *Kidney International;* **67:** 2089–2100

7. Couchoud C, Pozet N and Labeeuw M. Screening early renal failure: cut-off values for serum creatinine as an indicator of renal impairment. **1999.** *Kidney International;* **55**: 1878–1884

8. Santulli G, Cipolletta E, Sorriento D, Giudice G D, Anastasio A, Monaco S, Maione A S, Condorelli G, Puca A, Trimarco B, Illario M and Iaccarino G. Cam MK4 gene deletion induces hypertension. **2012.** *Journal of American Heart Association*; **1(4)**: e001081

9. Santulli G, Trimarco B and Iaccarino G. G-protein-coupled receptor kinase 2 and hypertension: molecular insights and pathophysiological mechanisms. **2013.** *High Blood Pressure Cardiovascular Prevention*; **20(1):** 5-12.

10. Steven M B, Glenn M, Elizabeth D, Ankers and Edmund G. Shorter dialysis times are associated with higher mortality among incident hemodialysis patients. **2010.** *Kidney International;* **77**(7): 630–636

11. Abram S and Anju V. Assessment of quality of life in patient on haemodialysis and the impact of counseling. **2012** *Saudi Journal of kidney Diseass and Transplantation*; **23:** 953-957

12. Unruh A, Kurella M, Brett T, Larive C, Rastogi A and James S. Impact of Sleep Quality on Cardiovascular Outcomes in Hemodialysis Patients: Results from the Frequent Hemodialysis Network Study. **2011**. *American Journal of Nephrology*: **33**: 398-406 13. Hodges V M, Rainey S, Lappin T R and Maxwell A P. Pathophysiology of anemia and erythrocytosis. **2007**. *Critical Reviews in Oncology/Hematology*: **64**: 139–158

14. Al-Khoury S, Afzali B, Shah N, Thomas S, Tatomir P G, Goldsmith D and Covic A. Diabetes, kidney disease and anaemia:

time to tackle a troublesome triad. **2007**. *International Journal of Clinical Practice*; **61**: 281–289

15. Hamilton R W, Gardner L B, Penn A S and Goldberg M. Acute tubular necrosis caused by exercise-induced myoglobinuria. **1972.** *Annals of. Internal Medicine;* **77**(1): 77–82

16. Kurzer F and Senderson P M. Urea in the history of organic chemistry. **1956**. *Journal of Chemical Education*; **33(9)**: 452-459

17. Gamperling N, Hagbloom M B and Houwen B. Performance Evaluation of the Sysmex KX-21 [TM] Automated Hematology Analyzer. **1998.** *Sysmex Journal International;* **8:** 96-101

18. Lascano M E and Poggio E D. Kidney function assessment by creatinine-based estimation equations. **2010.** Dieases management project

19. Astor B C, Muntner P, Levin A, Eustace J A and Coresh J. Association of kidney function with anemia: the Third National Health and Nutrition Examination Survey (1988–1994). **2002** *Archives Internal Medicine*; **162**:1401-1408.

20. Hida M, Saito H, wakabayashi T and Satoh T. Age and sex distribution in chronic renal failure patients at dialysis induction. **1985.** *The Tokai. Journal of Experimental and Clinical Medicine;* **10(6):** 581-588

21. Hayrullah Y, Mehmet B, Mustafa B K, Yesim G A and Sadik B. The effects of dialysers on some blood biochemical parameters in hemodialysis patients. **2011.** *Africian Journal of Pharmacy and Pharmacology*; **5(22)**: 2513-2516

22. Kaysen G A, Tom G, Larive B and Ravindra L. The Effect of Frequent Hemodialysis on Nutrition and Body Composition: Frequent Hemodialysis Network Trial. 2012. *Kidney International Journal*; **82(1)**: 90–99

23. Schieppati A and Remuzz G. Chronic renal disease as a public health problem: epidemiology, social, and economic implications. **2005.** *Kidney International Supplement;* **98:** 7-10.