Evaluating Serum Urea, Creatinine and Hemoglobin Level in Chronic Renal Failure of Pre and Post Dialysis at St. Paul's Hospital Millennium Medical College, Addis Ababa, Ethiopia.

Abstract

Objective: The objective of this study was to evaluate serum urea, creatinine and hemoglobin level in chronic renal failure pre and post dialysis at St. Paul's Hospital Millennium Medical College, Addis Ababa, Ethiopia.

Results: A total of 33 chronic kidney patients participated in this study. Out of this only 26 patients (78.79%) attend the dialysis unit for four months the rest either passed away or kidney transplantation done. The study population comprised 80.8 % male and 19.2% female. Before the dialysis, 12 (46.2%) patients serum urea level was 101-122 mg/dl, however after dialysis, 14 (53.8%) patients had serum urea level were between 20 – 50.99 mg/dl and 11 (42.3 %) patients had serum urea level were between 51 – 100 mg/dl. Most of the patients, (53.8%) undergoing hemodialysis serum creatinine level before dialysis were between 7.6 – 10.5 mg/dl. The majority of patients' (42.3%), serum creatinine level after dialysis. The majority (73.1%) of the patient hemoglobin level was between 7.0 – 11.0 mg/dl and 23.1% of the patients were between 11.1 – 14.0 mg/dl. Patients with chronic kidney disease have high serum urea and creatinine level before hemodialysis.

Conclusion: Hemodialysis decreases the burden of kidney in chronic kidney disease patients.

Keywords: ***Urea, Creatinine, Hemoglobin, After and Before Hemodialysis***

Introduction

The main function of the kidneys is to regulate the volume and composition of the extracellular fluid. The processes of filtration, reabsorption and secretion are regulated homeostatically so as to minimize changes in extracellular fluid composition; in achieving this, urine of appropriate volume and composition is produced [1]. The kidneys also maintain the blood creatinine in a

normal range. Creatinine is a waste product in human blood that is a result of muscle metabolism. It is normally removed from blood by kidneys. Normal range of creatinine in the blood is approximately 0.6 to 1.2 milligrams (mg) per deciliter (dl) in male adults and 0.5 to 1.1 milligrams per deciliter in female adults. But when kidney function slows down, the creatinine level rises. Increased value of creatinine level signifies impaired kidney function or kidney disease. As the kidneys become impaired for any reason, the creatinine level in the blood rises due to poor cleaning of creatinine by the kidneys. Abnormally high levels of creatinine thus warn of possible malfunction or failure of the kidneys. It is for this reason that standard blood tests routinely check the amount of creatinine in the blood. Dialysis is a process by which the blood is cleaned by an artificial kidney [2]. Urea is also an organic compound, playing a vital role in the metabolism of nitrogen-containing compounds. It was also artificially synthesized by Friedrich Wohler in 1828 as of an inorganic forerunner. In different studies, chronic kidney disease (CKD) showed as one of the major public health problems worldwide [3]. it has been estimated that about twenty six million adults having on-dialysis dependent kidney disease in the also in the developed country, United States [4]. In another study, it has been estimated that more than 13% of thus population to have chronic renal disease. Furthermore, the prevalence of CKD is expected to increase with time worldwide [5, 6]. 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. 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].

Haemodialysis is considered as a good therapeutic option in the context of the renal replacement therapies. Body waste product including urea, creatinine and free water are removed from the blood in case of impaired kidneys. From an economic point of view, dialysis is considered cheaper compared with the high cost of renal transplant. So, dialysis has superiority over renal transplant particularly, when the possibility of rejection is taken into account [8,9].It has been observed that chronic Kidney Disease (CKD) is associated with anemia since erythropoietin production is reduced as a consequence of impaired function of kidneys in case of chronic renal failure [10, 11]. The effect of haemodialysis on the elimination of excess body waste as well as hemoglobin level of patients was investigated. Investigating the impact of haemodialysis on the removal of excess body waste and hemoglobin level important to know how much the dialysis decreases the metabolic waste product. Therefore, this study could give evidence about

efficiency of haemodialysis on chronic kidney patient at St. Paul's Hospital Millennium Medical College (SPHMMC) by evaluating the creatinine and urea level before and after dialysis, and the prevalence of anemia in chronic renal failure patients.

Main text

Methods

Cross sectional study design was conducted From February to May 2017 in all chronic kidney failure patients by excluding those infected with hepatitis and HIV in the Ethio-Egyptian Nephrology unit in SPHMMC Addis Ababa Ethiopia. It is the only governmental hospital providing service for patients with acute kidney infection (AKI) since May 2013 and CKD since September 2016. The unit has 18 dialysis machine: 6 for AKI and 12 for CKD patients each CKD patient spent four hours during dialysis and three times per week. SPHMMC is a referral and teaching hospital. Four data collectors were recruited and trained for five days. The training address issues such as how to collect blood sample from the patient and how to fill the questioner. Socio-demographic factors like age, sex, income, family history, occupation, etc. and clinical factors like hypertension, diabetes mellitus and the likes. Blood samples were collected by using standard sampling tube; 5 ml of the blood will be obtained from each patient before and after dialysis. Then the samples were transported to SPMMC Laboratory for analysis.

In SPMMC Laboratory, each sample was divided into two; half of the blood was placed in tubes containing anticoagulant (EDTA) and half in clot activator tubes. Clotted blood was centrifuged to separate serum and used for the estimation of creatinine and urea. Non-clotted blood samples were used for complete blood count and hemoglobin in blood Analyzer Sysmax KX-21. Percentages of reduction in urea and creatinine values were calculated using the values of blood samples withdrawn from each patient before and after each hemodialysis sessions.

1. **Urea estimation by using cobasintegra 400 plus system**

Urea was measured by diacetylmonoxime colorimetric method and Berthelot reaction. In this method the urea was converted to ammonia by an enzyme called urease. The ammonia produced was 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.

$$\text{Urea} + 2H_2O \xrightarrow{\text{Urease}} 2NH_4^+ + CO_3^{2-}$$

The ammonia formed then reacts with α- ketoglutarate and NADH in the presence of GLDH to yield glutamate and NAD^+.

$$\text{2-Oxoglutarate} + NH_4 + \text{NADH} \xrightarrow{\text{GLDH}} \text{L-glutamete} + \text{NAD+} + H_2O$$

The rate of decrease in NADH concentration is directly proportional to the urea concentration in the specimen. It is determined by measuring the absorbance at 340nm.

2. Creatinine estimation by using cobasintegra 400 plus system

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 was determined photometrically. The intensity of produced colored is directly proportional to the amount of creatinine in the sample.

$$\text{Creatinine} + \text{Picric acid} \xrightarrow{\text{alkaline } P^H} \text{Yellow-orange complex}$$

In solution creatinine forms a yellow orange complex with picrate. The rate of dye formation is proportional to the creatinine concentration in the specimen.

3. Hemoglobin level

Non-clotted blood was used to complete blood count and hemoglobin in blood Analyzer Sysmax KX-21.Furthermore, different association risk factors with chronic kidney disease in patients who started renal dialysis was assessed through pre-tested and structured questionnaire survey method. Then, Data were entered into and cleaned by running frequency using EPI-info to make ready for analysis. Once the data was ready for analysis, it was exported to SPSS-20 version. The data were summarized in percentages, tables and graphs as appropriate

Ethical clearance was obtained from the IRB of St. Paul's Hospital Millennium Medical College (SPHMMC). Data collection procedure was carried out with full consent of the study participant. Each study subject was also been assured that the information provided on the request form should be confidential and used only for the purpose of research.

Results

A total of 33 chronic kidney patients participated in this study of this only 26 patients (78.79%) attend the dialysis unit for four months; soon after commencing the study, six patients underwent kidney transplantation and one patient passed away. The study population comprised 80.8 % male and 19.2% female. The mean age of the study participants were 42.5 years (standard deviation + 12.97) and their age range from 18 to 68 years. Of the respondents, the majorities 18 (69.2%) were married, 6 (23.1%) were single, 1 (3.8%) were divorced and 1 (3.8%) widowed. In terms of their residency 24 (92.3%) were urban and 2 (7.7%) were living in rural area. Concerning other socio-demographic factors, 14 (53.8%) were secondary school, 5(19.2%) were higher education.

Table 1: Socio-demographic characteristics of the study participants, 2017.

Variables	Frequency (n=26)	Percent (%)
Gender		
Male	21	80.8%
Female	5	19.2%
Age in Year		
15-24	1	3.8%
25-34	6	23.1%
35-44	7	26.9%
≥45	12	46.2%
Residence		
Urban	24	92.3%
Rural	2	7.7%
Marital Status		
Single	6	23.1%
Married	18	69.2%

Divorced	1	3.8%
Widowed	1	3.8%
Education Level		
Illiterate	3	11.5%
Primary school	4	15.4%
Secondary school	14	53.8%
Higher education	5	19.2%
Occupation		
Private employee	4	15.4%
Gov't employee	4	15.4%
Merchant	1	3.8%
Farmer	1	3.8%
Others	16	61.5%

Hemodialysis on serum urea level CKD Patients

From the total of 33 patients admitted to SPHMMC dialysis unit 26 patients serum urea level were analyzed for four months (once per month) before and after dialysis. In CKD patients serum urea level before dialysis was significantly higher than the normal serum urea level (6 – 20 mg/dl). From the total patients of 26 (78.8 %) who participated in this study the serum urea level analyzed before dialysis in 12 (46.2%) patients serum was between 101-122 mg/dl, 9 (34.6%) patients had their serum urea level before dialysis greater than 123 mg/dl and 5 (19.2%) patients had their serum urea level before dialysis between 80 – 100 mg/dl (Fig1).

Hemodialysis had significant change in reduction of serum urea level. When we saw the result of serum urea level in CKD patients attending SPHMMC hemodialysis unit after dialysis 14 (53.8%) patients had serum urea level between 20 – 50.99 mg/dl, 11 (42.3 %) patients had serum urea level between 51 – 100 mg/dl and one (3.38%) patient had serum urea level reduced to less than 20 mg/dl. So, after dialysis there was clear reduction on serum urea level (Fig2).

Hemodialysis evaluation on serum Creatinine level CKD patients

Creatinine is produced as a waste product of creatine and phosphocreatine. Because much of the creatinine is produced in muscle, the amount of creatinine that is measured in blood is proportional to the patient's lean muscle mass. The waste product creatinine enters the blood supply where it is removed through the kidney. The patients admitted to SPHMMC dialysis unit during the study time had their serum creatinine level assessed by using cobasintegra 400 plus system. The mean serum creatinine level before dialysis was 8.86 with a standard deviation of 2.07. The serum creatinine level was higher than the normal range (0.6 – 1.2 mg/dl) in CKD patients undergoing hemodialysis. Most of the patients undergoing hemodialysis their serum creatinine level before dialysis were between 7.6 – 10.5 mg/dl (53.8%) , 23.1% of the patients participated in this study had their serum creatinine level before dialysis between 10.6 – 12.75 mg/dl this is still higher than normal serum creatinine level. The remaining 23.1% patients' serum creatinine level before dialysis was less than 7.5 mg/dl (Fig 3).

Hemodialysis has positive impact on removing the metabolic waste product creatinine. When we saw the serum creatinine level of patients admitted to SPHMMC dialysis unit their serum creatinine level were reduced towards normal level (0.6 – 1.2 mg/dl). Results showed that the mean serum creatinine level after dialysis were 2.11 with a standard deviation of 0.77. The majority of patients' serum creatinine level after dialysis were between 3.0 – 3.92 mg/dl (42.3%), 34.6% of the patients serum creatinine level after dialysis were greater than 4 mg/dl and for the remaining 23.1% of the patients participating in this study their serum creatinine level after dialysis were between 1.47- 2.9 mg/dl (Fig4).

Hemodialysis on Hemoglobin level in CKD patients

Chronic renal failure induces a slow and progressive function of kidney. As a result the patients admitted to dialysis unit to remove their metabolic by product by using dialysis machine. During this procedure patients remove their blood to the machine which reduces their hemoglobin level. Non- clotted blood were collected from the patients to measure their hemoglobin level in chronic kidney patients who participated in this study by using blood analyzer KX-21. During the study period the mean hemoglobin level of chronic kidney patients were 10.46 with a standard deviation of 1.53. The majority (73.1%) of chronic kidney patients who participated in this study their hemoglobin level were between 7.0 – 11.0 mg/dl, 23.1% of the patient's hemoglobin level were between 11.1 – 14.0 mg/dl and only one patient (3.8%) in this study had hemoglobin level greater than 14 mg/dl.

Discussion

Haemodialysis is considered as a good therapeutic option in the context of the renal replacement therapies. Body waste product including urea, creatinine and free water are removed from the blood in case of impaired kidneys. Therefore evaluating urea, creatinine and hemoglobin level before and after dialysis is essential to see how much the dialysis machines remove their metabolic waste products. In this study an attempt was made to evaluate urea, creatinine and hemoglobin level in chronic kidney failure patients before and after dialysis at SPHMMC dialysis unit.

From the total patients who participated in this study 80.8% were male and 19.2% were female this shows that chronic kidney failure is most common in male than female. A comparable result was found in Pakistan and Jordan [15, 20]. During the study period it was also observed that people are more affected with CKD when their age increases (46.2%, Age≥45). This finding was consistent with the study done in Pakistan [15]. This may be because of the functionality of nephron which decreases when the age increase, susceptibility for hypertension, diabetes or because of some age related problem.

In this study, among the total participant, 46.2% had serum urea level before dialysis between 101-122 mg/dl, 34.6% had serum urea level before dialysis greater than 123 mg/dl and 19.2% had serum urea level before dialysis between 80 – 100 mg/dl. Which was lower than in a study

done in Pakistan where 53% had serum urea level before dialysis between 200-300 mg/dl and also the study done in Tikrit, Iraq (Mean 29.40 ± 6.40) mmol/L). But in our finding values are still higher than normal range of serum urea level (6-20 mg/dl). In this present study, after dialysis 53.8% patients had serum urea level between 20 – 50.99 mg/dl and 42.3 % patients had serum urea level between 51 – 100 mg/dl. This was still less than in a study done in Pakistan where 40% had a serum level between 101-200 mg/dl and 26% between 1-100 mg/dl [15]. The reason may be less intake of protein meal by patients in our country or the efficiency of the dialysis machine was high.

In this study it was observed that most of the patients undergoing hemodialysis their serum creatinine levels before dialysis were between 7.6 – 10.5 mg/dl (53.8%). 23.1% had a serum creatinine level between 10.6 – 12.75 mg/dl and for the remaining 23.1% their level was less than 7.5 mg/dl. Mean creatinine value before dialysis was 8.85 ± 2.07. Our current study results differ from the study done in Kirkuk Iraq in which the Mean was 0.9±0.15 mmol/L and this is higher than our result. However, the present finding was higher than the one found in India (Mean creatinine value before dialysis = 4.76± 2.25). A comparable result was found in Jordan [21]. In this study, the mean creatinine level after dialysis was 2.11±0.77 which was less than the result from Pakistan, Iraq and Jordan [15, 20,21]. Even if our current result of serum creatinine level after dialysis is less than the result mentioned by other authors still the serum creatinine level after dialysis of all authors is less than the serum creatinine level before dialysis. This result shows that hemodialysis has positive impact on serum creatinine level. Actually, our result and the result of different authors are still higher than the normal value of creatinine (0.6-1.2 mg/dl). This higher creatinine level than normal indicates impairment of renal function. Removal of metabolic waste product during dialysis also depends upon proper timing of dialysis, patient awareness and appropriate dietary habits of the patients.

During the study period the mean hemoglobin level of chronic kidney patients were 10.46 with a standard deviation of 1.53. This result is in accordance with the result mentioned by other studies [15, 20-22]. This shows that serum hemoglobin level of chronic kidney patients is less than the normal value. This low Hb level mostly led to the development of anemia. The main reason for less Hb level in chronic kidney patient is due to reduced production of erythropoietin from impaired kidney.

This study revealed high serum urea and creatinine level in chronic kidney disease. Hemodialysis reduced the level of metabolic waste product like urea and creatinine. Patient with CKD requires evaluation and treatment. So governmental and non-governmental organizations should make effort to increase the number of dialysis machine.

Declarations

Ethics approval and consent to participate

Informed written permission was obtained from St. Paul's Hospital Millennium Medical College Institutional Review Board (IRB) and submitted to the head of the laboratory department. Verbal informed consent was taken from each participant. Any data generated from the specimens protected the patent privacy, confidentiality and anonymity**.**

Consent for publication

Not applicable.

Availability of data and materials

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

References

1. Guyton and hall (2011). Text book of medical physiology 12th ed. SAUNDERS ELSEVIR Philadelpia, 1091pp.

2. Amin N, Mahmood RT, Asad MJ, Zafar M, and Raja AM. Evaluating urea and creatinine levels in chronic renal failure pre and post dialysis: a prospective study. JCvD, 2014.

3. 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.

4. 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

5. 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.

6. 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

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, 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.

9. 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.

10. Ethiopian Public Health Association (EPHA). Emerging Public Health Problems in Ethiopia: Chronic Non-Communicable Diseases. May 2012.

11. John W Stanifer, Bocheng Jing, Scott Tolan, Nicole Helmke, Romita Mukerjee, Saraladevi Naicker, Uptal Pate. The epidemiology of chronic kidney disease in sub-Saharan Africa: a systematic review and meta-analysis. Lancet Glob Health 2014.

12. Suresh M , Mallikarjunareddy N, Sharan B Singh M, Hari Krishna Bandi, Shravyakeerthi G, Chandrasekhar M, Hematological Changes in Chronic Renal Failure. 2012. International Journal of Scientific and Research Publications, Volume 2, Issue 9.

13. Noor ul Amin, Raja Tahir Mahmood, M. JavaidAsad, Mudassar Zafar, and AsadMehmood Raja. Evaluating Urea and Creatinine Levels in Chronic Renal Failure Pre and Post Dialysis. 2014. Journal of cardiovascular disease Vol. 2, No.2.

14. M.Z. Molnar *et al.* Estimated glomerular filtration rate at reinitiation of dialysis and mortality in failed kidney transplant recipients. Nephrol Dial Transplant (2012) 27: 2913–2921.

15. Yazar H., Balci M., Basarali K. M., Gocmen A.Y and Buyukbas S. The effects of dialysers on some blood biochemical parameters in hemodialysis patients 2011. Afr. J. Pharm.

16. Fiseha *et al.:* Chronic kidney disease and under diagnosis of renal insufficiency among diabetic patients attending a hospital in Southern Ethiopia. BMC Nephrology 2014.

17. KDIGO Clinical Practice Guideline for Acute Kidney Injury: volume 2, March 2012.

18. Nadia Khasawnah, Jaafar Abdulrahman Abu Abeeleh. Hematological and biochemical findings among Jordanian patient with end stage renal disease. E.Sc.J: 2015 edition vol.11.

19. EntedharRifaat Sarhat1 and Nawal Abdullah Murtadha. Biochemical Changes in Chronic Renal Failure Pre and Post Hemodialysis. Journal of Environmental Science and Engineering A 5 (2016) 190-195.

20. A.L Furqan et al: Evaluate some biochemical changes associated with chronic renal failure patients undergoing hemodialysis in al najaf al ashraf governorate. International Journal of Scientific and Research Publications, Volume 4, Issue 11, November 2014.