ORIGINAL RESEARCH

Life Science Journal of Pakistan
http://www.lifesciencejournal.pk

Biochemical profile of patients with chronic kidney disease (CKD) undergoing regular hemodialysis

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Abstract

Kidneys play a vital role in the removal of metabolic waste products in the form of urine. Chronic kidney disease (CKD) is the decline in kidney function for more than 3 months. This study was designed to investigate comorbidities associated with CKD and to evaluate biochemical parameters of patients undergoing regular hemodialysis from different areas of Punjab. This is a population-based study, conducted at Tahir Heart Institute, Chenab-Nagar, Pakistan. In which 26 (15 males and 11 female) patients (mean age 56 ± 6 years) diagnosed with CKD stage-v and initiated dialysis in a regular manner. Their renal function tests, liver function tests, electrolytes, albumin, and vitamin-D were performed, and appropriate statistical analysis was done. Results showed that CKD affects more males than females. Hypertension is leading comorbidity with CKD around 46%, hypertension, and diabetes both 26.9%, diabetes 15.4%, cardiovascular diseases 7.69% and other 3.8%. Level of urea, creatinine, potassium, and phosphorus was higher in a patient with no significant gender difference. Iron and vitamin–D were deficient in all these patients and this deficiency was higher in female patients. Our findings provide comorbidities that leads towards kidney failure and an overview of routine biochemical parameters of CKD stage-v patients with gender differences.

Keywords: chronic kidney disease, comorbidities, hypertension, biochemical parameters

Life Sci J Pak 2019; 1(01):03-09. doi:10
(Received 23 Sep 2018 – Accepted 21 March 2019 – Publilshed May 5, 2019)

Introduction

Chronic kidney disease is an emerging health issue worldwide. CKD stage v or end-stage renal disease is the decrease in GFR below 15mL/min per1.73m^2 for more than 3 months estimated based on creatinine-based GFR. CKD is also a prognostic disease for many premature cardiovascular diseases (CVDs) and congestive heart failure (CHF) that are a stimulator of each other (1).

Hypertension is leading comorbidity associated with death due to CKD (2, 3). Mortality rate due to hypertension is about 40% worldwide (4). It is commonly noticed with CKD and is poorly controlled in patients undertook hemodialysis (5). Hyperactivity of the renin-angiotensin system (RAS) is associated with the progression of kidneys damage. Kidneys release renin in case of sudden change in blood pressure that converts angiotensin to active form angiotensin I in kidneys that elevate blood pressure, it is converted into angiotensin II by angiotensin-converting enzyme (ACE) in lungs. Angiotensin II acts directly on blood vessels and cause vasoconstriction and elevate blood pressure (6, 7). CKD affects more than 23% of patients who have diabetes mellites and cause numerous complications including cardiovascular diseases (8). The death rate increase in patients having diabetes than those without diabetes (9). CKD increases with age as it affects more to older individuals (10, 11).

There are different biochemical parameters that indicate reduced kidney function. Electrolytes perform many important functions in the body within normal limits. Kidneys remove excess of these electrolytes and other uremic toxins. In kidney failure or reduced kidneys function several complications produced due to low fluid excretory capacity. Control of potassium is too much important in cardiac patients (12). Hyperkalemia and hyperphosphatemia are also associated with an increased mortality rate (13).

Measurement of blood urea nitrogen or serum creatinine has been used to assess renal function. Urea comes from the protein in the diet or body's metabolism system. Creatinine comes from muscular activity. Serum creatinine concentrations are affected by several diagnostic interferences; it depends on muscle mass critically. Additionally, creatinine concentration is affected by age, gender, culture, body habitus and nutrition (14). Another study reported that the delay in serum separation from venous blood may alter some creatinine measurements, that cause misclassification of CKD (15). Hemodialysis led to a reduced level of these uremic toxins in these patients and decrease the burden on the kidneys (16).

Patients with CKD usually suffer from the mineral-bone disorder. It is due to modifications in vitamin-D metabolism, one of the key features of mineral bone disorder that has foremost medical and research consequences. CKD patients have a vitamin-D deficiency. So, they are usually prescribed vitamin-D supplements. Deficiency may be due to reduced sun exposure (17), reduced synthesis of vitamin-D due to kidney disease (18) and nutritional restrictions contribute to the high occurrence of vitamin-D deficiency and severe loss of vitamin-D binding protein leads to increased kidney loss of vitamin-D metabolites (19). Iron deficiency is also most common among CKD patients, and this leads toward anemia. It is associated with high hospitalization and high mortality rate (20). This study was designed to investigate about biochemical parameters of CKD patients undergoing regular hemodialysis and find out comorbidities associated with CKD among both males and females.

Methodology

This is a population-based study; conducted at Tahir Heart Institute, Chenab Nagar, Pakistan. A total of twenty-six (15 male; 11 female) patients were selected for the study with age limit 40–60 years. Patients had been informed by written consent following WHO ethics rules 2007. All patients were diagnosed with CKD stage-v and initiated regular hemodialysis from Sharif Dialysis Centre, Tahir Heart Institute before January 2016. Patients excluded from the study if they had passed through a recent surgical procedure or those with reactive hepatitis-B or hepatitis-C. Patients who were recommended any kind of special treatment by a physician also excluded.

Demographic (age, height, weight, blood pressure and body temperature), physical and medical or medication data were collected by questionnaires. Patients were considered hypertensive if they had blood pressure higher than 140/90 mmHg or were using antihypertensive drugs. All patients were advised dialysis 3 times a week by physician and followed-up for a comprehensive period of 10 months. Pre-dialysis 10ml blood sample (5 ml in EDTA vacutainer and 5 ml in serum separating vacutainer) collected after every 12 sessions of dialysis. The analysis was performed at Masroor Diagnostic Centre, Tahir Heart Institute. For hematological examination EDTA vacutainer was kept on a homogenizer for 10-20 minutes and analysis done at Sysmex XN-1000 analyzer.

Renal function tests (urea, creatinine) and electrolytes (sodium, potassium, magnesium, phosphorus, and calcium) performed by serum separating vacutainer using Elecsys 2010, cobas c311 automated analyzer, Roche diagnostic, Pakistan. Vitamin–D and hepatitis viral load evaluation were performed during follow-up period using electrochemiluminescence immunoassay ECLIA Elecsys 2010, cobas e411 automated analyzer, Roche diagnostic, Pakistan. Patients were advised neither to take cold drinks nor any type of fast food or special treatment. They were provided standard food during each dialysis session. Column statistics was applied using Microsoft Excel 2016.

Demographic data

Total 26 patients studied (males 15; females 11). Mean ± S.D age of these CKD patients was 55.8 ± 5.7 years. For male patients, these values were 55.3 ± 7.5 years, for female patients 56 ± 4.4 years. Average body weight was 64 ± 7.6 kg and 55.7 ± 14.6 kg for male and female patients respectively. Their height was 170.9 ± 9.1 cm and 158.3 ± 10.3 cm respectively. Their body temperature has not shown much deviation. All patients had a normal body temperature. These values were 98 ± 0.6 ^{o}F and 97.7 ± 0.6 ^{o}F for male and female patients. Blood pressure showed much deviation because most of the patients were hypertensive. Average systolic blood pressure measured was 157 ± 26.8 mmHg and 160 ± 20.5 mmHg, and diastolic blood pressure 89 ± 17.3 mmHg and 83 ± 7.1 mmHg for male and female patients respectively. Represented in Table 1.

Table No. 1: Demographic data of male and female CKD patients

Demographic Parameters		Male (n=7)			Female (n=3)		
		Mean ± S. D	Min.	Max.	Mean ± S. D	Min.	Max.
Age (Years)		55.3 ± 7.5	50	65	56 ± 4.4	52	61
Weight (kg)		64 ± 7.6	58	78	55.7 ± 14.6	40	69
Height (cm)		170.9 ± 9.1	154.9	182.9	158.3 ± 10.3	152.4	170.2
Body Temp. (^{O}F)		98 ± 0.6	97	99	97.7 ± 0.6	97	98
Blood Pressure (mmHg)	Systolic	157 ± 26.8	131	187	160 ± 20.5	137	175
	Diastolic	89 ± 17.3	73	120	83 ± 7.1	76	90

Min: Minimum, **Max:** Maximum, **S.D:** Standard Deviation, **temp:** temperature

Table No. 2: Hematological Examination of CKD patients

Parameters	Units	Male (n=7)			Female (n=3)		
		Mean ± S. D	Min.	Max.	Mean ± S. D	Min.	Max.
RBC's	(10^6/µL)	4 ± 0.4	3.25	4.44	3.8 ± 0.4	3.47	4.21
WBC's	(10^3/µL)	6.4 ± 1.3	4.76	8.53	6 ± 2.7	3.66	9.01
Platelets	(10^3/µL)	185.5 ± 54.2	138	291	163.6 ± 58.3	101.4	217
HGB	(g/dL)	11.3 ± 1.5	9.02	13.68	11.3 ± 1.2	9.95	12.31

Min: Minimum, **Max**: Maximum, **S.D:** Standard Deviation

Results

Hypertension was the major comorbidity associated with CKD 46% (n; 12 = 7M, 5F), Followed by hypertension and diabetes combined 26.9% (n; 7 = 4M, 3F), diabetic nephropathy 15.4% (n; 4 = 2M, 2F), cardiovascular diseases 7.69% (n; 2 = 2M) and other 3.8% (n; 1 = 1F). Present in Figure 1.

Hematological parameters are most important in studying CKD. Red blood cells, white blood cells, platelets and hemoglobin were 4 ± 0.4 (10^6/µL), 6.4 ± 1.3 (10^3/µL), 185.5 ± 54.2 (10^3/µL), 11.3 ± 1.5 (g/dL) for male CKD patients and 3.8 ± 0.4 (10^6/µL), 6 ± 2.7 (10^3/µL), 163.6 ± 58.3 (10^3/µL), 11.3 ± 1.2 (g/dL) for female CKD patients respectively. Represented in Table 2. Urea and creatinine (mg/dL) were 124 ± 23, 8.6 ± 1 and 127 ± 29, 7.3 ± 0.9 among male and female patients respectively. Represented in Table 3, Figure 2(a & b). Electrolytes were normal for both genders except potassium and phosphorus, that was noticed high among patients. Phosphorus was (mmol/L) 6 ± 1.5 and 6 ± 1.3 for male and female patients respectively. Sodium, chloride, potassium, calcium and magnesium were (mmol/L) 134 ± 3, 94 ± 3, 5 ± 0.6, 2 ± 0.2, 1 ± 0.1 and 137 ± 1.6, 96 ± 2, 5 ± 1, 3 ± 0.8, 1 ± 0.2 in male and females respectively. Represented in Table 3, Figure 3(a & b). Liver function tests; alanine transferase, aspartate transferase, alkaline phosphate, albumin and bilirubin were 17 ± 4 (U/L), 26.4 ± 7.9 (U/L), 75 ± 3.3 (U/L), 4 ± 0.5 (g/dL), 0.29 ± 0.08 (mg/dL) in male and 15 ± 6 (U/L), 21 ± 5.9 (U/L), 91 ± 8 (U/L), 3.2 ± 0.6 (g/dL), 0.29 ± 0.1 (mg/dL) in female patients respectively. Represented in Table 3.

Iron and Vitamin-D ware seemed severely deficient in these patients. Their mean ± S.D values were 55 ± 8 (g/dL), 15.8 ± 1.8 (pg/mL) for male and 40 ± 8.9 (g/dL), 13.4 ± 1.3 (pg/mL) for females respectively. Represented in Table 3, Figure 4 (a & b).

Table No. 3: Biochemical examinations of male and female CKD patients.

Parameters	**Units**	**Male (n=7)**			**Female (n=3)**		
		Mean ± S. D	**Min.**	**Max.**	**Mean ± S. D**	**Min.**	**Max.**
Urea	mg/dL	124 ± 23	93.6	161.4	127 ± 29	117	158
Creatinine	mg/dL	8.6 ± 1.1	7	9.9	7.3 ± 0.9	6.5	8.9
Sodium	mmol/L	134 ± 3	130	137	137 ± 1.6	136	139
Potassium	mmol/L	5 ± 0.6	4.2	5.9	5 ± 1	3.9	5.4
Chloride	mmol/L	94 ± 3	91	98	96 ± 2	94	98
Calcium	mmol/L	2 ± 0.2	1.6	2.3	3 ± 0.8	2	3.5
Magnesium	mmol/L	1 ± 0.1	0.9	1.2	1 ± 0.2	1.1	1.4
Phosphorus	mmol/L	6 ± 1.5	3.4	8.4	6 ± 1.3	4	7
ALT	U/L	17 ± 4	13.1	24.1	15 ± 6	10	26
AST	U/L	26.4 ± 7.9	14.6	31.7	21 ± 5.9	12.9	25.9
ALP	U/L	75 ± 3.3	70	77.9	91 ± 8	78	99
Albumin	g/dL	4 ± 0.5	3.1	4.4	3.2 ± 0.6	2.7	3.8
Bilirubin	mg/dL	0.29 ± 0.08	0.24	0.45	0.29 ± 0.1	0.21	0.46
Iron	µg/dL	55 ± 8	43.3	64.6	40 ± 8.9	32	53.9
Vit-D	pg/mL	15.8 ± 1.8	13.3	16.6	13.4 ± 1.3	12	14.5

ALT: alanine transferase, **AST**: aspartate transferase, **ALP**: alkaline phosphate

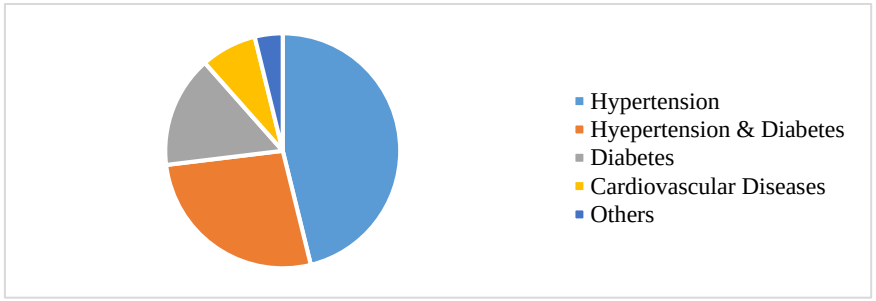
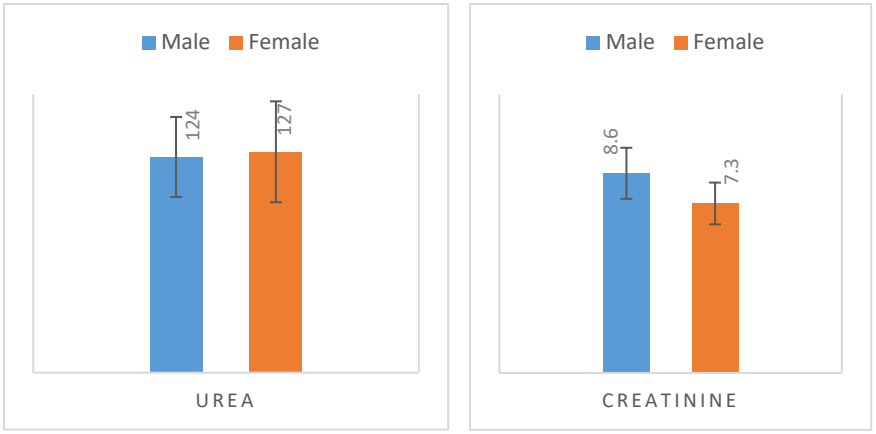
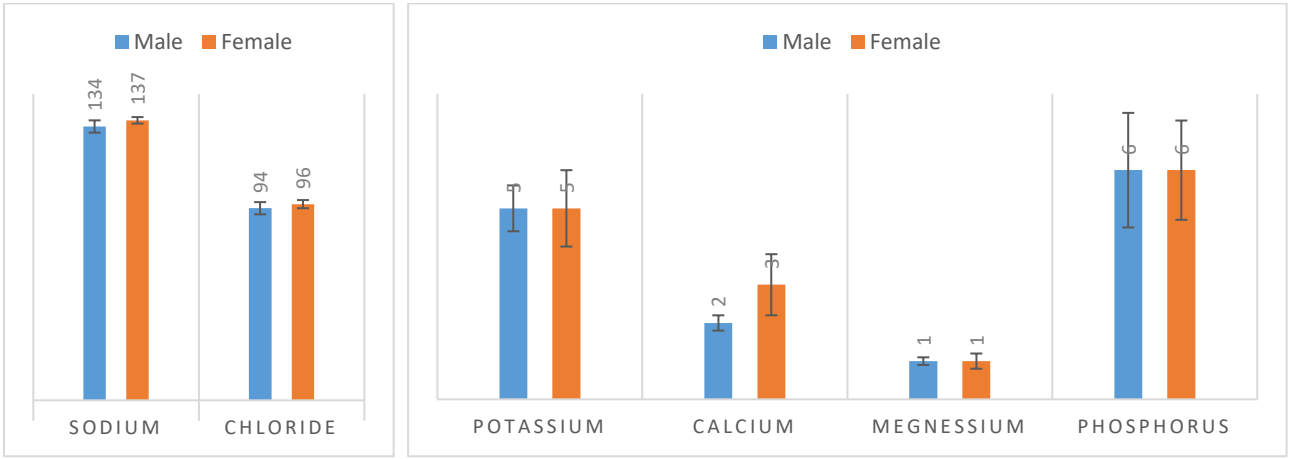


Figure 1 Comorbidities associated with CKD patients.



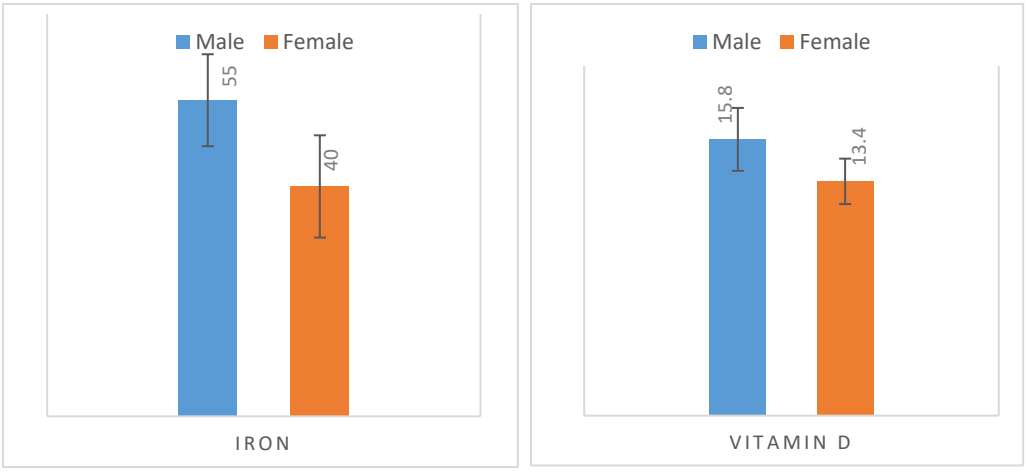
(a) **(b)**

Figure: 2 Comparative graph of renal function tests **(a)** urea and **(b)** creatinine, of male and female CKD population.



(a) **(b)**

Figure: 3 Comparative graphs of electrolytes **(a)** sodium and chloride **(b)** potassium, calcium, magnesium, and phosphorus of male and female CKD patients.



(a) **(b)**

Figure: 4 Comparative graphs of **(a)** iron and **(b)** vitamin-D of male and female CKD patients.

Discussion

This study found hypertension as leading comorbidity with CKD similar to the findings of Collins et al. (10). Its occurrence persists very high among patients with CKD stage-V. Hypertension noticed among 70% population with CKD. Twelve patients had hypertension (46%) and 7 patients had hypertension along with diabetes mellitus (26.9%) as comorbidities. Management of hypertension is very difficult in hemodialysis patients because much difference exists in pre, inter and post-dialytic period. Systolic blood pressure was prominent in these patients. Males with 157 ± 26.8 mmHg and females with 160 ± 20.5 mmHg which is noticeably very high. One of the possible causes could be the low fluid excretory capacity and volume excess in the body. Hypervolemia causes Hypertension up to 90% in dialysis patients (21). Hemodialytic hypertension is principal cause of cardiovascular mortality. Cardiovascular diseases are a common cause of death in CKD patients (22). During follow-up, one patient died with myocardial infraction having comorbid hypertension.

Diabetes mellitus is the second major cause of CKD. Combined prevalence was 40% in CKD dialysis population. Four patients had diabetes (15.4%) and 3 had diabetes along with hypertension (26.9%) as comorbid disease. Grundy et al. (23) described that diabetic nephropathy affects around 20 – 40 % of people who have diabetes (23).

Kidneys play a vital role in homeostasis by regulating the extracellular fluid composition by plasma filtration constantly in the body, thereby protecting the body's internal environment. Any damage to kidney leads towards the reduced capacity to filter blood that rise the level of metabolic byproducts. Among these, blood urea and serum creatinine concentration are important by-products that indicate kidney function (24). Both were noticed very high among these hemodialysis patients; Male patients showed a high level of serum creatinine 8.6 ± 1.1 (mg/dL) than females (7.3 ± 0.9).

Phosphorus and potassium are also important in CKD. Both were noticed high in the patients due to reduced renal excretory capacity. Potassium mineral controls nerve and muscular function. The heart beats at a normal rhythm because of potassium. Potassium is essential for keeping fluid and electrolyte balance and pH level. To achieve these functions, its level must be kept between 3.5-5.5 mEq/L. Hyperkalemia causes several complications within the body. The kidneys support keeping potassium at a normal level. But due to low excretory capacity, these patients show an increase in electrolytes in the body. Control of hyperkalemia is much important in patients of CVDs (12) so, patients directed to have potassium-free diet. Hyperphosphatemia is related to an increase in CVD risk factor in cardiac patients (25, 26). Patients under investigation showed an increased level of potassium and phosphorus. Sever increase in phosphate level in some patients also reported mineral-bone disorder and very disturbed condition for having joint pain and discomfort.

Modern studies revealed that vitamin-D deficiency is very common in CKD patients' dependent upon dialysis. It can be due to a restricted diet and low exposure to sunlight or metabolic disorders like reduced ability to convert 25-(OH) vit-D into the active form, 1, 25 dihydroxy-vit-D. Vitamin-D deficiency occurs in both male and female patients but the level of vitamin-D significantly lower in female patients (27). These findings are similar with this study as all the patients either male or female, showed vitamin-D deficiency and females were noticed more deficient in vitamin D 13.4 ± 1.3 pg/mL than males 15.8 ± 1.8 pg/mL. Vitamin-D supplements in nutrition should be prescribed to CKD patients on hemodialysis to overcome this deficiency.

Hemoglobin deficiency is also due to deficiency of iron in the blood which has a fundamental role in hemoglobin structure. To overcome this RBCs deficiency in

body erythropoietin therapy was given to every patient after each dialysis session. This study found comorbidities with biochemical parameters urea, creatinine and electrolytes (potassium, phosphorus) were higher in CKD patients underwent hemodialysis. Vitamin D and iron were deficient, and this deficiency was higher in female gender than males.

Conclusion

Hypertension was the major comorbid disease in CKD population, following by diabetes and hypertension combined. Biochemical analysis revealed the increased concentration of urea, creatinine, and electrolytes (potassium and phosphorus) and severe deficiency of vitamin D and iron among all patients. Females were noticed more deficient than male CKD population. They found to have a very poor quality of life due to a disturbance in these parameters and for being machine dependent. This study can help healthcare experts to treat CKD population effectively by understanding the complications associated with these subjects.

Acknowledgments

We would like to acknowledge all the team of Tahir Heart Institute especially Maj. Gen ® Prof. Dr. M. Masudul Hasan Nuri (Consultant Cardiologist), and Dr. Nighat Qureshi (Consultant Nephrologist), Tahir Heart Institute, Chenab Nagar, Pakistan for their cooperation and discussion during the study and providing us such a friendly environment to conduct this research work.

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