Comparative Analysis Of Biochemical And Hematological Variations In Chronic Kidney Disease Patients In District Peshawar, KP, Pakistan

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Abstract
Chronic kidney disease (CKD) is a worldwide public health problem. It is associated with various biochemical and hematological abnormalities that leads to morbidity and mortality. The aim of this study was to evaluate the biochemical and hematological parameters in chronic kidney disease patients in District Peshawar, KP, Pakistan. CKD has undergone significant demographic change over the past two decade as a result of globalization and climate change, the disease now poses a greater threat to human. By comparing the hematological and biochemical parameters in chronic kidney disease patients, this study seeks to better understand the ongoing endemic CKD disease in Peshawar, KP. This study was carried out as case-control study and observational research from March 2023 to September 2023. 200 patient samples that tested for chronic kidney disease was gathered and examined. According to the findings, males and female between the age of 20 and 80 are more likely to prone to kidney diseases. The elevated creatinine, urea, estimated glomerular filtration rate and ESR level was observed high in all patients. The study also discovered an increase in biochemical parameter with marginally lower potassium levels, and lower hemoglobin level which raises the possibility of an underlying improper function of kidney.

Keywords: CKD, ESR, GFR, kidney, potassium

INTRODUCTION

Chronic kidney disease (CKD) is a medical condition characterized by abnormal kidney function and a gradual decrease in glomerular filtration rate (GFR) [1]. Chronic renal failure patients exhibit lower hematological indices due to impaired erythropoietin production, as well as other factors such as hemolysis, suppression of bone marrow erythropoiesis, hematuria and gastrointestinal blood loss [2]. The concentration of serum creatinine is also found to have a negative correlation with all hematological parameters, with the degree of changes dependent on the severity of renal failure [3]. Anemia is found to be the most common hematological abnormality in chronic renal failure, with normochromic normocytic anemia being the most frequently observed [4]. The major risk factors for CKD include hypertension, Diabetes mellitus and obesity. Biochemical and hematological parameters are affected in CKD and becomes more evident as the disease progresses [5]. As the kidneys play a significant role in the regulation of body fluids, electrolytes and acid-base stability, CKD and ESRD predictably result in more than one derangements consisting of hyperkalemia, metabolic acidosis and hypophosphatemia which, in turn result in severe complications such as bone-mineral disorders, muscle wasting, vascular calcification and mortality[6]. Derangement in biochemical parameters as sodium, potassium, calcium, magnesium and chloride may be life threatening, hence these parameters should be kept within physiological range. 3-5[7]. Various hematological parameters such as hemoglobin (Hb), hematocrit (Hct), Red blood cell (RBC) count, and total leukocyte count (TLC) and platelet count are deranged in CKD. These alterations are due to marrow suppression by retained uremic products and aluminum toxicity associated with hemodialysis. Anemia in CKD is mostly due to reduced erythropoietin production from the kidney leading to decreased erythropoiesis [8]. Other factors for anemia include hemolysis, chronic blood loss, nutritional deficiency, inflammation and hyperparathyroidism. The major risk factors for CKD include hypertension, Diabetes mellitus and obesity. Obesity is a significant contributing factor to the development of essential hypertension, diabetes, and other comorbid conditions that increase the risk of chronic kidney disease [9]. CKD and ESRD predictably result in more than one derangement consisting of hyperkalemia, metabolic acidosis and hypophosphatemia which, in turn result in severe complications such as bone-mineral disorders, muscle wasting, vascular calcification and mortality [10]. This study focuses on chronic kidney disease (CKD) in Peshawar, KP, Pakistan. It examines the biochemical and hematological parameters in CKD patients at MMC to gain a better understanding of the disease in this specific population. Overall, this research provides valuable insights for the diagnosis, treatment, and prevention of CKD patients.

MATERIALS AND METHODS

Study Design

A case-control and observational study was conducted for six months from March to September 2023 in the Biochemistry and Pathology departments of Maqsood Medical Complex (MMC) Peshawar, and Medical laboratory Technology (MLT) Abasyn University Peshawar.

Sample Size

The study was included 200 patients from both male and female of age ranging from 20 to 80 years.

Inclusion/ Exclusion Criteria:

Patients over 20 years of age with documented CKD and serum creatinine >1.5 mg/dL were included. A control group of 100 age and sex-matched healthy volunteers were included.
Patients with acute illness, bleeding disorders, pregnancy, chronic inflammatory diseases, hematological malignancy, and serum creatinine within the last 3 months were excluded.

Data Collection

Data was collected from the population of interest through a pre-designed questionnaire for information about their life style and previous history of presentation.

Samples Processing:

The samples were analyzed in the MMC General Hospital laboratory. A 23G x 1½ needle was used to collect 5ml of venous blood, which then transferred into three test tubes: one Serum Separating Tube (SST) and one ESR tube (type AFMA-Disg), 3rd tube is EDTA which was gently mixed three to four times. The tube with ethylene diamine tetra-acetic acid (EDTA) was used to prevent blood coagulation. Each Test tube was labeled with a sticker containing the patient serial number, name, time and place of collection. The blood samples were processed for the ESR test, CBC, while another test tube were screened for blood urea, serum creatinine and electrolytes analysis. [11].

Samples Assessment:

The assessment was performed in laboratory using a chemistry analyzer Cobas C311 to measure serum creatinine, urea, eGFRs, and electrolytes with Easy Lyte Plus. Additionally, the ESR was measured using the Westergren method and the CBC was analysed using the Sysmex KX21 machine [12].

Test for Complete blood count (CBC)

Principle

The test principle for CBC involves a blood test that measures various components of the blood, including white blood cells and red blood cells, platelets, haemoglobin, haematocrit, and mean corpuscular volume [13].

Procedure

To conduct the test, 2 ml of blood was collected in an EDTA test tube, mixed well for 3 to 4 times, and then analysed using a haematology analyser. The results was printed out and include all indices.

Test for Erythrocyte Sedimentation rate (ESR)

Principle

The erythrocyte sedimentation rate (ESR) is a widely used hematological test that detects non-specific inflammation associated with infection, certain cancers, and autoimmune diseases. This test measures the rate at which red blood cells (RBCs) settle in a test tube over a period of 1 hour. During the procedure, a blood sample will be taken and monitored for 1 hour to determine the rate at which the RBCs fall to the bottom of the test tube [14].

Procedure

The Wintergreen method measures the distance (in millimeters) at which red blood cells in anticoagulated whole blood fall to the bottom of a standardized, upright, elongated test tube over one hour due to the influence of gravity. The test tube used for the test is called the Westergren tube [15].

Electrolytes

Principle

The key principle that electrolytes rely on is that certain chemical elements can naturally hold a positive or a negative electrical charge. When those elements are dissolved in a liquid, that liquid can then conduct electricity. An example of this is salt water, which conducts electricity easily [16].

Procedure

To measure the electrolyte levels in a blood sample, 2 ml of blood was collected in a Serum separating tube and centrifuged for 10 minutes. After centrifugation, the upper serum portion of the sample was analyzed using the Easy Lite Plus to detect levels of sodium (NA), potassium (K), and chloride.

Blood Urea Test

Principle:

The urea test is utilized to evaluate kidney function by measuring the amount of urea in a blood sample. The test works by hydrolyzing urea to ammonia and Carbon dioxide using urease, after which the resulting ammonia reacts with a phenolic chromogen and hypochlorite to form a green-colored complex. The intensity of the color produced is directly proportional to the concentration of urea present in the sample [17].

Procedure:

Standard Test Reconstituted Reagent 3ml Pre-warm at 37^{o}C for 2 minutes. and added Standard 0.025ml - Sample (serum) - 0.025 After exactly 30 seconds. Read and recorded absorbance A1 against distilled water at 340 nm. At exactly 60 seconds, read and recorded the absorbance A2 and determine ΔA.

Creatinine blood test

Principle:

A creatinine test is a measure of how well your kidneys are performing their job of filtering waste from your blood. Creatinine is a chemical compound left over from energy-producing processes in your muscles. Healthy kidneys filter creatinine out of the blood. Creatinine exits your body as a waste product in urine. A measurement of creatinine in your blood or urine provides clues to help your doctor determine how well the kidneys are working [18].

Procedure:

To measure the creatinine levels in blood sample, 2 ml of blood was collected in a serum separating tube and centrifuged for 10 minutes. After centrifugation, the upper serum portion of the sample was analyzed using the Cobas c311 to detect creatinine level.

Glomerular filtration rate test:

Principle

Kidneys are the body's main organs of filtration system. They remove waste products from the blood and excrete them via urine. The Glomeruli are the small filters inside the kidneys. If the kidneys aren't working properly, glomeruli won't filter as efficiently. The doctor may order a glomerular filtration rate (GFR) test if they suspect that the kidneys aren't working properly. This is a simple blood test [19].

Formula:

$$\text{Creatinine clearance} = \frac{[140 - \text{age (years)}] \times \text{LBW (kg)} \times 1.23 \text{ (if male) (mls/min)}}{\text{Serum creatinine (umol/L)}}$$

RESULTS

In this case-control study, a total of 100 of chronic kidney disease confirmed patients of both males and females were included in which males were 70%(n=70) and females were 30%(n=30) as Shown in Figure (1). Age ranges from 20 to 80 years with a mean and standard deviation of 40.6 ±16.2. The minimum age was 21 years and the maximum age was 80 years. Shown in table 4.1.

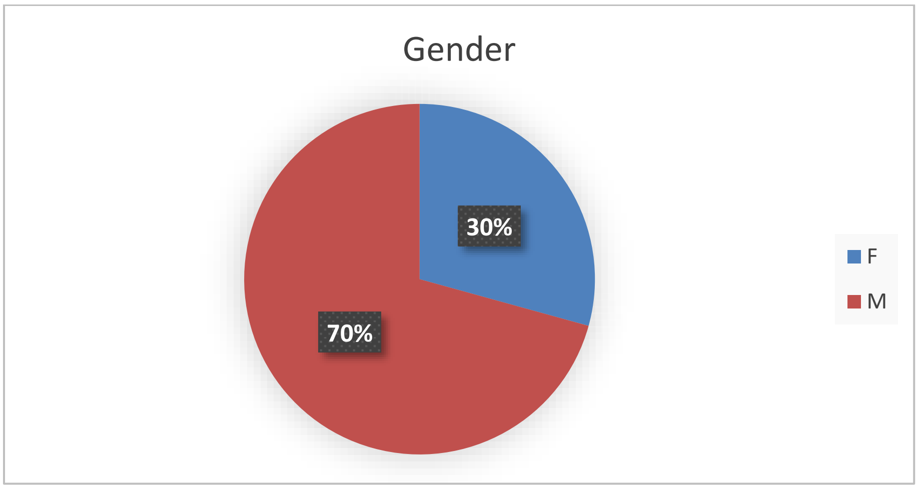

Figure 4.1: Gender wise distribution of chronic kidney disease patients.

Table 4.1: Distribution of CKD patients according to age and gender of case.

Age	Male	Female	Total (%)
21-40	41	19	60 (60%)
41-60	17	07	24(24%)
61-80	12	04	16(16%)
Total	70	30	100(100)

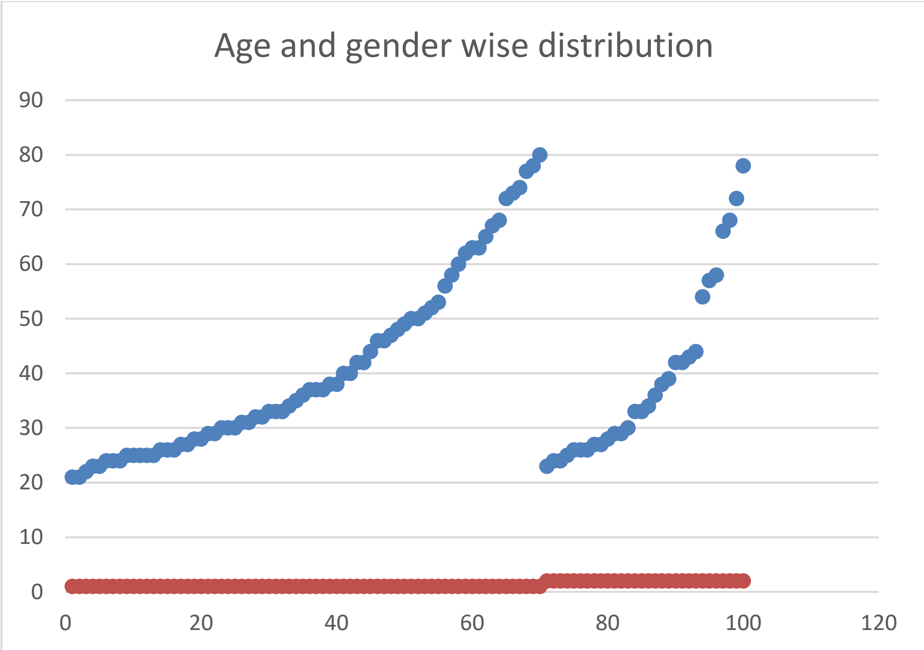

Figure 4.2: Age and gender wise distribution.

In the study, the most common CKD patients in males were aged between 40-60 years, and female were 21-40 years shown in the figure (2).

The normal value for creatinine was 0.7-1.3 mg/dl, urea 20-40 mg/dl, Hb% gm/dl, sodium (Na) 135-145 mmol/l, potassium (K) 3.6–5.2 mmol/l, chloride (Cl) 95–105 mmol/l, erythrocyte sedimentation rate (ESR) 0 – 15 ml/h, Estimated glomerular filtration rate (eGFR) 60–120 ml/m.

The descriptive studies showed that creatinine has a minimum value of 1.5 mg/dl and a maximum is 17.8 with a mean and standard deviation of 8.7±3.3 indicating variation in kidney among the CKD individuals. The urea has a minimum value of 53 and a maximum is 468mg/dl, with a mean and standard deviation of 15.6±3.3, Hb% have minimum value is 5.7 and the maximum value is 13.6, with mean and standard deviation is 9.73±1.49 This shows variability in blood oxygen-carrying capacity among the individuals, sodium (Na) have minimum value is 132 and the maximum is 149 mmol/l, with mean and standard deviation is 140.5±3.0, potassium (k) have minimum value is 2.0 and the maximum value is 3.2 with mean and standard deviation is 2.6±33, chloride (Cl) have minimum value is 96 and the maximum value is 105, with mean and standard deviation is 99.3±10.0, Estimated glomerular filtration rate (eGFR) have minimum value is 2 and maximum value is 58, with mean and standard deviation is 9.8±9.5 pointing to diverse kidney function across the population, erythrocyte sedimentation rate (ESR) have minimum value is 6 and maximum value is 56, with mean and standard deviation is 17.8±8.8 suggesting differences in inflammatory or infection responses among the individuals. shown in Table (2).

Table 4.2: Descriptive statistics of Case study

S. No	Variables	Minimum	Maximum	Mean	SD
1	AGE	21	80	40.64	16.295
2	CREAT	1.5	17.8	8.706	3.3600
3	HB%	5.7	13.6	9.732	1.4943
4	Na	132	149	140.58	3.079
5	K	2.0	3.2	2.626	.3335
6	Cl	3	105	99.39	10.012
7	GFR	2	58	9.80	9.579
8	ESR	6	56	17.58	8.873

Results show that most investigated parameters show a significant difference between the case and control groups. Patients with CKD have higher levels of creatinine and urea, which point to reduced kidney function. In comparison, their hemoglobin levels are lower, which means anemia brought on by renal disease. In addition, the eGFR, which calculates renal filtration rate, is considerably lower in the CKD group than in the control group. Lower potassium levels are also seen in the case group, which may be related to compromised renal excretion. The observed variations in potassium levels further suggest that CKD patients may be at risk for electrolyte imbalances. Additionally, the minor rise in ESR raises inflammation in CKD patients, underscoring the significance of taking care of these other health issues. The levels of salt and chloride show only modest changes between the two groups shown in Table (3).

Table 4.3: Frequency Distribution of Biochemical and Hematological parameters among CKD patients and control group.

S. No	Parameter	CKD mean and SD	Control Mean and SD
1	Creatinine(mg/dl)	8.71±3,36	0.89±.19
2	Urea (mg/dl)	151.6±67.4	30.97±1.33
3	Hb% (gm/dl)	9.37±1.49	13.14±1.33
4	Sodium (mmol/l)	140.58±3.07	140.35±2.23
5	Chloride(mmol/l)	100.29±2.44	101.05±2.44
6	Potassium(mmol/l)	2.63±.33	4.09±.30
7	eGFR (ml/m)	9.8±9.57	111.12±30.55
8	ESR (ml/h)	17.58±8.87	14.27±2.62

The Friedman two-way analysis shows that a significant correlation in chronic kidney disease (CKD) with a p-value is p< 0.05. There strong association between renal function low hemoglobin (Hb%) and reduce Estimated glomerular filtration rate (eGFR). In electrolytes, sodium (NA) has increased with reduced potassium (K) levels. Show significant association in kidney disease (CKD) is Shown in Table (3).

DISCUSSION

Chronic kidney disease is characterized by continuous reduction in glomerular filtration rate (GFR) thus by estimating GFR we can diagnose an unknown person with stages of chronic kidney disease (CKD) [20]. This toxic waste products needs to be filtered out by our kidneys otherwise its increase level leads to accumulation of various nitrogenous metabolites in the blood including urea and creatinine [21]. In this study, the mean level of urea and creatinine among study patients was high respectively which were significantly high in patients with CKD as compared to control. Similar study was done by Amin and and Khasawnah [22, 23] in which they observed that urea and creatinine levels in patients with CKD were significantly elevated. Creatinine is generated from creative with the aid of non-enzymatic dehydration. Creatinine is synthesized in our body at a continuous manner and is excreted from our body through kidney glumerular filtration unit. Reduced kidney function can have an effect on the rate at which creatinine is filtered by means of the kidneys and may be used as a measure of kidney function. Due to inability of kidney to clear creatinine through urine excretion, kidney function deteriorates which results in increased levels of creatinine in blood serum [24]. Urea is the major end product of protein catabolism in maximum animals it is produced in a sequence of reactions in the liver referred to as the urea cycle. In the urea cycle, ammonia is transformed to urea, which is carried by means of blood to the kidneys for its elimination from the body. Elevated levels of urea within the blood may additionally indicate renal failure. Accumulation of urea and creatinine concentrations in blood of CKD patients leads the body very un-wellness excreted from the blood streams through kidneys [25]. In the present study, the serum sodium level was normal and potassium level was decreased in cases. The mean value of serum sodium and potassium in controls were 140.35±2.23 mmol/l and 4.09±.30 mmol/l respectively. chloride level was normal in both cases and control. Estimation of electrolytes should be frequently completed in CKD patients to avoid delay in correction of dysnatremias which might also cause serious complications and increase the frequency of morbidity and mortality among CKD patients [26]. In their study located statistically nonsignificant decreased in serum sodium inside the CKD patients as compared to controls. As we are aware of the fact that the kidneys are principally responsible for the maintenance of fluid and electrolyte balance, acute or chronic changes in renal function can result in various imbalances [27]. Severely, the rapidity of beginning of renal deterioration makes nursing evaluation and intervention critical to the prevention of complications and potentially fatal outcomes. Our data showed the combination of diabetes and hypertension is the main lead among the risk factors of CKD followed by chronic glomerulonephritis, Anemia, Fluid and electrolyte imbalance, Malnutrition and weight loss [28]. The major factor for reduction of these red blood cell parameters is impaired erythropoietin production along with other factors that suppress marrow erythropoiesis and shortened red cell survival. Erythropoietin is the hormone which regulates red blood cell production and maintain the viability of RBC by retarding the cleavage of DNA [29]. In the absence of erythropoietin, DNA cleavage is rapid and leads to cell death. In CKD due to impaired production of erythropoietin and destruction of red cells Hb and Hct concentration fall which is evident even in patients with mild to moderate renal insufficiency. In this study Erythrocyte sedimentation rate (ESR) was high which a simple diagnostic tool for estimating systemic inflammation as similar study was by van [30] and the finding correlated to other studies conducted on level of ESR in CKD patients which have reported 75% to 100% prevalence of raised ESR in CKD patients.

CONCLUSIONS

This study concluded that CKD patients have high range of biochemical parameter of urea and creatinine, and low eGFR reports compare to healthy individuals. The range of erythrocyte sedimentation rate (ESR) of CKD positive patients was increased sometime as compared to healthy individual while range of hemoglobin (Hb%) of CKD positive patients was decreased as compared to healthy individuals. The range of sodium and chloride were normal but potassium level was lowered as compare to healthy individuals. To control these abnormalities close monitoring of renal profile, therapeutic medication under the supervision of physicians, Regular intake of sufficient fluid are very mandatory.

References

1. Elendu, C., Okah, M.J., Fiemotongha, K.D., Adeyemo, B.I., Bassey, B.N., Omeludike, E.K. and Obidigbo, B., 2023. Comprehensive advancements in the prevention and treatment of diabetic nephropathy: A narrative review. Medicine, 102(40), p.e35397.
2. Kalantar-Zadeh, K., Jafar, T.H., Nitsch, D., Neuen, B.L. and Perkovic, V., 2021. Chronic kidney disease. The lancet, 398(10302), pp.786-802.
3. Goncalves, S., Pecoits-Filho, R., Perreto, S., Barberato, S.H., Stinghen, A.E., Lima, E.G., Fuerbringer, R., Sauthier, S.M. and Riella, M.C., 2006. Associations between renal function, volume status and endotoxaemia in chronic kidney disease patients. Nephrology Dialysis Transplantation, 21(10), pp.2788-2794.
4. Sanni, M. and Verdolini, E., 2022. Eco-innovation and openness: Mapping the growth trajectories and the knowledge structure of open eco-innovation. Sustainable Futures, 4, p.100067.
5. Rumano, M., Elezi, B. and Rumano, E., 2021. Biochemical and Hematological Parameters in a Group of Chronic Kidney Disease Patients in Albania. The Eurasia Proceedings of Health, Environment and Life Sciences, pp.39-45.
6. Prabhu, S.R., 2023. Imbalances in Fluids and Electrolytes, Acids and Bases: An Overview. Textbook of General Pathology for Dental Students, pp.111-114.
7. Mehmood, H.R., Khan, Z., Jahangir, H.M.S., Hussain, A., Elahi, A. and Askari, S.M.H., 2022. Assessment of serum biochemical derangements and associated risk factors of chronic kidney disease. Journal of Taibah University Medical Sciences, 17(3), pp.376-383.
8. Habib, A., Ahmad, R. and Rehman, S., 2017. Hematological changes in patients of chronic renal failure and the effect of hemodialysis on these parameters. Int J Res Med Sci, 5(11), pp.4998-5003.
9. Luyckx, V.A., Tuttle, K.R., Garcia-Garcia, G., Gharbi, M.B., Heerspink, H.J., Johnson, D.W., Liu, Z.H., Massy, Z.A., Moe, O., Nelson, R.G. and Sola, L., 2017. Reducing major risk factors for chronic kidney disease. Kidney international supplements, 7(2), pp.71-87.
10. Singh, S. and Bhatta, S., 2018. Biochemical and hematological parameters in chronic kidney disease. Journal of Manmohan Memorial Institute of Health Sciences, 4(1), pp.4-11.
11. MUSA, M. M. I. (2021). A TECHNICAL REPORT ON STUDENT INDUSTRIAL WORK EXPERIENCE SCHEME (SIWES) (Doctoral dissertation, DEPARTMENT OF MICROBIOLOGY, BAYERO UNIVERSITY, KANO).
12. Fares, A. K. (2001). Performance evaluation of two haematology analysers: The Sysmex KX-21 and the Beckman Coulter AC. T diff. Sysmex Journal International, 11(1).
13. Becker, M., Moritz, A., & Giger, U. (2008). Comparative clinical study of canine and feline total blood cell count results with seven in-clinic and two commercial laboratory hematology analyzers. Veterinary clinical pathology, 37(4), 373-384.
14. Tishkowski, K., & Gupta, V. (2023). Erythrocyte sedimentation rate. In Stat Pearls [Internet]. Stat Pearls Publishing.
15. Kahar, M. A. (2022). Erythrocyte sedimentation rate (with its inherent limitations) remains a useful investigation in contemporary clinical practice. Ann. Pathol. Lab. Med, 9, R9-R17.
16. Conlisk, A. T. (2012). Essentials of micro-and nanofluidics: with applications to the biological and chemical sciences. Cambridge University Press.
17. Francis, P. S., Lewis, S. W., & Lim, K. F. (2002). Analytical methodology for the determination of urea: current practice and future trends. TrAC trends in analytical chemistry, 21(5), 389-400.
18. Hameed, I., Rahman, A., Umar, M., Kamal, F.T.Z., Alam, M., Nisar, M., Bano, T. and Manshoor, N., 2023. Preparation of Solanum Virginianum (L.) And Acacia Nilotica (L.) Leaves Methanolic Extracts and Assessment of Their Anti-Inflammatory and Anti-Oxidant Potentials. Journal of Survey in Fisheries Sciences, 10(3), pp.437-441.
19. Akbari, A., Swedko, P. J., Clark, H. D., Hogg, W., Lemelin, J., Magner, P., ... & Ooi, D. (2004). Detection of chronic kidney disease with laboratory reporting of estimated glomerular filtration rate and an educational program. Archives of internal medicine, 164(16), 1788-1792.
20. Ruiz-Ortega, M., Rayego-Mateos, S., Lamas, S., Ortiz, A. and Rodrigues-Diez, R.R., 2020. Targeting the progression of chronic kidney disease. Nature Reviews Nephrology, 16(5), pp.269-288.
21. Romagnani, P., Remuzzi, G., Glassock, R., Levin, A., Jager, K. J., Tonelli, M., ... & Anders, H. J. (2017). Chronic kidney disease. Nature reviews Disease primers, 3(1), 1-24.
22. Amin, T., Mahmood, T., Tariq, A., Naseem, S., &Siddique, K. (2014). Impact of haemodialysis on the removal of excess body waste and hemoglobin level of patients with chronic renal failure. Journal of the Pakistan Medical Association, 64(9), 1024-1027.

23. Khasawnah N, Alrahman Abu Abeeleh JA. Hematological and biochemical findings among Jordanian patient with end stage renal disease. European Scientific Journal. 2015; 11(3): 135-140.
24. Traynor, J., Mactier, R., Geddes, C. C., & Fox, J. G. (2006). How to measure renal function in clinical practice. Bmj, 333(7571), 733-737.
25. Salmean, Y. A. (2013). The effects of added fiber to the diets of chronic kidney disease patients on quality of life, clinical markers and, gastrointestinal and kidney function. University of Florida.
26. Suresh M, Mallikarjunareddy N, Sharan B Singh M, Hari Krishna Bandi, Shravyakeerthi G, Chandrasekhar M. Hematological Changes in Chronic Renal Failure. International Journal of Scientific and Research Publication 2012; 2(9):1-4.
27. Chambers, J. K. (1987). Fluid and electrolyte problems in renal and urologic disorders. Nursing Clinics of North America, 22(4), 815-826.
28. Thomas, M. C., Brownlee, M., Susztak, K., Sharma, K., Jandeleit-Dahm, K. A., Zoungas, S., ... & Cooper, M. E. (2015). Diabetic kidney disease. Nature reviews Disease primers, 1(1), 1-20.
29. Koury, M.J., 2014. Abnormal erythropoiesis and the pathophysiology of chronic anemia. Blood reviews, 28(2), pp.49-66.
30. van Atteveld, V.A., Van Ancum, J.M., Reijnierse, E.M., Trappenburg, M.C., Meskers, C.G. and Maier, A.B., 2019. Erythrocyte sedimentation rate and albumin as markers of inflammation are associated with measures of sarcopenia: a cross-sectional study. BMC geriatrics, 19, pp.1-8.