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Assessment of Haematological Markers in Relation with Blood Urea Nitrogen and Serum Creatinine in Pre-dialysis Patients with Chronic Kidney Disease

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ABSTRACT

Background: *To investigate the hematological and biochemical parameters in pre – dialysis chronic kidney disease (CKD) patients and compared with the normal individuals. Methods: The samples of CKD patients (n= 30) belong to both genders were collected from different tertiary care hospitals of Karachi, Pakistan and compared with normal individuals (n = 30) not suffering from any disease used as control.* ***Results:*** *18 of CKD patients and 19 from normal groups were male and 12 from CKD and 11 from normal group were female. The average age (yr) was 38 ± 12.06 for normal group and 44 ± 09.10 for CKD. The mean height (cm) of normal subjects was 163 ± 6.87 and body weights (kg) were 71.04 ± 10.12. Mean height of CKD group was 165.3 ± 7.79 and weights were 64.35 ± 12.23. Higher magnitudes of blood urea nitrogen (BUN) and serum creatinine were found as 85.63 ± 56.11 and 6.86 ± 3.42 mg/dL respectively in CKD group. Hemoglobin, red blood cells (RBCs), pack cell volume, lymphocytes and eosinophils were found significantly (p<0.01) very low while white blood cells, monocytes and neutrophils were found high (p<0.01) in CKD patients.* ***Conclusions****: Findings concluded that hematological parameters were severely affected in CKD patients as compared to normal controls. Kidney dysfunction in turn not only affects the erythropoietin synthesis that normally stimulates the bone marrow to produce RBC's but also the synthesis of rennin and Vitamin D that normally regulates blood volume and blood pressures and involves in making bones respectively.*

Key words: *Chronic kidney diseases, Hematological parameters, Blood urea nitrogen.*

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INTRODUCTION

Progressively growing chronic kidney diseases (CKD) is a worldwide public health problem. Different biochemically and physiological linked intermediary metabolisms as well as mechanisms of body are dependent on the essential and effective functioning of kidney. The deviation of glomerular filtration rate (GFR) from the normal functioning is among the major contributor of CKD and kidney failure.[1,2] The threat of this health problem is markedly increasing in the world including Pakistan is a big victim of this problem because of its escalating risk factors CKD especially adopting sedentary life-style, diabetes, hypertension, etc.[3, 4] Numerous scientific literatures from past archives provide

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evidences that chronically persistent kidney problems not only decrease the quality of life but also finally lead to the mortality.[5] Biochemical markers are important to investigate different pathological conditions because they appropriately depict the significant association with the metabolic processes of the body.[6] Similarly, preliminary assessment of hematological parameters provide indication of any kind of dysfunction going on in biological system like the investigation relevant with white blood cell count (WBC) worked as a strong indicator of the defense mechanism of the biological machinery.[7, 8] Whereas, level of hemoglobin is also use to evaluate the anemic profile of biosystems, hematocrit (HCT) or packed cell volume (PCV) is referred as the integral part of human complete blood count that provides the concentration or amount of volume (space) of red blood cell (RBC) in blood due to this PCV is also termed as Erythrocyte Volume fraction (EVF).[8,9] In hematological reporting three indices of RBC provide complete status, it includes; mean cell volume or mean corpuscular volume (MCV) is quantification of the red blood cells (RBC) size that use to classify types of anemia (as microcytic, normocytic or macrocytic anemia) in anemic or associated pathological problems.[7] Mean corpuscular hemoglobin (MCH) is the mean mass of conjugated protein containing heme residue (hemoglobin) per erythrocyte cell and also use to distinguished anemic profile of patients[10], and mean corpuscular hemoglobin concentration (MCHC) is the determination of the magnitude of hemoglobin in a given volume of packed red blood cells.[10,11] The smallest cells platelets (thrombocytes) are important blood clotting markers, the increase in thrombocytes count increases the blood clot in vessels and increases the chance of arthrosclerosis and other related diseases.[7,12] Differential leucocytes count provides a broad picture about the working capacity of immune system, major types of WBC with their values helps in the diagnosis of different infection, allergies or toxicities related to drugs or chemical compounds.[7]

Assessment of renal kidney function can mainly be determined by the blood urea nitrogen test (BUN), which reflects the amount of urea (nitrogen) in blood therefore BUN is an important test to assess the kidney efficiency.[6,13] Similarly, kidney maintains the normal creatinine level in the body but in case of pathologies related to the abnormal kidney functioning elevated levels of creatinine always found [13-15] Present study was undertaken to investigate the BUN and creatinine markers with relation to hematological parameters in pre - dialysis CKD patients. In future, a country wide sampling and investigation related to CKD patients will perform to strengthens and validate the current findings.

METHODS

Study Population and Study Site

The current study was conducted in Department of Biochemistry, University of Karachi from July 2012 to June 2014 with the approval of departmental research committee (DRC) which regulates all ethics in animal and human trials according to the international guidelines. The sample of (n=30) population were collected from chronic kidney diseases (CKD) patients belong to both gender from different tertiary care hospitals of Karachi. Informed verbal consent was taken from study subjects before taken the samples, with an assurance for confidentiality of information and their other details. Test samples were run against the blood collected from normal subjects (n=30), which were not suffering from any type of diseases. CKD patients in this study were included with following criteria.

Inclusion Criteria

Patients of either sex have recently diagnosed chronic kidney disease with no past dialysis treatment. Control subjects have no diagnosed disease or not suffering from any kind of disorders were included.

Exclusion Criteria

Pregnant and lactating women, children, patients with any kind of cancers, HIV infected, burns ward, muscle problems, autoimmune disease, prostatic association, or those patients that have any record of bleeding disorders were excluded.

Biochemical Analysis

From the blood samples of all patients, sera was separated and used to analyze biochemical parameters including blood urea nitrogen (BUN) and serum creatinine on Beckman Coulter AU 480 completely automated, random access Clinical chemistry analyzer.

Hematological Analysis

Complete blood profile of all patients includes hemoglobin (Hb) estimation, Packed Cell Volume (PCV), Mean Corpuscular volume (MCV), Mean Corpuscular Hemoglobin (MCH), Mean Corpuscular Hemoglobin Concentration (MCHC), Erythrocyte count (RBC), Leucocytes (WBC) and its differential count (Neutrophils, Lymphocytes, Eosinophils, Monocytes,) and Platelets (PLTs) counts were performed by the *automated Analyzer, Sysmex (XS-1000i)*.

Statistical Analysis

The data were analyzed by student's t-test through *Graphpad* Software, Quick calcs Online Calculators for Scientists. Differences were considered significant with $p \leq 0.05$. Values are expressed as mean ± standard deviation (SD).

RESULTS

Study subjects

Among thirty (n=30) normal individuals nineteen (n=19) were male and eleven (n=11) were females. Eighteen (n=18) male and twelve (n=12) females were included in CKD patients. The demographic profile of both groups (normal individual and CKD patients) is shown in Table 1. Average age in years of normal individuals was 38 ± 12.06 and for CKD patients this range was of 44 ± 09.10. Mean height (cm) of normal individual was 163 ± 6.87 with average body weight (kg) of 71.04 ± 10.12 and for CKD group this range was in between 165.3 ± 7.79 cm with average body weight of 64.35 ± 12.23 kg with recently diagnosed CKD and have no previous dialysis treatments (Table 1).

Biochemical Parameters

There was marked elevated level of BUN observed in CKD patients while a sustained and significant decrease ($p<0.01$) in the same parameter was observed in normal controls. BUN level in both male and female gender CKD patients were observed individually to signify the findings, it was validated that in both gender of CKD group there was marked increase ($p<0.01$) in BUN levels as compared with normal control (Table 2). Similarly, high values of serum creatinine observed in CKD group as compared with normal subjects. Both male and female CKD patients showed significantly ($p<0.01$) increased level of serum creatinine, while both included gender of controls represents its values in normal range (Table 2).

Hematological Profile

RBC count of normal patients was increased while in CKD patients it was reduced. It was also validated that both gender subjects of CKD patients have reduced RBC count, hence it represents a significant ($p<0.01$) decreased in erythrocyte quantity (Table 3). WBC quantity of CKD patients was increased significantly ($p<0.05$) as compared with the normal subjects. The PLTs count in CKD subjects is lowered significantly ($p<0.01$) as compared with the normal subjects (Table 3). The Hb levels of (Table 3) CKD patients were markedly decreased ($p<0.01$) in both male and female subjects, while a cumulative total represents that half of its level decreased as compared to control group. Similarly, there was much decrement ($p<0.01$) observed in PCV level of CKD patients while these findings were much improved in normal controls. Gender based assessment of PCV also confirmed these findings. MCV of both CKD and normal subjects has sustained levels. MCHC was decreased in CKD patients and this significant ($p<0.01$) reduction was also confirmed the individual comparison of male and female CKD patients with normal individuals. A significant reduction ($p<0.01$) in MCHC ($p<0.01$) levels was observed in CKD patients as compared with normal controls (Table 3).

Differential Leucocytes Count

There was a much reduction ($p<0.01$) observed in percent lymphocytes and eosinophilic counts of CKD patients as compared with normal subjects. Whereas percent neutrophils and monocytes levels were much elevated in CKD subjects and this marked ($p<0.01$) increment were also individually confirmed in both male and female CKD subjects, however it was significantly ($p<0.01$) improved in normal subjects (Table 4).

Table. 1. Demographic Profile of Study Subjects

Characteristics	Normal Control	Chronic Kidney Patients
Male	19	18
Women	11	12
Average Age in years	38 ± 12.06	44 ± 09.10
Mean Height in cm	163 ± 6.87	165.3 ± 7.79
Average Body weight (Kg)	71.04 ± 10.12	64.35 ± 12.23
CKD	Nil	Diagnosed
Co-morbid disease	No	Diabetes, hypertension, idiopathic

DISCUSSION

Kidney - the vital organ of the body perform variety of functions, besides being involve in removing the waste products from the blood, kidneys are also play a major role in the formation of many other important hormones such as erythropoietin (EPO), renin and calcitriol (1,25 dihydroxy-vitamin D). Many developing countries are facing a silent epidemic of chronic kidney disease.[16] CKD progression include not only to kidney failure but also complications of reduced kidney function and increased risk of other pathological problems such as bone resorption, cardiovascular disease, etc and all-cause mortality overall, although patients with CKD are far more likely to die, principally from cardiovascular disease, than to develop kidney failure.[5]

Investigations based on previous researches clearly established risk factors for kidney diseases.[1] The baseline-adjusted predictor of developing CKD included age, glomerular filtration rate, hematuria, hypertension, diabetes, serum lipids, obesity, smoking status, and consumption of alcohol.[1,5,17,18] Diabetes and hypertension are strong predictors for the development and progression of chronic kidney disease.[19] It seems likely that the underlying risk factors for atherosclerosis, such as obesity, physical inactivity, smoking and alcohol consumption, might also predict the risk of chronic kidney disease.[19,20] Physical activity has been associated with a lower rate of nephropathy and renal dysfunction.[21] The initial conventional treatments includes diuretics that effects different parts of nephrons like loop diuretics, osmotic diuretics such as mannitol, drugs that alter the pH of urine including ammonium chloride, sodium citrate, potassium citrate and drugs that alter the excretion of organic molecules like probenecid, sulfinpyrazone [15] but in severe cases dialysis and kidney transplantation has to be recommended.[22]

Glomerular filtration rate (GFR) is considered as best indicator of renal function in health and disease states. As GFR is difficult to measure in clinical practice, thereby estimating serum creatinine, uric acid and urea are more approachable markers to asses kidney function.[23] Although these can be affected in other conditions like concentration of urea can be increased by high protein diet, creatinine in muscular dysfunction, uric acid in gout/ arthritis.[6,13] In addition, globally well-spread chronic condition diabetes also alter the concentration of all these three parameters. [3] Thus, a reduction in GFR along with increase in serum uric acid and creatinine levels indicating chronic kidney disease.[14,23] The aim of this research was to study the biochemical and hematological parameters in CKD patients. Selected biochemical parameters including blood urea nitrogen (BUN) and serum creatinine levels were used to select CKD patients that showed above 20 and 2 mg/dL respectively. However hematological parameters including hemoglobin (Hb), packed cell volume (PCV), red blood cells (RBCs), lymphocytes (L) and eosinophils (E) were found significantly low and monocytes (M) and neutrophils (N) were found high in CKD patients ($p<0.01$). Mean cell

Table 2: Biochemical Parameter in Normal and CKD Patients

Parameter	Control Group			CKD Group		
	Male	Female	Total	Male	Female	Total
Blood Urea Nitrogen (mg/ dl)	17 ± 8	15 ± 7	15.50 ± 4.76	116.33**± 60.36	48.80**±14.41	85.63** ± 56.11
Serum Creatinine (mg/ dL)	1.3 ± 0.7	1.0 ± 0.4	1.05 ± 0.18	7.98** ± 4.06	5.52** ± 2.12	6.86** ± 3.42

Values are mean ± standard deviation, ***p* ≤*0.01* when compared with normal subjects.

Table 3: Hematological Parameter in Normal and CKD Patients

Parameter	Control Group			CKD Group		
	Male	Female	Total	Male	Female	Total
Haemoglobin (g/dL)	15.75 ± 1.51	13.25 ± 1.51	14.50 ± 2.45	8.56**± 1.94	8.74**± 0.88	8.64 **± 1.48
Red Blood Cells (10^{12}/L)	5.5 ± 1.0	4.8 ± 1.0	4.80 ± 0.62	2.98**± 0.68	3.11**± 0.46	3.05**± 0.56
White Blood Cells (10^9/L)	6.30 ± 3.14	7.90 ± 3.98	7.50 ± 2.44	10.63 ± 4.38	9.78 ± 7.94	10.25 ± 5.92
Platelets (10^9/L)	290.12 ± 89.19	354.40 ± 76.67	300.00 ± 108.01	283.66 ± 124.04	180.40 ± 66.97	212.18 ± 102.04
PVC (%)	45.3 ± 3.2	41.2 ± 4.0	42.50 ± 6.45	26.71**± 5.40	27.48**± 2.82	27.06**± 4.23
MCV (Fl)	90 ± 6	89 ± 6	88.50 ± 5.33	90.10 ± 6.02	89.06 ± 8.79	89.62** ± 7.02
MCH (Pg)	30 ± 2	30 ± 2	30.00 ± 2.23	28.66 ± 1.19	28.30 ± 2.32	28.50 ± 1.70
MCHC (%)	34 ± 1	33 ± 1	33.25 ± 1.22	31.96 ± 1.88	31.90 ± 2.15	31.93 ± 1.90

Values are mean ± standard deviation, ***p* ≤*0.01* when compared with normal subjects.

Table 4: Differential Leucocytes Count in Normal and CKD Patients

Groups	Neutrophills (%)	Lymphocytes (%)	Eosinophills (%)	Monocytes (%)
Normal Patients	55 ± 9.09	35 ± 9.0	3.50 ± 1.87	4 ± 1.58
Chronic kidney Patients	72.90** ± 15.63	17** ± 13.13	2.27** ± 1.35	7.82** ± 4.07

Volume (MCV), mean cell hemoglobin concentration (MCHC), platelets and white blood cells (WBCs) were not found statistically significant though MCV and WBCs were high in CKD patients.

Therefore, it has been concluded that hematological parameters were severely affected in CKD patients as compared to normal. Kidney dysfunction in turn affects the synthesis of erythropoietin, rennin and Vitamin D because of which not only it affects the synthesis RBCs in bone marrow and become the major cause of anemia but also it effects blood volume & blood pressure that also increases the risk of cardiovascular diseases. In addition, as vit D synthesis is affected thus bone rigidity may also severely affected and may become one of the causes of osteoporosis. Anemia is a common, recognized complication of CKD and was previously considered as a late complication of CKD when the GFR falls below 60 ml/min or at stage 3.[1,18,24] An important aspect of the management of anemia in patients with CKD is a careful assessment of iron status.[24] There is strong evidence that development and progression of CKD are outcomes of exposure to cardiovascular disease risk factors.[19] There is convincing evidence that CKD can be prevented or its progression delayed, if effective management is initiated on time. Hence, identifying patients with CKD and providing prompt intervention play an important role in appropriate management of CKD.

CONCLUSION

Therefore, it has been concluded that hematological parameters were severely affected in CKD patients as compared to normal. Kidney dysfunction in turn affects the synthesis of erythropoietin, rennin and vitamin D which not only affects the synthesis RBCs in bone marrow and become the major cause of anemia but also alter blood volume & blood pressure. In addition, bone rigidity may also severely be affected and may become one of the causes of osteoporosis.

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