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RESEARCH ARTICLE

Hematological disturbances associated with chronic Kidney Disease and kidney transplant patients

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Abstract

The present study was focused on the double comparison of hematological disturbances in the patients suffering from chronic kidney disease (CKD) & in kidney transplant (KT) patients as compared to normal healthy individuals, as these disturbance remains considered as a frequent complication, associated with morbidity and mortality causing decline in quality of life.

This observational study included 20 subjects with CKD at different stages of the disease, 20 of kidney transplant patients and 20 healthy adults were recruited into the study. The complete hematological profile including Hemoglobin, CBC count, differential WBC count and Absolute indices were examined using automated Hemato-analyzer.

The results showed that the differences between the mean of RBCs, Hb and PCV were significantly lowered both in chronic kidney disease patients and in kidney transplant patients, similarly MCH and MCHC indices also decreased significantly in both the types of patients however no change was observed in MCHC level in kidney transplant patients. WBC count increased in CKD patients and slightly increased in kidney transplant patients but not statically significant, the differential WBC count like lymphocytes decreased in both types of patients but Monocytes decreased in CKD and increased in kidney transplant patients and platelets, MCV and granulocytes were normal in both types of patients.

In conclusion, the present study suggests altered hematological profile in both experimental groups and the increase in disturbances depicts the severity of illness in chronic kidney disease and kidney transplant patients.

Introduction

Chronic kidney disease (CKD) is considered as a rapidly growing global health problem, characterize by progressive destruction of renal mass with irreversible sclerosis and loss of nephron. In case of end-stage renal disease and/or chronic renal failure, Kidney transplantation is a treatment of choice for patients through a surgical procedure to take over the task of purifying the blood and remove the waste materials (Wasti AZ et al., 2013; Strom T. et al., 1994).

The Kidney Disease Outcomes Quality Initiative designates 5 stages of CKD, with stage 5 being ESRD, the point at which patients' loss of kidney function need dialysis or kidney transplant. Patients at higher risk for CKD include patients with diabetes, hypertension, or a family history of hypertension, diabetes, or CKD (Peter WL. et. al., 2007). Most people with chronic kidney disease die of a co-morbid condition, usually cardiovascular disease, before experiencing complete kidney failure requiring dialysis or transplantation. However, the onset and progression of chronic kidney disease are highly preventable, and early treatment of complications can significantly improve long-term patient outcomes (Sarah L. et al., 2008).

Hematological disturbance such as anemia is considered as a frequent complication occurs in chronic kidney disease and is associated with morbidity and mortality and a decline in quality of life. (Weiss G et al., 2005). The severity of anemia is directly proportional to the degree of renal function. One of the important aspects of chronic kidney disease management is the correction of anemia and the maintenance of hemoglobin level by using (ESA) Erythropoietin–stimulating agents. Furthermore, the measurement of erythropoietin levels is useful only for anemic patients with hemoglobin levels of <10 g/dl. However, any interpretation of an erythropoietin level in anemia of chronic disease with a hemoglobin level less than 10 g per deciliter must take into account the degree of anemia. (Aronoff GR et. al., 2009)

Muirhead N *(*1999) has reported that after transplantation, the hemoglobin (Hb) levels will generally increase but in patients with a graft that functions sub optimally anemia can persist. Fatema K et al., (2013) have reported that the prevalence of these anemic patients is 38.6% however, 25% were suffering from severe anemia, meaning their hemoglobin value is less than 11 or 10 g/dl for males or females, respectively. In allograft recipients, several factors are known to induce anemia such as sepsis, CMV, prophylactic and immunosuppressive agents, ACE inhibitors, kidney injury during the transplantation procedure, poor graft function, and surgical problems in the recipient after transplantation.

Anemia may also negatively affect long-term outcome in kidney transplant recipients, moreover, in patients who undergo dialysis, it has been linked to the development of left ventricular hypertrophy, and is believed to be a major contributor to cardiovascular risk. In post-transplant recipients, anemia may also be a cardiovascular risk factor and is particularly worrying because these cardiovascular events are known to be the main cause of death in transplant recipients (Vanrenterghem Y. et al., 2003; Vincenti F. et al., 2003).

Several factors have been found to affect hemoglobin variability, including those that are drug related, such as pharmacokinetic parameters, patient-related differences in demographic characteristics and factors affecting the clinical status, as well as clinical practice guidelines, treatment protocols and reimbursement policies.

Iron deficiency contributes to anemia after transplantation besides other causes of anemia in renal transplant patients. The main cause of iron deficiency anemia after renal transplantation is linked to some factors like blood loss during dialysis, regular blood sampling prior to transplantation, blood loss during the operation, bleeding due to abnormal coagulation and rarely due to postoperative gastrointestinal bleeding (Zheng S. et al., 2009). Additionally the magnitude of iron loss from blood loss in the pre-transplantation period has not been quantified. In majority cases anemia is diagnosed by lowering hemoglobin which can be defined as "A condition in which blood is deficient in red blood cells, hemoglobin or in total volume" so low hemoglobin means that the patient has anemia.

Approximately 15 to 20% of maintenance dialysis patients had average hemoglobin levels <11 g/dl ± 1.1 to 1.3 g/dl (SD), although average hemoglobin levels have steadily increased, may be due to the introduction of ESA. Moreover, the recommended target hemoglobin levels ranged between 11 to 12 g/dl, according to the National Kidney Foundation (KDOQI)-Kidney Disease Outcomes Quality Initiative guidelines, Whereas hemoglobin >13 g/dl should be avoided since it may be associated with poor clinical outcomes several in Chronic Kidney Diseases. Additionally the target range between 10 and 12 g/dl remains unchanged according to the recent expert review established by the Food and Drug Administration, because hemoglobin variability (both low and high hemoglobin levels) seems to be associated with increased death risk (Aronoff GR et. al., 2009).

The present study plan to evaluate the hematological disturbances which may appears more frequently in the patients suffering from chronic kidney diseases and kidney transplant patients.

MATERIALS AND METHODS

The blood samples of kidney disease patients were collected from different kidney and Urology clinics and hospitals from all over Karachi-Pakistan, and compared them to the normal healthy individuals (n=20). Automated Hemato-analyzer (ABX-Micro 60) was used to determined hematological parameters, including hemoglobin, hematocrit, RBC and differential counts and absolute indices. The cell viability was performed to determine the number of apoptotic and non-apoptotic cells by differential count, in chronic Kidney Disease and transplant patients.
However, 20 apparently healthy and non smoking subjects were selected at random used as controls to compare the result. Patients suffering from conditions such as diabetes mellitus, hypothyroidism, liver or kidney disease and a history of familial dyslipidemia were excluded from the study.
Statistical analysis was performed using standard statistical software (SPSS version 16.0). All data are expressed as mean ± SD. The data were also tested using student's t-tests; the significance level was set as $p < 0.05$.

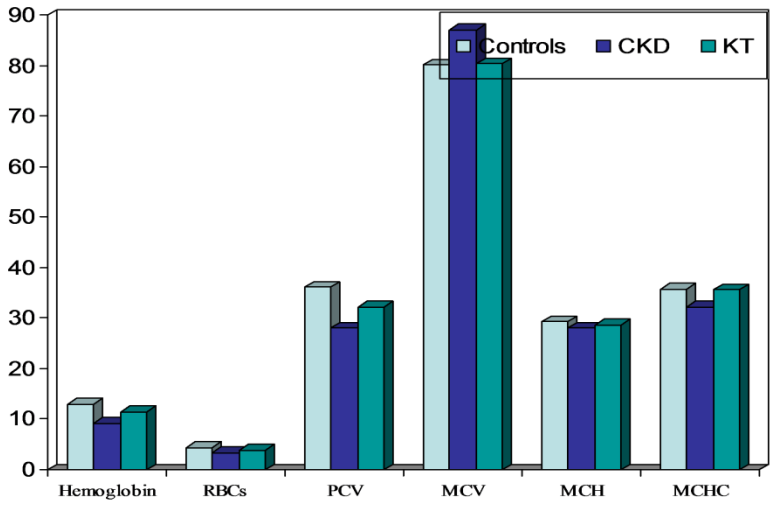
RESULTS

The present study was based on the analysis of hematological indices in kidney transplant patients and chronic kidney disease patients.

Table-1 shows the differences in hematological and absolute blood indices in both the experimental groups - CKD & kidney transplant patients as compared to normal healthy controls. Significant ($p>0.0001$) decrease was observed in the Hemoglobin and RBCs count in both CKD & kidney transplant patients as compared to the control group. The PCV level was significantly ($p>0.0001$) decrease in both CKD & kidney transplant, while MCHC level in CKD patients was observed to be significantly decreased ($p>0.0001$) but not significant in kidney transplant patients. A slightly significant decrease was observed in MCH level in CKD patients as compared to the control group however, this decrease was not significant in kidney transplant patients. MCV did not show any significant difference in both CKD & kidney transplant patients (Figure-1).

Table-2 depicts the differences in WBCs and differential counts in both the experimental groups. WBCs count was observed to be a significant increase ($p>0.001$) in both CKD and in kidney transplant patients as compared to the normal group. The Lymphocyte count was decreased in both CKD & kidney transplant patients while the Monocytes count was significantly ($p>0.00001$) decreased in CKD patients when compared to control group however, was significantly increase in kidney transplant patients. The Granulocytes count did not show any significant differences in both CKD & kidney transplant patients. The platelet count did not show any significant differences both in kidney transplant patient and CKD patients as compared to control group.

Figure-1 Comparison of hematological profile in Chronic Kidney Diseases & Kidney Transplant patients Vs Normal controls**.**



Hb- hemoglobin (g/dl), RBC- Red blood cell concentration ($10^3/mm^2$), PCV-Packed cell volume (%), MCV-Mean cell volume (fl), MCH-Mean cell hemoglobin (pg), MCHC- mean cell hemoglobin concentration (%),WBC-White blood cell concentration ($10^3/mm^2$).

TABLE 1: Comparison of Hematological/Absolute Indices in Chronic Kidney Diseases & Kidney Transplant patients as compared to controls.

Parameters	Controls	Chronic Kidney Disease Patients	Kidney Transplant Patients
Hemoglobin (g/dl)	12.985±0.901	9.225±2.355	11.435±1.692
RBCs ($\times 10^3$/mm ^{3})	4.406±0.391964	3.3715±0.6633	3.929±0.6832
PCV (%)	36.170±3.338	28.075±7.223	32.170±5.690
MCV (μm^3)	80.15±3.937	87.125±12.15	80.40±8.65
MCH (Pg),	29.355± 1.583	28.100± 4.212	28.710 ±3.599
MCHC (gm/dl)	35.765± 1.440	32.165± 1.348	35.780± 2.191

TABLE 2: Comparison of Differential Indices in Chronic Kidney Diseases & Kidney Transplant patients as compared to controls**.**

Parameters	Control	Chronic Kidney Disease Patients	Kidney Transplant Patients
WBCs ($\times 103/mm^3$)	6.955±1.145	9.080±3.162	8.300±3.584
Lymphocytes (%)	32.875±6.894	27.500±13.567	27.650±7.538
Monocytes (%)	10.100±1.168	6.995±3.913	17.870±5.132
Granulocytes (%)	59.155± 7.654	63.70 ±15.203	55.455± 9.721
Platelets ($\times 10^3/mm^3$)	258.60±73.31	290.80±120.18	253.25±119.33

DISCUSSION

Chronic kidney disease is a major public health problem and a major cause of morbidity and mortality worldwide. CKD is diagnosed on the basis of presence of markers of kidney damage and kidney function. This study was done to assess the hematological profile in CKD and to assess the impact of various renal replacement therapies on the hematological profile including the hemoglobin, red blood cells, and mean cell hemoglobin. White blood cells count with differential count was also performed.

Significant alterations were observed in the hematological profile in the present study, depicts the severity of hematological side effects in both chronic kidney disease and kidney transplant patients. Consistent with the finding of Alghythan K. et al., (2012), the RBCs count, Hb and PCV levels in CKD patients, were significantly lower as compared to their healthy controls. 23% decrease was observed in RBCs count in patients suffering from chronic kidney diseases while 10% decrease observed in kidney transplant patients as compared to their respective controls, suggesting anemia.

The hemoglobin level in chronic kidney disease patients decreased is 28.9% and in kidney transplant patients is 11.9% as compared to that of control group however, the level of PCV decreased in chronic kidney disease patients is 30.6% and in kidney transplant patients in 11% as compared to that of control group further confirmed the presence of anemia.

This decrease in RBC count and Hb attributed to anemia because kidney secrete hormone called erythropoietin which makes red blood cells and whenever any kidney disease occur the red blood cells count decrease and anemia developed. (Alghythan AK et al., 2012). It may be due to iron deficiency which may occurs when iron stores are depleted as a result of loss or decreased intake; however, functional deficiency occurs when there is a need for a greater amount of iron to support hemoglobin synthesis than can be released from iron stores, reported by (Koshy S. et al., 2007)

Classically, the anemia in chronic kidney disease has been uncomplicated as the morphology of RBC remains unchanged or normocytic normochromic, predominantly because of an erythropoietin deficiency (Arun S et al., 2012).

EPO deficiency and iron deficiency are the leading causes regardless of dialysis status. Other causes contributing to anemia in CKD patients are inflammation, chronic blood loss, hyperparathyroidism, aluminum toxicity, hemoglobinopathies, vitamin deficiencies (B12 and folate), hemolysis and adverse effects of cytotoxic or immunosuppressive drugs and Angiotensin converting enzyme inhibitors.

These studies also suggest that the of MCH level as measured in this study showed statistically significant decreased in chronic kidney disease patients is 4.2% and decreased in kidney transplant patients is 2.1% as compared to that of control group is, the decreased in MCH reflects not only decreased in hemoglobin synthesis but also in the size of the cell. The MCHC level decreased in chronic kidney disease patients is 10% however, did not show not show any difference in kidney transplant patients but the decrease in MCHC in CKD patients would reflects the decreased of saturation of hemoglobin in the cell as a result of the iron i.e. hypochromia. The study also showed that there were no significant differences between mean of MCV both in chronic kidney disease and in kidney transplant patients. Pereira R. et al., (2010) reported similar observations though but they did not find any significant change in the MCH value while Malyszko J et al., (2001) reported similar results from their studies.

The findings of this study also indicated the differences between the mean of WBCs and differential counts i.e. the WBCs count increased in chronic kidney disease patients is 29.8% which is due to many reasons like Anemia, Bone marrow tumors, Infectious diseases, Inflammatory disease, Leukemia, Tissue damage however, slightly increased was observed in kidney transplant patients (19.35%) but not significant.

The Lymphocytes count also decreased in CKD patients 16.3% and was also decreased in kidney transplant patients is 15.8% our results in contrast to the finding of the study done by Agarwal R et al., (2011), where a majority of the patients had a normal lymphocyte count. The decreased in lymphocytes count may be due to chronic infections, severe stress (Hyperadrenocorticism), kidney failure, or prolonged use of gluco-corticoid (Cortisone) injections.

The monocytes count decreased in chronic kidney disease patients is 30.7% however, it was marked increased in kidney transplant patients 76.9% , this increase in Monocytes in kidney transplant patients showing that they are activated in these patients, which may be due to chronic infection of the stomach, tuberculosis or a chronic inflammation condition like inflammatory bowel disease and malignancy or an abscess and in chronic kidney disease decrease count usually non significant (Alghythan AK. et al., 2012).

The granulocytes count did not show any significant changes in both chronic kidney disease & in kidney transplant patients. The finding of this study also indicated that platelet count did not show any change in both the experimental groups.

CONCLUSION

We suggests the use of stringent hematological testing in the patients suffering from Chronic kidney disease and in kidney transplant, in order to decrease morbidity and mortality related with this disease conditions. It is also concluded that in chronic kidney patients, impaired erythropoietin because as high as 90% of erythropoietin is produced in the juxta glomerular apparatus of the kidney while 10% are produced in the liver and other organs. The severity of affectation depends on the stage of renal failure. Changes in red cell indices are due to a number of factors aside erythropoietin productions, deficiencies of iron, vitamin B12 and folate as a result of nutritional insufficiency or due to increased blood loss are contributory factors. Shortened red cell survival, hyperparathyroidism, mild chronic inflammation and aluminum toxicity have also been implicated is the main reason for the decrease in red blood cells count, hemoglobin concentration, packed cell volume and in leukocyte count.

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