ORIGINAL ARTICLE

Evaluation of Iron Studies in patients with Chronic Kidney Diseases

MUHAMMAD RIZWAN HAFEEZ[1], SIBGHA BASHIR[2], UMAIR ARIF[3], *ADEEL ZAFAR[4], SHABZAIN ISHRAT[5], SARA KHAN[6]*
[1]Assistant Professor Medicine,
[2]Assistant Professor Chemical Pathology,
[3]Assistant Professor Medicine, QAMC/BVH, Bahawalpur
[4]Assistant Professor of Pathology,
[5]Senior Demonstrator of Pharmacology, Shahida Islam Medical & Dental College, Lodhran
[6]Assistant Professor Chemical Pathology, CMH Medical, Bahawalpur
Correspondence to Dr. Muhammad Rizwan Hafeez Email: drrizwanhafeez@gmail.com

ABSTRACT

Aim: To analyze different types ofbiomarkers, primarily serum iron, serum ferritin and total iron binding capacity of the patients, who have been diagnosed with chronic kidney diseases.
Study design: Cross sectional study
Place and duration of study: Shahida Islam Medical & Dental College, Lodhran during June 2018 to January 2019.
Methods: The data was collected from those patients who visited the OPD of the hospital regularly for dialysis process. Ten millilitres of blood was collected from participants of this study for serum creatinine, erythrocyte sedimentation rate (ESR), serum iron, TIBC, ferritin levels, and TSAT. Estimated glomerular filtration rate (eGFR) was calculated using modification of diet in renal disease.
Results: These patients were in CKD stage 3-5. The age of the patients ranged from 15 to 79years. Diabetic nephropathy, hypertension and chronic glomerulonephritis found to contribute 37(54.4%), 19(27.9%) and 9(13.2%) cases respectively. Two patients had lupus nephritis (2.9%). One patient had autosomal dominant polycystic kidney disease (1.5%). There was a significant difference between Hgb concentration (8.71±2.70 vs. 12.93±8.7, *P*<0.001) and packed cell volume (26.64±12.17 vs. 38.05±6.11, *P*<0.001) between the predialysis CKD and control groups.
Conclusion: Conclusively, it can be explained that in order to perform detailedinvestigation of patients with chronic kidney diseases or on dialysis, regarding the presence of iron deficiency, it is essential that they must project the patient to aforementioned diagnostic procedures.
Keywords: Evaluation, Chronic kidney disease, Diagnosis

INTRODUCTION

Among the most widely prevalent diseases and the life-threatening conditions, Anemia is also considered as one of such diseases which is widely responsible for inducing multiple number of other diseases within patients because of its association with several mechanisms going within the body. In particular, patients with chronic kidney diseases are also more prone towards development of iron deficiency among them as a risk factor associated with anemia. The core objective of this research study is to find out the relationship between reduced levels of iron within the patients of chronic kidney failures, or patients with dialysis and what are some of the methods and markers which are useful for diagnosing the patients with iron deficiency because of kidney diseases[1].

Anemia is one of the most common and prevalent underlying disease which is associated with chronic kidney diseases in patients. However, before the advent and introduction of erythropoietin stimulating agents ESA's, erythropoiesis was considered as the primary factor and reason for causing anemia in the patients with chronic kidney diseases. However, after multiple researches and new innovations in this field, it has been analyzed that along with erythropoiesis, numerous other factors are responsible for causing anemia in patients with chronic kidney disease. One of such conditions is disturbed and disruptive hemodynamics of iron metabolism and absorption in patients with CKD. Since, one of the major and most prevalent types of anemia is iron deficiency anemia, which leads to malabsorption and production of iron within the patients which leads to reduced levels of iron within the patients. This leads to lack of iron to a great extent in these patients, and this might be associated with number of other diseases and occurrence of serious incidents, which might even lead to death. However, in such conditions, it is essential to regularly monitor and evaluate the markers which represent iron deficiency among the patients so that it could be rapidly detected, and patients could be provided with the medication treatment accordingly[2].

Some of the biomarkers which are used to detect the condition of iron deficiency among patients with chronic kidney diseases are ferritin, transferrin and Total Iron Binding Capacity (TIBC). With the help of these markers, it can be easily detected the conditions of a patient, and how anemia can be treated by providing them the respective therapy and medication treatment to reduce the underlying symptoms and diseases from the patient's body[3].

Received on 24-05-2019
Accepted on 13-12-2019

PATIENTS AND METHODS

This cross sectional study was conducted in Shahida Islam Medical & Dental College, Lodhran during June 2018 to January 2019. This study was done with the approval of ethical committee of hospital. The data was collected from those patients who visited the OPD of the hospital regularly

for dialysis process. Inclusion criteria were newly diagnosed CKD patients or those on conservative management who were ≥18 years of age and gave informed consent to participate in the study while exclusion criteria were CKD patients on renal replacement therapy (RRT) and those with HIV infection, hemoglobinopathies, chronic infections, malignancy, history of cigarette smoking, use of erythropoiesis-stimulating agents, iron products, or history of blood transfusion in the previous four weeks to the time of evaluation for study. Ten millilitres of blood was collected from participants of this study for serum creatinine, erythrocyte sedimentation rate (ESR), serum iron, TIBC, ferritin levels, and TSAT. Estimated glomerular filtration rate (eGFR) was calculated using modification of diet in renal disease. The data was analyzed through SPSS-20.

RESULTS

These patients were in CKD stage 3-5. The age of the patients ranged from 15 to 79 years. Diabetic nephropathy, hypertension and chronic glomerulonephritis found to contribute 37(4.4%), 19(27.9%) and 9(13.2%) cases respectively. Two patients had lupus nephritis (2.9%). One patient had autosomal dominant polycystic kidney disease (1.5%). There was a significant difference between Hgb concentration (8.71±2.70 vs. 12.93±8.7, *P*<0.001) and packed cell volume (26.64±12.17 vs. 38.05±6.11, *P*<0.001) between the predialysis CKD and control groups. The ESR and serum ferritin levels were significantly higher in the predialysis patients than the controls (*P*<0.001). There was no statistical difference in the mean values of the serum iron, TSAT, and TIBC between the CKD and control groups. The mean serum creatinine was significantly higher in the CKD group compared to the control group (3.28±2.75mg/dL vs. 0.90±0.78mg/dL; *P*<0.001) while the mean eGFR in the CKD patients was significantly lower compared to the control group.

Fig. 1: ROC curve of group A

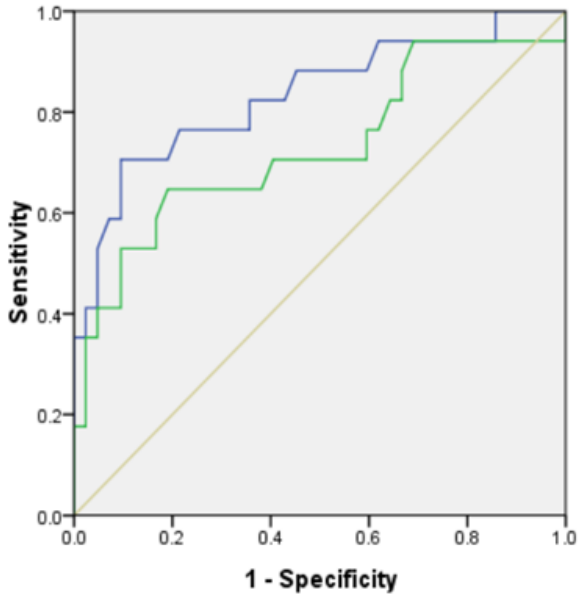

Fig. 2: ROC curve of group B (control)

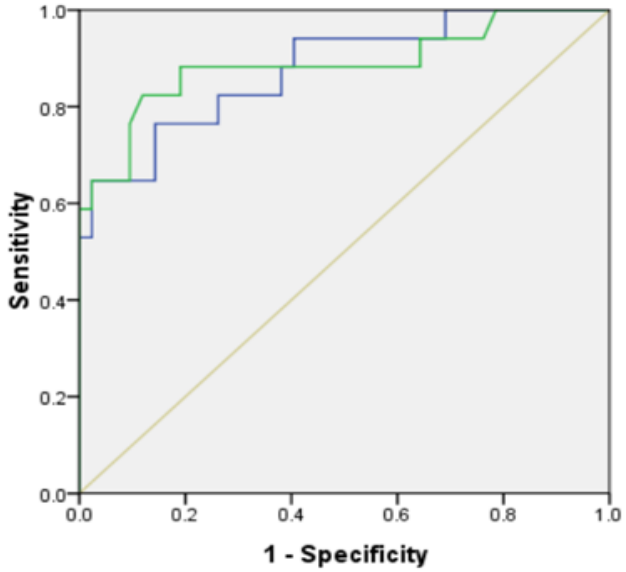

Table 1: Hematological indices of chronic kidney disease and control groups (*n* =190).

Variable	Predialysis CKD patients	Controls	P value
Hb concentration (g/dL)	8.71±2.70	12.93±8.7	<0.001
Packed cell volume (%)	26.64±12.17	38.05±6.11	<0.001
ESR (mm/h)	51.99±32.74	17.50±8.59	<0.001
Serum iron (µg/dL)	101.67±57.16	99.47±34.77	0.752
Serum ferritin (ng/mL)	223.23±121.90	158.82±68.06	<0.001
TIBC (µg/dL)	281.05±238.01	259.91±78.20	0.422
TSAT (%)	45.94±45.83	46.95±48.17	0.882
Creatinine (mg/dL)	3.28±2.75	0.90±0.78	<0.001
eGFR (mL/min/L73m^2)	35.74±26.26	114.19±41.24	<0.001

CKD = Chronic kidney disease, Hb = Hemoglobin
ESR = Erythrocyte sedimentation rate, TIBC = Total iron binding capacity, TSAT = Trasnferrin saturation

DISCUSSION

According to multiple researches and discoveries, it has been investigated that Anemia is one of such conditions which mainly occurs due to disruption and errors in three natural mechanisms of human bodyEither it occurs because of reduced production of endogenous erythropoietin, oreduced survival rates of erythrocyte. Additional condition is decreased levels of natural nutrition's among patients which are folate or vitamin B12. Since many years, the primary treatment which had been provided to the patients with chronic kidney diseases for the treatment of anemia was regular blood transfusion. However, there were multiple drawbacks and adverse effects associated with blood transfusion to the patients, which mainly include dependence on external sources for blood requirements, as well as due to rapid and frequent transfusion of blood in the patients, it also leaded to over load of iron withinpatients' body. In addition, the free radicals of iron were also considered as poisonous and dangerous for patient's health leading to severe hazardous effects. In order to reduce the dependency on blood transfusion for patients with CKD, an additional treatment had been introduced by the researchers, which is known as recombinant human erythropoietin (rHuEpo). However, the transfusion of recombinant human erythropoietin also

leaded to occurrence of certain adverse events in patients like damaging the other cells through their free radicals as well as being the oxygen carrier, due to which most of the oxygen supply had been diverted to fulfill their requirement, resulting in reduction of oxygen supply to other organs of the body[4].

In healthy and young individuals, the iron production and homeostasis is usually maintained by the seminescnet erythrocytes, in which the cells are being deteriorating or become older and weak, the iron which is released from these cells are then taken back to the bone marrow through the reticuloendothelial system, where it readily gets absorbed in the bone marrow and then combines with erythroblasts. In addition, normal iron homeostasis is also maintained and balanced with the help o the process of absorption of iron from the daily dietary nutrition provided to the human body and this iron is then being stored and transported to the bone marrow for further processing. However, in patients with dialysis or chronic kidney diseases conditions, usually patients are meant to go through regular blood replacement, filtration and transfusion in dialysis which is a great mode of excessive iron loss from patient's body. In addition, there are certain condition in chronic kidney diseases due to which there is malabsorption of iron in gastrointestinal tract of the patient. Thus, usually in patients with chronic kidney disease there is a severe loss and lack of iron, which might also be referred to as natural iron deficiency and it leads to blockage of iron fromreaching to the site of erythroblast production. Even if iron is present inexcessive amount and stored within the body in their respective reserves, it is unable to reach to the site of production of erythroblast due to blockade of reticuloendothelial cell iron[5].

Thus, conclusively, because of the multiple mechanisms and pathways for iron deficiency and reduced iron absorption in patients with CKD, it somehow becomes difficult and complex for patients with CKD to diagnose the real pathway and root cause for iron deficiency among patients with Anemia. This leads to challenges in diagnosing the respective biomarkers of iron deficiency for patients with CKD. The core objective and primary focus of this research study is to focus upon the levels and evaluation of serum iron, serum ferratin and Total Iron Binding Capacity of an individual, so that levels for each of these biomarkers can be analyzed and based on these readings and findings, the right kind of therapeutic treatment can be provided to the patients[6].

CONCLUSION

Conclusively, it can be explained that in order to perform detailed investigation of patients with chronic kidney diseases or on dialysis, regarding the presence of iron deficiency, it is essential that they must project the patient to aforementioned diagnostic procedures. The primary functions and process involved in leading to anemic condition for a patient is reduced erythropoiesis. In addition, the iron absorption of patients from the dietary intake and nutrition also decreases which leads to reduced levels of iron in patient's body. Moreover, patients who are on dialysis, has to go through blood transfusion and filtration of the blood from their entire body regularly, which also leads to reduced levels of iron and loss of iron radicals from their body.

REFERENCES

1. Andriopoulos B Jr, Corradini E, Xia Y, et al. BMP6 is a key endogenous regulator ofhepcidin expression and iron metabolism. Nat Genet 2009; 41:482.
2. Aoun M, Karam R, Sleilaty G, Antoun L, Ammar W. Iron deficiency across chronic kidney disease stages: Is there a reverse gender pattern?. PLOS ONE 2018;13(1):e0191541.
3. Babua C, Kalyesubula R, Okello E, et al. Cardiovascular risk factors among patients with chronic kidney disease attending a tertiary hospital in Uganda. Cardiovasc J Afr 2015; 26:177-80.
4. Cases A, Egocheaga M, Tranche S, Pallarés V, Ojeda R, Górriz J et al. Anemia of chronic kidney disease: Protocol of study, management and referral to Nephrology. Nefrología 2018;38(1):8-12.
5. Collins AJ, Li S, St Peter W, et al. Death, hospitalization, and economic associationsamong incident hemodialysis patients with hematocrit values of 36 to 39%. J AmSocNephrol 2001; 12:2465.
6. Gaweda A. Markers of iron status in chronic kidney disease. HemodialysisInt2017;21:S21-S27.
7. Iyawe IO, Adejumo OA, Iyawe LI, Oviasu EO. Assessment of iron status in predialysis chronic kidney disease patients in a Nigerian Tertiary Hospital. Saudi J Kidney Dis Transpl 2018;29:1431-40
8. Macdougall I. Intravenous iron therapy in patients with chronic kidney disease: recent evidence and future directions. ClinKidJ2017;10:i16-24.
9. Macdougall I, Bircher A, Eckardt K, Obrador G, Pollock C, Stenvinkel P et al. Iron management in chronic kidney disease: conclusions from a "Kidney Disease: Improving Global Outcomes" (KDIGO) Controversies Conference. KidInt2016;89(1):28-39.
10. Rambod M, Kovesdy CP, Kalantar-Zadeh K. Combined high serum ferritin and low ironsaturation in hemodialysis patients: the role of inflammation. Clin J Am SocNephrol2008; 3:1691.
11. Reddy GC, Devaki R, Rao P. Iron Indices in Patients with functional anemia in chronic kidney disease. *EJIFCC*. 2013;24(3):129-36.
12. Saxena S, Venkatesan M, Kumar A. Evaluation of iron status in patients of chronic kidney disease - A study to assess the best indicators including serum transferrin receptor assay. Indian JNephrol2019;29(4):248.
13. Thomas DW, Hinchliffe RF, Briggs C, et al. Guideline for the laboratory diagnosis offunctional iron deficiency. Br J Haematol 2013; 161:639.