Estimation of Serum Iron and Ferritin in Patients with Chronic Renal Failure

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Abstract

Background: The incidence of renal failure, and potentially of CRF, is increasing steadily in Sudan. Anaemia is an accompaniment and independent risk factor for the development of cardiac dysfunction along with other complications. It is also responsible for 40-50% deaths in CRF patients. For this reason, the quick and accurate diagnosis of anaemia should help in decreasing the morbidity caused by CRF. The correction of anaemia, e.g. by the administration of iron supplements and/or erythropoietin, should help improving the general outcome of CRF.

methods: Fifty patients with chronic renal failure, already diagnosed clinically and on laboratory basis were selected as a sample group. Another 50 healthy individuals not known to have renal disease were selected as a control group. 5 ml of venous blood was collected in lithium heparin container for iron and ferritin. Concentration of iron was measured by colorimetric method by using SPINREACT™ and serum ferritin by Turbilatex-Ferritin kit. The data obtained were analyzed by using statistical package for social science (SPSS) on programmed computer. **Results:** The mean ± SD of serum ferritin was calculated in patients and controls and it was found 72 µg/L ± 16.2 for patients and 96 µg/L ± 19.7 for controls the (*p-value* 0.000). Also the mean ± SD of serum iron was obtain from patients and controls and was found 41µg/dL ± 29.2 and 87 µg/dL ± 47.5 respectively with (*p-value* = 0.000). There were a weak negative correlation between serum iron and serum ferritin concentrations in patients and controls (R -0.161). **Conclusion:** The study concludes that serum iron and ferritin levels in CRF patients are significantly low in comparison to healthy controls.

Keyword: Ferritin, CRF, Iron

Introduction

CRF is progressive loss of renal function over a period of months to years. High blood pressure and diabetes mellitus are the most important causes of CRF. CRF can lead to cardiovascular disease and anaemia [(1)]. Anaemia is a major and severe haematological complication in these patients. CRF can only be detected

by blood test for creatinine and when it is high it indicates decrease in glomerular filtration rate (GFR) as a result of decreased capacity of the kidney to excrete waste product. Signs and symptoms of kidney failure are hypertension because of increased fluid overload (also leading to swelling and oedema), decrease in calcium level [(1)], metabolic acidosis and erythropoietin synthesis defect which leads to anaemia [(2)]. Anaemia in patients with CRF is due to many factors. Erythropoiesis and iron homeostasis are impaired as a result of a complex chain of events, including the relative deficiency of erythropoietin, chronic inflammation, blood loss, decreased iron absorption and utilization [(3)]. Anaemia is an independent risk factor for the development of cardiac dysfunction like increased cardiac output, cardiac enlargement, left ventricular hypertrophy and congestive heart failure. It also decreases the quality of life and exercising capacity [(4)]. Haeme is an iron-containing porphyrin derivative (an iron chelate of the protoporphyrin IX) that gives haemoglobin its red colour. Functionally, haeme is a prosthetic group for many proteins and enzymes involved in oxygen metabolism and electron transfer reaction. Most (2500mg) of serum iron is bound to the red blood cells haemoglobin, 3mg is bound to transferrin, 500mg is bound to myogloblin and some enzymes (e.g. cytochromes) and 600-1000mg are stored as ferritin or haemosidren [(3)].

Iron is stored inside a protein called ferritin and thus serum ferritin test provides information about the iron level inside the body. Ferritin serves to store iron in a nontoxic form, to deposit it in a safe form, and to transport it to areas where it is required [(5)]. The function and structure of the expressed ferritin varies in different cell types and can be used to diagnose anaemia. The ferritin levels measured have usually direct correlation with the total amount of iron stored in the body. If the ferritin level is low, there is a risk for lack of iron, which could lead to anaemia [(5)]. The normal serum ferritin values are as follow: in children 6 month to 15 years = 7-140mcg/L, in men = 18-270mcg/L and in women = 18-160 mcg/L. Ferritin levels, chronic renal failure, anaemia and their relationship are some of the most researched topics in biomedical field. A study conducted by Khanam *et al.* in Bangladesh (2013) revealed that serum iron & serum ferritin in CRF was significantly low [(6)]. In 2002, Hsu *et al.* published a study on the epidemiology of anaemia associated with chronic renal insufficiency among adults in the USA. The result showed that serum ferritin in 47% of woman and 44% of men was lower than reference value [(7)]. In 2013 Rao *et al.* found that haemodialysis patients had serum ferritin ≥100 mg/L compared to a median patient value of 436 mg/L [(8)]. A Russian study published in 2013 reported a strong correlation between the diastolic dysfunction and left ventricular hypertrophy seen in patients with end-stage renal failure and the severity of renal anaemia. Adequate correction of renal anaemia (and arterial hypertension) has helped in the alleviation of patients' symptoms and it has also resulted in significant reduction in number of cases [(9)].

Materials and methods

This study is a laboratory analytical case control study, which was conducted in Suba University Hospital in Khartoum State, during the period of 3 months. A number of 100 subjects were enrolled in this study, they were classified into two groups, 50 patients already diagnosed clinically and on laboratory basis were selected as a case group. Another 50 healthy individuals not known to have renal disease were selected as a control group. Five mL of venous blood were collected (using 70 % ethanol as skin disinfectant) in lithium heparin. Blood was centrifuged for 3-5 minutes at 4000 rpm/min and plasma was then collected.

Concentration of iron was measured by FerroZine - Colorimetric method. Also the concentration of ferritin was measured by Turbilatex Ferritin methods using SPINREACT™ (manufactured by Spinreact, Santa Coloma, Spain) for iron and ferritin. For internal quality control, normal and pathological control sera were analyzed to monitor the performance of manual assay procedures. The data obtained were analysed by using statistical package for social science (SPSS). T-test was used to compare between control and patients and the results were expressed as (mean ± SD). Also regression analysis was used and the results were expressed as (R) and (R2).

Results

This study was carried out on 50 patients diagnosed as having chronic renal disease and 50 healthy individuals not known of having any renal diseases or a history of other disease.

Table (1) shows comparison of the mean value of serum ferritin level between CRF patients and the control groups. It can be seen there was a significant decrease in serum ferritin in CRF when it was compared with the control group (*p-value* = 0.000).

Table (2) compares the mean value of serum iron in CRF patients and control group, it also shows a significant decrease in serum iron in CRF patients than control (*p-value* = 0.000).

Figure (1) demonstrates a weak negative correlation between serum iron and serum ferritin concentrations in the CRF patients (R= - 0.161).

Table 1: Comparison of mean value of serum ferritin in CRF patients with that in the control group determined by using (Turbilatex-Ferritin) method

T-test	Type	N	Mean	Std. Dev	SEM	P-value
Serum ferritin µg/L	Patients	50	72	16.2	2.1	0.000**
	Control	50	96	19.7	3.4	

P-value less than 0.05 is considered as statistically significant.

**Significant.

Table 2: Comparison of the mean value of serum iron in CRF patients with that in the control group determined by using (FerroZine. Colorimetric) method

T-test	Type	N	Mean	Std. Dev	SEM	P-value
Serum iron µg/L	Patients	50	41	29.2	4.1	0.000**
	Control	50	87	47.5	8.3	

P-value less than 0.05 is considered as statistically significant.

**Significant.

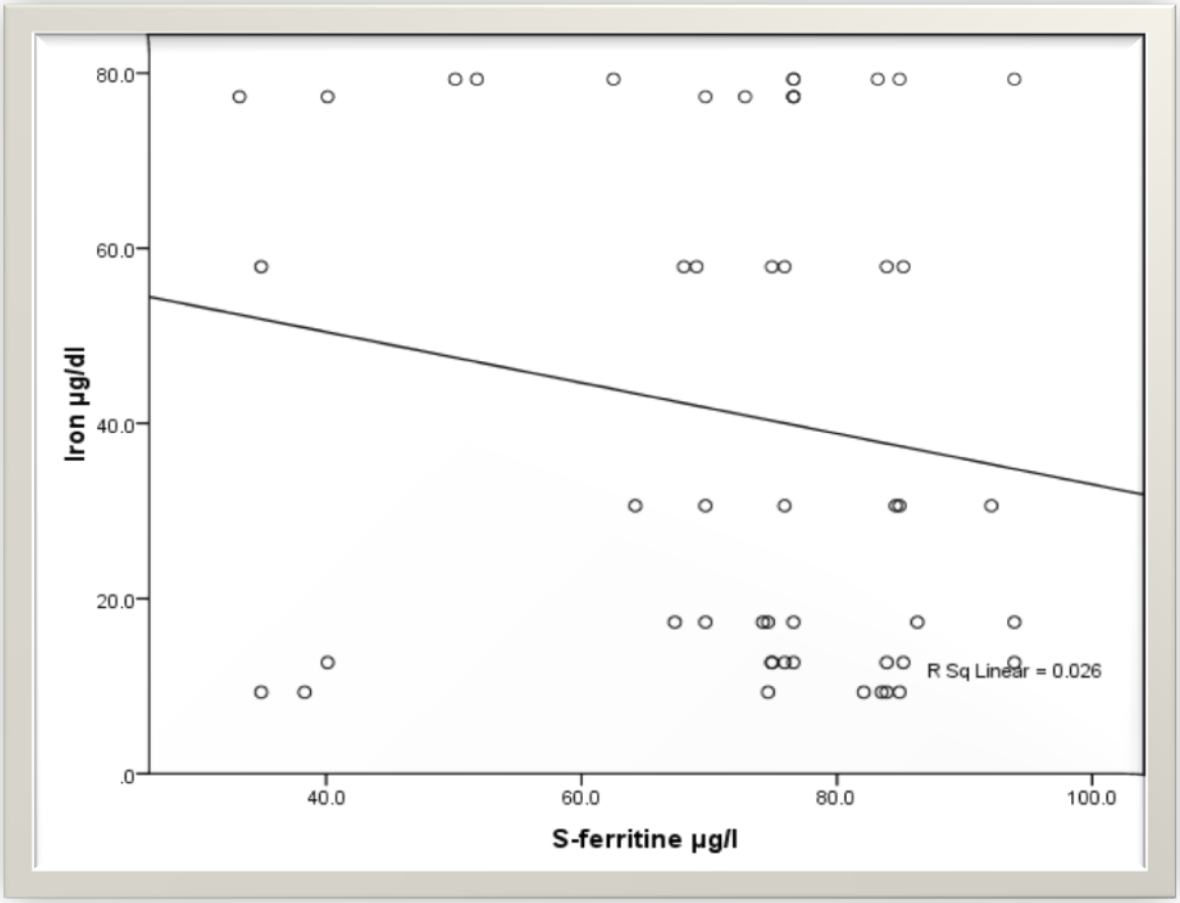

Figure 1: Demonstrates correlation between serum iron and serum ferritin concentrations in the CRF patients

Discussion

Chronic renal failure is a worldwide health problem and a big burden on national health systems. Anaemia is one of the most common complications encountered during the course of the disease. Furthermore, anaemia is a significant risk factor for the development of cardiovascular disease, faster progression of renal failure and decreased quality of life. The present study was undertaken to estimate serum iron and ferritin levels in end-stage renal failure (CRF) patients suffering from anaemia. For this purpose, 50 CRF patients with anaemia were selected as a study group provided that they haven't been put on iron therapy. Another 50 healthy individuals were selected as a control group. The results showed that serum iron levels in CRF patients were significantly lower when compared to healthy individuals, a finding that agrees with results reported by Taralov *et al.* [(10)]. The results of the present study also agree with those of the studies done by Folia *et al.* [(11)], Barry *et al.* [(12)] and Hsu *et al.* who reported that serum iron and ferritin levels were significantly lower in CRF when compared to healthy individuals. Lopez-Sierra *et al.* reported that serum ferritin and serum iron levels were significantly lower in elderly patients hospitalised for chronic diseases when compared to healthy individuals [(13)]. They also concur with Skali *et al.* who found that serum ferritin level was significantly lower in patients suffering already from cardiovascular disease as a result of CRF when compared to healthy individuals [(14)]. A report from Russia showed that serum ferritin levels were significantly

lower in CRF patients when compared to healthy individuals [9]. In addition to the above mentioned studies, the findings of this study concur with Kalantar-Zadeh *et al.* [15], Kaufman *et al.* [16] Milman *et al.* [17], Hutchinson *et al.* [18] Fernandez-Rodriguez *et al.* [19], Patruta *et al.* [20] and Kshirsagar *et al.* [21] who all showed that serum iron and serum ferritin were significantly decreased in patients of CRF. Some conflicting results were obtained by Rao *et al.* [8] and Al-Mukhtar *et al.* [22] and showed that serum ferritin was significantly increased in patients with CRF. This might be due the use of different calculation techniques and the adoption of different cut-off value in their measurements. On the other hand, the results of the present study are similar to the results obtained by, Malovrh *et al.* [23] who used low-dose iron replacement to correct anaemia in haemodialysis patients, Pouresmaeil *et al.* [24] who encountered significantly low levels of iron and ferritin in the course of studying lead levels in haemodialysis patients. In addition, the studies done by Atkinson *et al.* [25], Cuevas *et al.* [26], Rafi *et al.* [27] and Małyszko *et al.* [28], Kalantar-Zadeh *et al*. [29] have all reached similar results. Some researchers suggested that erythropoietin deficiency due to decline in functional renal tissue is a causative factor for decrease in RBC production in CRF patients suffering from anaemia. In addition, they suggested that various factors might be involved in lowering of iron status in patients suffering from CRF associated with anaemia [11]. Some investigators also reported that for the re-establishment of effective erythropoiesis by erythropoietin therapy, it is necessary to ensure sufficiently available iron in patients suffering from CRF [12]. Erythropoietin deficiency is mostly the primary cause of anaemia in CRF. The findings of this study may support the idea that gradual destruction of erythropoietin secreting cells of the kidney in different stages of CRF is the reason behind anaemia, despite the fact that erythropoietin levels in test subjects was beyond the scope of this study. The lowering in serum ferritin occurs in CRF patients is due to changes in iron status and these changes vary with severity of CRF and thus, this may be the reason of the association of severe CRF with chronic infection.

Conclusion

In conclusion, the study shows that serum iron and ferritin levels in CRF patients are significantly low in comparison to healthy controls, most probably due to changes inflicted by CRF and the duration of anaemia. This also indicates the importance of measures that can be taken to correct anaemia (e.g. by erythropoietin) in order to maintain effective erythropoiesis and to achieve target normal level of iron. Further studies should be done to measure serum iron and ferritin levels in different stages of renal failure with large sample size.

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