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Correlation of serum ferritin and proteinuria in patients of chronic kidney disease

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Abstract

Chronic Kidney disease (CKD) is emerging to be an important chronic disease globally. Hypertension and diabetes are the frontrunner causes of these two chronic diseases. Being highly populous country, it can cause damage to the fabric of healthcare and economy. By any imagination 229 per million populations in India are at End Stage Renal Disease (ESRD) and more than I lac new patients enter renal replacement programs annually in India. Because of scarce resources only 10% cases in ESRD receive any renal replacement therapy. Lack of awareness and cost of treatment make it difficult to approach by common man. Serum ferritin, as a marker of iron status in individual with Chronic Kidney Disease (CKD), is also an inflammatory marker. Proteinuria also called albuminuria is condition in which urine contains an abnormal amount of protein. It is a sign of CKD which can result from diabetes, high blood pressure, and the diseases that cause inflammation in kidneys. So protein in the urine forms an essential part of routine medical assessment. In patients with Proteinuria, disturbances in Iron metabolism may occur as consequence of increased urinary excretion of transferrin which is iron binding protein, transferrin. Decreased serum transferrin levels may lead to increased level of free non-transferrin bound iron in the urine which could give rise to free radical mediated lipid peroxidation and ensuing injury of vascular endothelial cells. Within cells iron is stored in complexes with ferritin. Serum ferritin levels are supposed to reflect body iron stores. Elevated levels of ferritin are supposed reflect body iron stores. Elevated levels of ferritin may signal iron overload, as seen in patients with haemochromatosis. The potential role of free iron-mediated endothelial cells cell injury has gained more attention due to recent studies that have incriminated serum ferritin as an independent predictor of coronary artery disease. The present study was aimed to measure correlation of serum ferritin and Proteinuria in patients of chronic kidney disease.

Aims and objectives

1. Measure filtration rate (GFR in patients with chronic kidney disease.)
2. Estimate the level of serum ferritin in chronic kidney disease patients.

3. Estimate 24 hrs urinary protein and / or Microalbumin in CKD patients.

4. Find any correlation between Proteinuria and ferritin according to various stages of GFR.

Keywords: Ferritin, ESRD, CKD, Transferrin, Proteinuria, Hemochromatosis, Endothelial injury

Introduction

Ferritin is the major storage protein found in human tissues. Iron serum concentration tends to increase moderately in the presence of inflammation and the simultaneous combination of these two conditions, also referred to as malnutrition-inflammation-cachexia syndrome is observed frequently in CKD patients. Iron treatment should be withheld in patients with such moderately high ferritin levels. High ferritin levels, especially if combined with low iron saturation ratio, as it is more strongly associated with inflammation than with iron stores. In patients with Proteinuria, serum ferritin levels are elevated with overt Proteinuria. The independent negative relationship between serum ferritin and transferrin points to the process that increased ferritin level may compensate for the loss of transferrin, thus reducing the amount of free iron. In 2004 Fishbane S conducted study on serum ferritin in CKD found that IV iron therapy is a key component of the care of patients and upper level at which treatment is given should be withheld and potential benefits and risks to the patient. In 2004 Amanda JW conducted study on serum ferritin levels are increased in patients with overt Proteinuria. In 2013 Hsu Y.H found that subjects with diabetes with higher ferritin tended to have more metabolic disorders, increased hsCRP and higher levels of micro-albuminuria. In 2013 Wu Hon-Yen conducted screening for CKD in population that targeted screening is cost effective as compared to non-screening.so undergoing doing screening is cost-effective in high risk population of diabetes and hypertension.

Material and methods

The study was conducted in the department of Biochemistry in collaboration with department Medicine at GGS Medical College, Faridkot. A total of 69 patients were enrolled in the study. The patients of liver disease, lung disease and any other diseases that can affect the above parameters were ruled out.10ml of venous blood is taken in a dry disposable syringe under all aseptic conditions from anti- vein in a dry and sterile vial for biochemical analysis. Centrifugation was done at 2000 rpm for 10 minutes to separate the serum. The serum was used for assessment of various investigations. I investigations were done on fully auto analyser and fully automated Chemiluminiscence. Estimation of 24 hrs urinary was done by Biuret method. Serum ferritin was estimated by a solid -phase enzyme labeled Chemiluminiscence immunometric assay. Normal serum values in males are 28-365 ng/ml while in females 05-148 ng/ml was found.

Results and observations

We found the disease in males in majority (Table-1). The study group had average age as 20-65 years.

Table 1: Distribution of patients according to sex and age mean ± SD

Gender And Age	Frequency	Percentage %
F	22	31.9
M	47	68.1
Total	69	100.0
Age 20-65 Yrs.	Mean + SD Years	
	52.52 ±12.85	

As shown in Figure-1, 69 patients were involved in the study, levels of urea and Creatinine were higher (Mean±SD) 165.59±91.40 mg/dl and 6.54±4.33 mg/dl. Blood urea ranges were minimum 52.0 mg/dl and

maximum 451.0 mg/dl. Serum Creatinine showed minimum 1.40 mg/dl and maximum 20.70 mg/dl.

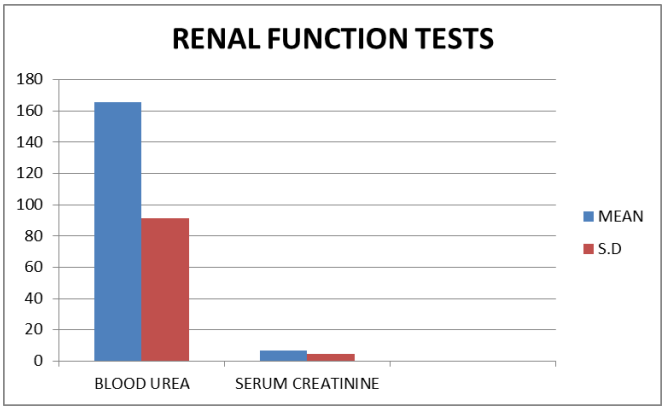

Figure 1

Table 2: estimation of renal function tests

Mean±SD	Mean±SD	Range mg %	
		Minimum	Maximum
Blood Urea mg%	165.59±91.40	52.0	451.0
Serum creatinine	6.54±4.33	1.40	20.70

The Table Shows Mean ± SD Of Blood Urea And Serum Creatinine Levels In CKD Patients

As shown in Figure-2, 69 patients involved in the study, levels of GFR, 24 hours urinary proteins and Ferritin were Mean±SD 19.70±13.91 ml/min, 1.24±0.44 g/day and 641.46±441.21 ng/ml. GFR, 24 hours urinary proteins and ferritin were minimum 3.09 ml/and maximum 56.00 ml/min, minimum range 0.10 g/day and maximum as 2.40 g/day and minimum range 49.0 ng/ml and maximum 1500.0 ng/ml.

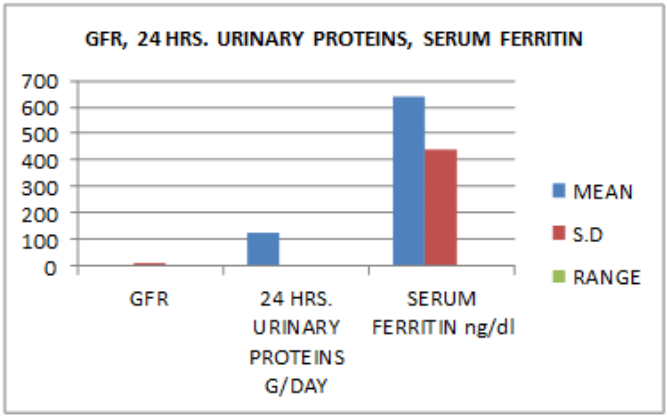

Figure 2

Table 3: Estimation of GFR, 24 hrs. Urinary proteins and serum ferritin levels in CKD patients

Parameters	Mean ±SD	Range	
		Minimum	Maximum
GFR ml/min	19.70±13.91	3.09	56.00
24 HR urinary protein g/day	1.24±0.44	0.10	2.40
Ferritin ng/ml	641.46±441.21	49.0	1500.0

Table 4: Comparison of Various Parameters According To Different GFR

Stages of GFR	Patients (n)	GFR ml/min	24 hrs. Urinary proteins g/day	Creatinine mg/dl	Serum ferritin ng/ml
1	-	-	-	-	-
2	-	-	-	-	-
3	15	42.56±8.48	1.43±0.39	2.31±0.50	393.80±278.7
4	21	19.88±3.46	1.24±0.34	4.35±0.73	510.90±328.95
5	33	9.19±3.64	1.17±0.50	9.86±0.46	837.12±482.29
Total patients	69	19.70±13.19	1.24±0.44	6.54±4.33	641.46±441.21

Table shows variations in parameters according to gfr staging

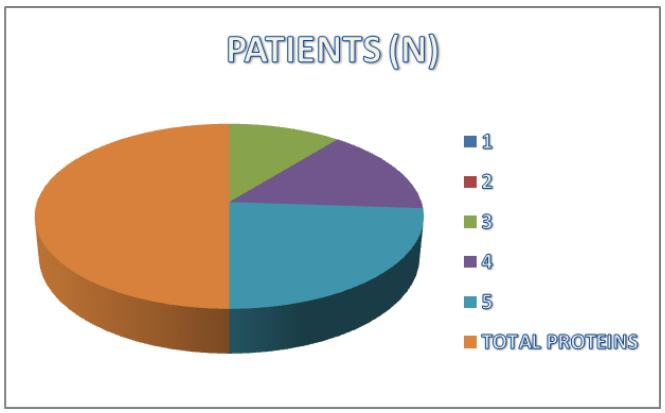

Figure 3: PIE graph: patient's distribution according to stages of GFR

Table 5: Correlation between 24 hrs. Urine proteins and ferritin

Parameters	Pearson correlation (4)	P value	Significance (2-tailed)
24 hrs. Urinary protein g/day	1	0.013	S
Serum ferritin -	0.29		

Table Shows Significant Relationship between 24 Hrs. Urine Protein And Ferritin with P=0.013, R =- 0.29

Discussion

Our data clearly indicate that serum ferritin levels are increased in patients with overt proteinuria. This observation is new and may seem somewhat unexpected in view of the reports that patients with a nephrotic syndrome are predisposed to iron deficiency because of the continued losses of the iron-binding protein transferrin. Further studies are warranted, in particular in view of recent data suggesting a relationship between cardiovascular morbidity/mortality and elevated ferritin levels. The stages of CKD should be based on combined indices of kidney function based (measured or estimated (GFR) on and kidney damage (Albuminuria/Proteinuria) irrespective of the underlying diagnosis e.g stage 2 CKD with microalbuminuria secondary to diabetic nephropathy. In India 60% of the patients suffering from chronic kidney diseases are either diabetic or hypertensive. Lifestyle changes are making it more vulnerable. The present study was carried out in GGS Medical College & Hospital, Faridkot. We enrolled 69 patients between age group 20-65 years. Maximum patients were found in (Table-1) 22 females (31.9%) and 47 males (68.1%) patients. The mean age of study group was (50.11 ±15.45) years. In the present study the renal function (Table-2) were rearranged with mean SD of blood urea as 165± 91.40 and creatinine was 6.54± mg/dl in the CKD patients. Serum creatinine Serum creatinine was significantly increased in (Table-5) as compared to stage 3 and 4. The present study results are also similar to the Study by Noor et al (2014). The Mean±SD of blood urea was 103.87±21.81. The mean of GFR in the study group was 103.87 ±21.69 and that of Creatinine was 6.42 ±1.81 mg/dl. In the study (Table-3) the mean GFR of the study group was 19.70±21.91 mg/dl. GFR was decreased with the disease progression. The mean GFR of the study group was 19.70±13.91ml/dl.GFR significantly as the disease progressed. 24 hrs protein (Table-3) has Mean±SD of 1.24±0.44 grams/day. 24 hrs urinary proteins (Table-4) showed no significant difference according to age. In the present study ferritin levels were found to be 641.46 ±441.21 ng/ml in patients of CKD It was significantly increased in stage 4 and 5 as compared to stage 3 (Table 5).Study of Dorine.W.Swinkles et al (2015) found that ferritin levels were increased in cases of proteinuria. In CKD patients' increased hepatic synthesis cannot compensate loss of smaller albumin losses of proteins transfer and so hypoalbuminemia and hypertransferrinemia of in

patients with proteinuria. However larger proteins as fibrinogen and ∞_2-macroglobulin.As ferritin is also large protein, so it will also rise as the production of liver increases. Kalantar-Zadeh et al in 2005 devised that in patients on hemodialysis serum ferritin levels increased to the range of 500 to 2000 mg/dl. It was found that ferritin level was of limited use in assessing iron stores keeping in view the varied interpretation (Coyne 2006,2008).Study group was divided into different (stages 3,4,5) based on GFR (Table-4). Comparative study was also conducted between stages of ferritin and proteinuria (Table56).

Summary And Conclusion

In present study serum ferritin levels were increased in all patients of CKD. This clearly indicates that inflammation is going on in CKD patients. Ferritin is also positively correlated with proteinuria which further aggravates renal damage. In conclusion, serum ferritin levels are raised in patients with nephrotic range proteinuria. We conclude that the rise in ferritin is on its part is aftermath of an increased non-specific protein synthesis in the liver. Ferritin synthesis is increased to make up for the loss of iron-binding transferrin, and makes up for unopposed free iron. In future the research should do to test our hypothesis and to evaluate the results of elevated ferritin levels in patients with the nephrotic syndrome. This is imperative because of the suggested ferritin related to any other vital comorbidity in heart and circulation.

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