ORIGINAL RESEARCH PAPER
Volume - 11 | Issue - 01 | January - 2022 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

EVALUATION OF SERUM IRON STATUS AND THYROID PROFILE IN PATIENTS OF CHRONIC KIDNEY DISEASE

Biochemistry

Dr. Srirekha. P Assistant Professor, Department of Biochemistry,kurnool Medical College ,kurnool

Dr. R. S. Swaroopa Rani Assistant Professor, Department Of Biochemistry,Guntur Medical College Guntur

Dr. Sarada U. Assistant Professor, Department of Biochemistry,kurnool Medical College ,kurnool

Dr. B. Ravindra Reddy* Associate Professor, Department of Biochemistry, Santhiram Medical College , Nandyal. *Corresponding Author

ABSTRACT

OBJECTIVE: To find the prevalence and association of thyroid dysfunction with anemia/body iron status among Chronic kidney disease patients,
MATERIALS AND METHODS: It is a cross-sectional study conducted in Government General Hospital ,Kurnool during the period from jan 2021-july 2021.. A total of 75 patients were included in our study who satisfied the diagnostic criteria of CKD and patients underwent clinical and renal parameters, haematological profile and iron status. For comparison of the results with the general population adequate number of controls were taken .
RESULTS: Our study results showed that out of the 75 patients with CKD 49 patients had low T3 syndrome which accounts for 65% of the patients, 14 patients had low T4 syndrome) which accounts for 18% of the patients and 12 patients had primary hypothyroidism TSH >20µIU/ml. it was found that nearly 43% of the patients did not have target serum ferritin of 100 ng/ml and 49.2% of study population did not have target TSAT of >20%.
CONCLUSION: The study demonstrates a high prevalence of thyroid abnormalities particularly hypothyroidism, accompanied by increased prevalence of anemia and iron deficiency indicating symbiotic relationship between thyroid gland function and body iron status. Thyroid Dysfunction occurred in the patients with chronic kidney disease, it does not indicate a state of hypothyroidism, but a reflection of the state of chronic illness/malnutrition.

KEYWORDS

chronic kidney disease, ferritin,Hypothyroidism, Anemia, Iron deficiency Anemia

INTRODUCTION

Chronic kidney disease (CKD) encompasses a spectrum of various pathophysiologic processes leading to abnormal kidney function, and a progressive decline in glomerular filtration rate (GFR).The approximate prevalence of CKD is 800 per million population, and the incidence of end stage renal disease (ESRD) is 150- 200 per million population.CKD is a worldwide epidemic associated with a number of comorbidities and hence a disease with high mortality.(1)

Anemia is an early complication of chronic kidney disease (CKD) and causes increased morbidity and mortality.(2) Although the primary defect is decreased erythropoietin production from the kidney, Decreased erythropoietin has recently linked with downregulation of hypoxia-inducible factor (HIF), a transcription factor that regulates gene expression of erythropoietin. a number of other factors may play contributory roles. For example iron, folate, vitamin B12 deficiency due to nutritional insufficiency or increased blood loss from hemodialysis, shortened RBC survival, hyperparathyroidism, mild chronic inflammation and aluminium toxicity,RBC fragmentation by injured renovascular endothelium in selected conditions such as glomerulopathy and malignant hypertension exacerbates the anemia.Early identification and treatment of anemia in CKD may improve cardiovascular morbidity and mortality.(3) Early treatment of anemia in CKD may postpone the onset of ESRD and improve survival.

Thyroid hormones are important for growth and differentiation, and modulation of physiological functions in all the tissues including the kidney. They also play a vital role in water and electrolyte homeostasis.(4).The kidney is responsible for degradation and excretion of thyroid hormones and iodine clearance, so understandably kidney dysfunction will interfere with thyroid hormone levels. CKD affects the hypothalamus pituitary thyroid axis. CKD affects thyroid function in many ways, including low circulating thyroid hormone levels, altered peripheral hormone metabolism, insufficient binding to carrier proteins, reduced tissue thyroid hormone content and altered iodine storage in the thyroid gland. Thus, in CKD, thyroid hormone metabolism is impaired.(5)

The objective of the present study was to see the relationship between chronic kidney disease and thyroid functional status and Serum Iron indices .and also to see the effect of CKD on thyroid hormonal status and to stratify the severity of renal disease by eGFR and to correlate stages of CKD with serum Iron indices,FT3, FT4 and TSH level.

MATERIALS AND METHODS-

This study was conducted at Government General Hospital ,Kurnool during the period from jan 2021-July 2021.. A total of 75 patients were included in our study who satisfied the diagnostic criteria of CKD and patients underwent clinical and renal parameters, haematological profile and iron status.Their GFR was assessed using the Cockcroft and Gault formula. Renal ultrasound scanning was also done in all the patients to look out for features suggestive of CKD.

Inclusion Criteria were:

1. CKD stage 2 to 4 as determined by Cockcroft & Gault Equation: Creatinine Clearance (ml/minute) = (140 – Age) x Weight 72 x Serum Creatinine (mg%) Multiply by a factor of 0.85 for females
2. Age above 18years
3. Patients must not have had renal replacement therapy.

Exclusion Criteria
Patients with:

a. Acute Renal Failure
b. Known Haemoglobinopathies
c. Glucose 6 phosphate Dehydrogenase(G6PD) deficiency
d. Hookworm infestation
e. Dyspepsia.
f. Coagulopathies
g. A history of any form of renal replacement therapy.
h. Pregnancy
I. Lactation
j. Blood transfusion in the preceding 3 months

After selection of patients, fulfilling the above criteria, about 5 ml of blood sample is collected in non-heparinised serum bottleBlood sugar, renal parameters (blood urea, serum creatinine), serum Electrolytes, thyroid profile .

Serum ferritin: The serum ferritin was determined by enzyme linked immunosorbent assay. Iron level was determined by Ferrozine method without deproteinization. Total iron binding capacity (TIBC) was determined by Spectrophotometric Assay.

Transferrin saturation calculated by using formula (TSAT);
TSAT = (serum iron/total iron-binding capacity) × 100.

The approval of the Ethics and Research Committee was obtained.

Statistical Tools

The information collected regarding all the selected cases were recorded in a Master Chart. Data analysis was done with the help of computer using Epidemiological Information Package (EPI 2010) developed by Centre for Disease Control, Atlanta. Using this software range, frequencies, percentages, means, standard deviations, chi square and 'p' values were calculated. Kruskul Wallis chisquare test was used to test the significance of difference between quantitative variables and Yate's chi square test for qualitative variables. A 'p' value less than 0.05 is taken to denote significant relationship.

RESULTS AND ANALYSIS

In our study 75 patients of CKD who were on conservative management fulfilling the criteria for CKD were studied, among these 59 were males and 16 were females, their age varied from 20 - 68 years

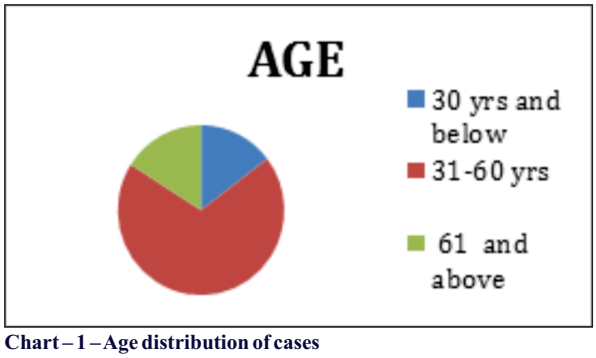

Chart – 1 – Age distribution of cases

Among the 75 patients in our study, patients who were 30 years old and below were 11 constituting 15%, between 31 - 60 years were 52 constituting 69 % and 60 years of age and above were 12 in number constituting 16% Distribution of creatinine clearance in ckd patients

Creatinineclearance (ml/minute	No. of patients	Percentage
<15	44	59
15-30	25	33
>30	6	8

Of the 75 patients, 44 patients had GFR of less than 15 ml/minute accounting to 59%, 25 patients had GFR ranging from 15 – 30 ml/minute accounting for 33% and patients had GFR ranging from more than – 30 ml/minute accounting for 8%. Among the patients studied most were in the range of creatinine clearance <15 ml/minute.

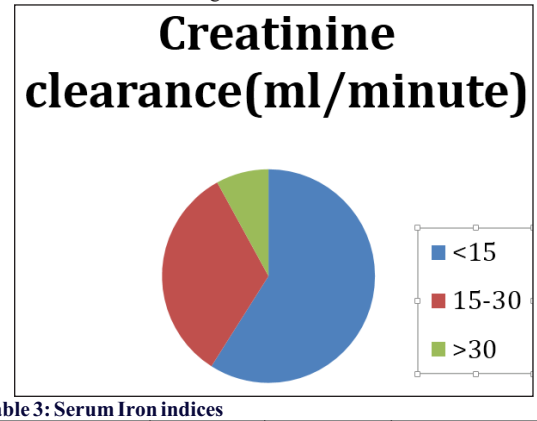

Table 3: Serum Iron indices

Serum Iron Indices	Study group		Control group		'p'
	Mean	SD	Mean	SD	
Iron (µg/l)	66.9	30.8	83.2	26.1	0.0196 Significant
TIBC(µg/l)	283.2	73.2	299.1	44.7	0.821 Not significant
TSAT %	29.56	17.3	29.2	11.2	0.341 Not significant
Ferritin(µg/l)	282.4	342.2	110.5	63.5	0.0485 Significant

Among the serum iron indices between study and control cases, Iron and Ferritin values were significantly different, (p <0.05). TIBC, TSAT values were not significantly different.

Table 4: Distribution Of Total T3 Free T4 And Tsh In Various Stages Of Ckd

Stages of CKD	Frequency	Mean Total T3	Mean free T4	Mean TSH
1-3	5	103.4±30.7	1.25±0.1	1.8±1.9
4	16	91±36.6	1.1±0.2	1.2±0.8
5	29	68.8±24	0.9±0.3	4.5±13.7

The above table 4 reveals the mean T3, free T4 and TSH levels in various stages of CKD. The mean T3 is decreased significantly with reduced creatinine clearance. The free T4 is also significantly decreased in stage 5 CKD.

Out of 75 patients in study, 20 patients (26%) had hypothyroidism, 12 patients (16%) had subclinical hypothyroidism, 19 patients (25%) had low T3 syndrome, 6 (8%) low T4 syndrome, while 2 patient (3%) found to be hyperthyroid. Out of 75,59 patients (78%) had some thyroid dysfunction.

RELATIONSHIP BETWEEN CREATININE CLEARANCE WITH TOTAL T3, FREE T4 AND TSH Relation with Cr. Clearance r Significance Total T3 0.320 P<0.05 Free T4 0.381 P<0.01 TSH -0.133 P>0.05

Relationship Between Creatinine Clearance

Relation with Cr. Clearance	r	Significance
Total T3	0.319	P<0.05
Free T4	0.385	P<0.01
TSH	-0.137	P>0.05

The above table shows positive correlation between total T3 and Creatinine clearance and it is statistically significant. The free T4 and creatinine clearance shows positive correlation and it is statistically significant. The above table shows negative correlation of TSH with creatinine clearance and it is not statistically significant.

DISCUSSION :

Patients with CRF often have signs & symptoms suggestive of thyroid dysfunction & hence the diagnosis of thyroid disease in these patients has obvious prognostic implications. In uremia the mean values of both serum T3 & T4 were significantly low. This is comparable to Ramiraz et al.(6) and Lim VS et al.(7)study. In our study, out of 75patients 19 patients 25%) had low T3 syndrome. The prevalence of low T3 in stage 1- 3 is 20 %, for stage 4 is 38%, and stage 5 is 70%. This observation is consistent with Sang Heon Song et al.(8) in which the prevalence of low T3 will be increased according to the increase in stage of CKD. In our study there is a positive correlation between Total T3 and creatinine clearance and it is statistically significant P<0.05.This shows serum T3 levels were associated with severity of CKD even in the normal TSH level. Overall prevalence of thyroid dysfunction was reported as 48%, 38.6% and 58% by Pakhle K et al,(9) Khatiwada S et al(10) and Manasa A.S. Gowda et al(11) respectively as compared to 78% in our study.

Thyroid stimulating hormone (TSH) is cleared by the kidneys and increased half-life of TSH is the norm in CKD; however even at lower glomerular filtration rates, TSH levels seem to remain normal in the majority of patients(12). The increased half-life of TSH seems to blunt TSH response to Thyroid releasing hormone (TRH). Reduction in glomerular filtration rate leads to reduced iodine clearance, contributing to enlargement and colloid degeneration of the of the thyroid gland.

Thyroid gland colloid degeneration is generally insidious, with very subtle clinical changes and not clinically relevant for most patients. Nevertheless, dialysis has been associated to an increased risk of thyroid nodules and thyroid cancer(13).

On the other hand, the uremic milieu can blunt thyroid hormones' bioavailability to peripheral tissues, leading to a state of thyroid resistance. T3 and T4 level abnormalities are the most common in CKD and low T3 levels is by far the most common abnormality observed inadvanced CKD stages(14)Although no tests are perfect indicators of the adequacy of iron stores, the TSAT and serum ferritin are the best measures of the body's iron status that we currently have Given the prevalence of iron deficiency in CKD patients, and the sensitivity and specificity of TSAT and serum ferritin in detection of

iron deficiency, the likelihood of iron deficiency is sufficiently high when TSAT is <20% and the serum ferritin is <100 ng/mL.(15) Therefore, the TSAT and serum ferritin should be maintained at a level of >20% and >100 ng/mL, respectively. In our study 43% of the patients did not have target serum ferritin of 100 ng/ml and 49.2% of study population did not have target TSAT of >20%.

In our study mean serum ferritin was 282.4 ng/ml and 10 cases had serum ferritin level >500ng/ml . Hence, a low ferritin level (*e.g.*, 200 ng/ml in hemodialysis patients or 100ng/ml in nondialyzed patients with CKD) is a reliable indicator of iron deficiency, whereas a normal to moderately high serum ferritin does not rule out iron deficiency or indicate adequate or too much Fe on board(16).

It is well known that occult inflammation is commonly present in CKD and may increase in prevalence with progressive disease. Inflammation has a profound effect on iron indices. Anemia in chronic kidney disease is a complex process that reflects an interaction of the erythropoietic processes of bone marrow with iron availability and inflammation.(17)) Serum ferritin value was measured in our patients and healthy controls and found to exist a significant difference between them. (P value 0.048). So every effort should be done to identify the cause of anemia in chronic kidney disease patients and treat the coexistent iron deficiency anemia in chronic kidney disease patients.

CONCLUSIONS

In summary, the present study finds thyroid dysfunction to be very common in CKD patients and reveals the significant association between CKD progression and thyroid dysfunction. The study also finds decreased serum Iron and ferritin in CKD. The study reveals that CKD patients with altered Serum Iron indices and Thyroid profile parameters have strong impact on mprbidity and further effects on quality of life.. so early treatment for Thyroid abnormalities and anaemia in CKD patients may lower the chance of developing complications later.

REFERENCES

1. Agarwal SK, Srivastava RK. Chronic kidney disease in India: challenges and solutions. Nephron Clin Pract. 2009;111(3):c197-203;
2. Gafter-Gvili A, Schechter A, Rozen-Zvi B: Iron Deficiency Anemia in Chronic Kidney Disease. Acta Haematol 2019;142:44-50. doi: 10.1159/000496492
3. Yu, PH., Lin, MY., Chiu, YW. *et al.* Low serum iron is associated with anemia in CKD stage 1–4 patients with normal transferrin saturations. *Sci Rep* **11,** 8343 (2021). https://doi.org/10.1038/s41598-021-87401-w
4. Shahid MA, Ashraf MA, Sharma S. Physiology, Thyroid Hormone. [Updated 2021 May 12]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK500006/
5. Khatiwada, Saroj et al. "Thyroid dysfunction and dyslipidemia in chronic kidney disease patients." *BMC endocrine disorders* vol. 15 65. 29 Oct. 2015, doi:10.1186/s12902-015-0063-9
6. . Ramirez G, O'Neill W, Jr, Jubiz W, Bloomer HA. Thyroid dysfunction in uremia: Evidence for thyroid and hypophyseal abnormalities. Ann Intern Med. 1976;84:672–6. [PubMed] [Google Scholar]
7. Lim VS. Thyroid function in patients with chronic renal failure. Am J Kidney Dis. 2001;38:S80–4. [PubMed] [Google Scholar]
8. Sang Heon Song, Ihm Soo Kwak, Dong Won Lee, Yang Ho Kang, Eun Young Seong, Jin Sup Park, The prevalence of low triiodothyronine according to the stage of chronic kidney disease in subjects with a normal thyroid-stimulating hormone, *Nephrology Dialysis Transplantation*, Volume 24, Issue 5, May 2009, Pages 1534–1538
9. Pakhle K, Parikh R, Jain A, et al. Thyroid dysfunctions in patients with chronic renal failure. Int J Res Med Sci 2017;5(6):2773-2778.
10. Khatiwada S, Rajendra KC, Gautam S, et al. Thyroid dysfunction and dyslipidemia in chronic kidney disease patients. BMC Endocr Disord 2015;15:65.
11. Gowda MAS. Evaluation of thyroid function status in patients with chronic kidney disease. JMSCR 2016;4(11):14235-14241
12. Rhee CM. The interaction between thyroid and kidney disease: an overview of the evidence. *Curr Opin Endocrinol Diabetes Obes*. 2016;23(5):407-415. doi:10.1097/MED.0000000000000275.
13. Prevalence and Incidence of Kidney disease and thyroid disorder. Right diagnosis from Health Grade.
14. Basu, Gopal, and Anjali Mohapatra. "Interactions between thyroid disorders and kidney disease." *Indian journal of endocrinology and metabolism* vol. 16,2 (2012): 204-13. doi:10.4103/2230-8210.93737
15. Dignass, A., Farrag, K., & Stein, J. (2018). Limitations of Serum Ferritin in Diagnosing Iron Deficiency in Inflammatory Conditions. *International journal of chronic diseases*, *2018*, 9394060. https://doi.org/10.1155/2018/9394060
16. The Fascinating but Deceptive Ferritin: To Measure It or Not to Measure It in Chronic Kidney Disease Kamyar Kalantar-Zadeh, Kourosh Kalantar-Zadeh, Grace H. Lee CJASN Sep 2006, 1 (Supplement 1) S9-S18;
17. Fishbane, Steven et al. "Iron indices in chronic kidney disease in the National Health and Nutritional Examination Survey 1988-2004." *Clinical journal of the American Society of Nephrology : CJASN* vol. 4,1 (2009): 57-61. doi:10.2215/CJN.01670408