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RESEARCH ARTICLE

THE STUDY OF PREVALENCE OF SUBCLINICAL HYPOTHYROIDISM AND ITS CORRELATION WITH SERUM ALBUMIN ON PATIENTS WITH CHRONIC KIDNEY DISEASE

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Abstract

Background: Chronic diseases have emerged as a important contributor to worldwide mortality and morbidity rates. The incidence of chronic kidney disease (CKD) stage-5 is 150–200 per million people and prevalence of CKD is approximately 800 per million people(1). In south Indian CKD patients diabetic nephropathy accounts for 29.6% , chronic interstitial nephritis (20.4%), chronic glomerulonephritis (17.4%), and hypertension nephropathy (11%) (2).It was discovered that CKD was related to a higher frequency of both subclinical and clinical primary hypothyroidism in the 3rd National Health and Nutrition Examination Survey participants. This finding was regarded to be quite interesting. So in our study we would like to see prevalence of subclinical hypothyroidism (SCH) and its relation with serum albumin in CKD patients.

Results: Out of the 100 CKD patients, the mean age was 53.45 ± 12.37 years. The mean of estimated GFR is 12.392 ± 8.81 ml/min per 1.73 m (range, 3 to 54.4 ml/min per 1.73 m), serum TSH is 9.59 ± 13.11 mIU/L (range, 0.17 to 100.6 mIU/L), and serum creatinine concentrations is 7.23 ± 3.73 mg/dl (range, 0.8 to 1.8 mg/dl).Among the study participants 45 patients (45%) have normal serum thyroid function test results. On the other hand, 54 patients (54%)have subclinical hypothyroidism(SCH).Overall, 5 (5%) patients have eGFR between 30 and 59 ml/min per 1.73 m2, 19 subjects had eGFR of 15 to 30 ml/min per 1.73 m2 and most patients 76 (76%) have an eGFR of <15 ml/min per 1.73 m2.The prevalence of subclinical primary hypothyroidism was increased in patients with progressively lower kidney function, ranging from 53.9% for persons with e GFR ≤ 15 ml/min per 1.73 m2 ,63.2% in persons with an eGFR 15-29 ml/min per 1.73 m2 in total stage 4 CKD patients and 20% in patients with eGFR between 30- 59ml/min per 1.73m2.Theserum albumin levels are decreased in 53 of patients with CKD and 47 patients have normal serum albumin levels(3.5- 4.5g/dl).

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Conclusions: In conclusion, in our study, the prevalence of SCH in study participants with CKD was 54%. Therefore, it may be wise to check the thyroid functions of all CKD patients regularly. In CKD patients, SCH is related to low serum albumin levels. There have been disagreements regarding whether thyroxine supplementation is necessary for SCH in CKD . Reduced thyroid function may serve as an adaptation for CKD patients to reduce protein catabolism. Therefore, attempts to treat it might be harmful to the patient. The issues surrounding thyroxin replacement in CKD patients with SCH, particularly when accompanied by hypoalbuminemia, may require additional, more extensive randomised trials and long-term follow-up.

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Introduction:-

Chronic diseases have emerged as a important contributor to worldwide mortality and morbidity rates. The incidence of chronic kidney disease (CKD) stage-5 is 150–200 per million people and prevalence of CKD is approximately 800 per million people(1). In south Indian CKD patients diabetic nephropathy accounts for 29.6% , chronic interstitial nephritis (20.4%), chronic glomerulonephritis (17.4%), and hypertension nephropathy (11%) (2).It was discovered that CKD was related to a higher frequency of both subclinical and clinical primary hypothyroidism in the 3rd National Health and Nutrition Examination Survey participants. This finding was regarded to be quite interesting.

When the blood thyroid-stimulating hormone (TSH) level is high (normal level : 4.2–10 IU/ml), but the corresponding serum-free thyroxine (FT4) level is within normal limits (normal level:0.93–1.7 ng/dl) then it is known as subclinical hypothyroidism (SCH)(3). An association between subclinical primary hypothyroidism and cardiovascular risk markers and cardiac dysfunction have been found in many studies which is very significant(4).SCH along with type 2 diabetes have been recognised as a reliable indicator of death from any cause in patients undergoing continuous dialysis, risk factor for cardiovascular events and renal failure(5).

However, there is a lack of sufficient quantitative evidence regarding the frequency of SCH in large populations of people at varying degrees of estimated glomerular filtration rate (eGFR). So, the purpose of this study is to determine the prevalence of SCH among ESRD patients in South India and its correlation with eGFR and serum albumin.

Materials and Methods:-

The study is conducted over a period of one year at a tertiary care centre in DR.PSIMS AND RF , Andhra Pradesh. It is a analytical study in which CKD patients of age more than 16 years with eGFR lessthan 60ml/min/1.73m2 attending outpatient and inpatients departments of Nephrology and general medicine are included. Out of which known hypothyroid and hyperthyroid patients, pregnant women and patients who were taking medications that affected thyroid function, such as lithium and high-dose steroids (hydrocortisone 100mg or equivalent dose of other commonly used steroids) are excluded from the study. As a result, the study cohort consisted of one hundred CKD patients who were consecutively examined. All the people who took part in the study had their demographic information collected, which included their age, gender, and whether or not they had diabetes, as well as their laboratory variables, which included their haemoglobin, blood urea nitrogen (BUN), serum levels of creatinine, albumin, phosphorus, and calcium.

All of the patients had their thyroid functions evaluated. TSH levels were determined using a Roche-Elecsys modular analytics E170 equipped with an electrochemi-luminescence immunoassay (ECLIA method). TSH has an analytical sensitivity of 0.005 IU/ml, while FT4 has an analytical sensitivity of 0.023 ng/dl.It was necessary to have normal FT4 levels (0.93–1.7 ng/dl) and high serum TSH levels (normal level: 0.27–4.5 IU/m) to diagnose SCH. Patients who have high TSH levels and low FT4 levels were classified to be having overt hypothyroidism, regardless of whether or not they exhibited symptoms of hypothyroidism.

Informed consent was taken from all the participants and the institutional ethics committee authorised the study.

Statistical Analysis

In terms of means ± SD and percentages, baseline characteristics of the study participants were expressed. It was also calculated (n%) how common SCH is. Concerning categorical and continuous variables, Student's t-test and the chi-square test were used to compare the two groups, namely patients with SCH and patients with normal TSH.

The use of simple and multiple logistic regression analysis allowed for examining the associations between patient factors such as age, gender, serum albumin, and SCH. Variables such as age, gender, and serum albumin were selected to be adjusted in the logistic regression model either because they were confounders in the association between SCH and CKD or through a process of forward selection of variables in which variables that had a significant association with SCH in the unadjusted analysis were included in the adjusted model.

After that, a multiple linear regression analysis was carried out to investigate the connection between SCH and serum albumin, with the additional factors of age and gender being considered. The selection of the variables for this logistic regression analysis was again very similar to what was detailed in the previous study.Multiple linear regression was used to obtain the numerical relationship between the factors of interest and SCH.

A statistically significant value was determined to be one with p less than or equal to 0.05. SPSS for Windows was utilised in order to carry out the statistical analysis (version 15.0; SPSS, Chicago, Ill., USA).

Results:-

In our study, out of 100 CKD patients mean age: 53.45 ± 12.37 years. In the whole sample, the mean value of estimated GFR is 12.392 ± 8.81 ml/min per 1.73 m2 range of eGFR varying from 3 to 54.4 ml/min per 1.73 m2. Serum TSH mean value is 9.59 ± 13.11 mIU/L range of serum TSH varying from 0.17 to 100.6 mIU/L. And mean value of serum creatinine 7.23 ± 3.73 mg/dl range of serum creatinine varying from 0.8 to 1.8 mg/dl as shown in table1. In our study overall 5 (5%) patients have eGFR between 30 and 59 ml/min per 1.73 m2 , 19(19%) patients have e GFR <30 ml/min per 1.73 m2 and most patients 76 (76%) have an eGFR of 15 to 30 ml/min per 1.73 m2 as shown in table 2.3Our study shows that 45% of the participants (n = 45) had serum thyroid function test results which are within the reference range. This means that their TSH values are within normal range from 0.35 to 4.5 mIU/L while their FT4 levels are within normal range 0.93-1.7ng/dl. On the other hand, 54% (n = 54) of the participants had subclinical biochemical hypothyroidism (i.e., TSH >4.5 mIU/L while their FT4 levels were normal as shown in table 3.

Table 1:- The Baseline characteristics of the study population.

	N	Minimum	Maximum	Mean	Std. Deviation
AGE	100	19.0	86.0	53.450	12.3749
HBgm	100	5.4	13.0	8.912	1.5638
TSH	100	.17	100.00	9.5908	13.11769
BUN	100	31.0	338.0	96.880	49.3841
CREATININE	100	1.3	21.3	7.234	3.7316
EGFR	100	3.0	54.4	12.392	8.8125
SALBUMIN	100	2.6	5.1	3.387	.4296
SPHOSPHORUS	100	2.47	12.24	5.1509	2.09891
CALCIUM	100	5.8	10.2	7.956	.8903
SURICACID	100	2.8	18.0	8.525	2.2747
Valid N (listwise)	100				

Table 2:- Number of patients in various stages of CKD.

Stages (eGFR ml/min)	Frequency	Percentage
Stage III(30-59)	5	5.0
Stage IV(15-29)	19	19.0
Stage V(<15)	76	76.0
Total	100	100.0

Table 3:- Thyroid disorders prevalence in the study population.

TSH levels (mlU/ml)	Frequency	Percentage
Hyperthyroidism	1	1.0
Normal	45	45.0
SCH	54	54.0
Total	100	100.0

In our study the prevalence of SCH is 53.9% for patients with eGFR ≤ 15 ml/min per 1.73 m2 in total stage V CKD , 63.2% in persons with eGFR between 15-29 ml/min per 1.73 m2 in total stage lV CKD patients. Only 20% of total stage III CKD patients which shows that prevalence of SCH have increased in patients with progressively lower kidney function which is indicated by eGFR as depicted in table 4.

Table 4:- Prevalence of subclinical primary hypothyroidism in the study population.

TSH levels (mlU/ml)	Stage III	Stage IV	Stage V	Total	P value
Hyperthyroidism	0	0	1(1.3)	1	0.4
Normal	4(80.0)	7(36.8)	34(44.7)	45	
SCH	1(20.0)	12(63.2)	41(53.9)	54	
Total	5	19	76	100	

In our study the serum albumin levels are decreased in 53 of patients with CKD and 47 patients have normal serum albumin levels(3.5- 4.5g/dl).Out of 53 CKD patients with SCH 36 patients have low serum albumin levels and only 18 patients have normal serum albumin as shown on table 5 which shows that albumin and thyroid function have significant correlation.The correlation of TSH with serum albumin and parameters are depicted in table 5.

Table 5- Serum albumin levels correlation with thyroid function in CKD patients.

Serum albumin in g/dl	Normal (greaterthan3.5g/dl	Decreased(lessthan 3.5g/dl)
Hyperthyroidism(n=1)	1	0
Normal Thyroid function (n=45)	28	17
SCH(n=54)	18	36
Total	47	53

Table 6- Correlation of variables with TSH

Variables	Pearson Correlation value	P value
Age	0.007	0.9
Hb (in gm)	0.11	0.2
BUN	-0.05	0.6
Creatinine	0.13	0.2
EGFR	-0.12	0.24
S.ALBUMIN	-0.015	0.9
S.PHOSPHORUS	-0.07	0.5
CALCIUM	-0.08	0.2
ALP	-0.27	0.2
A/C RATIO	0.9	1
S.URIC ACID	0.008	0.9

Discussion:-

According to our study, SCH is quite prevalent (54%) in CKD patients. Our findings are in accordance with many other research studies that have linked thyroid illness and renal impairment.

CKD staging system according to the National Kidney Foundation's, Lo et al analysis of hypothyroidism and various levels of estimated GFR led to the conclusion that impaired kidney function was linked to an increase in the prevalence of SCH and clinical hypothyroidism which is in accordance with our study with prevalence of SCH of 54 % in CKD patients with an eGFR of below 60 ml/min/1.73 m2(6).Similar findings were made by Chonchol et al, who found that 20% of CKD patients who did not need dialysis also had SCH(7).

According to Kang et al, SCH may be related to cardiac dysfunction and is prevalent in CKD patients receiving continuous ambulatory peritoneal dialysis(8). Thyroid hormones physiology is known to be changed in CKD patients. The baseline TSH rises, occasionally reaching values of 120 IU/ml and the response to exogenous thyrotropin-releasing hormone (TRH) is muted. The diurnal variation rhythm of TRH is disrupted and a decrease in serum T4 levels is seen(9).The greater prevalence of goitre and hypothyroidism in CKD patients may be explained by the Wolff-Chaikoff effect, which can impede thyroid hormone production by increasing total body inorganic iodide. These patients hypothyroidism may be brought on additionally by prolonged metabolic acidosis. (9). Brungger et al.used their experimental model to illustrate the potential pathways. They demonstrated that hypothyroidism is caused by metabolic acidosis, which greatly lowers serum thyroid hormone levels both tri-iodothyronine(T3) and tetra-iodothyronine (T4) and increases serum TSH levels in response(10).

A lower serum albumin concentration has been linked to an increased risk of SCH in CKD patients, according to our study. Compared to patients with normal TSH, our SCH patients exhibited considerably decreased serum albumin levels which is contrary to Kang et al. (8) study which found that patients with SCH have significantly higher serum albumin levels compared to individuals with normal serum TSH levels in their study cohort of 51 CKD patients on continuous ambulatory peritoneal dialysis. It is not understood what causes this discrepancy to exist. The key distinctions between our study and their study are that their study included patients undergoing continuous ambulatory peritoneal dialysis, whereas our study focused on haemodialysis patients and our study group is smaller than theirs. This makes it challenging to draw any conclusions. Gilles et al. found that patients with proteinuria have higher TSH levels which can be attributed to potential loss of thyroid hormones(T3, T4) in the urine(11). The relationship between hypoalbuminemia and other endocrine disorders in CKD has not been supported by evidence [12]. In CKD patients hypoalbuminemia is a separate risk factor for cardiovascular mortality, albeit et al [13].

There have been disagreements regarding whether thyroxine supplementation is necessary for SCH in CKD. Decreased thyroid function may serve as an adaptation for ESRD patients to reduce protein catabolism. Therefore, attempts to treat it might be harmful to the patient. The discovery that CKD patients who have thyroxine replacement were observed to have a negative nitrogen balance and enhanced leucine flow gives evidence for this statement (14). The cardiovascular risk in people with CKD, SCH, and hypoalbuminemia has not yet been established. Future randomized trials will be necessary to study the impact of thyroxine replacement in CKD patients.

Limitations :

We were unable to establish the temporality of connection between SCH, serum albumin and CKD due to the cross-sectional study design. Another limitation is small sample size which prevented us from assessing the effect modification due to gender, age, and diabetes status. There are questions about the accuracy of these estimations based on single measurements of all laboratory parameters. Additionally, because neither the aetiology of SCH nor the measurement of anti-thyroid antibodies was done in our study, we cannot determine if the SCH we found in our patients was linked to decline in eGFR or a primary thyroid pathology.

Conclusions:-

Our study revealed a 54% prevalence of SCH among a sample of CKD patients. Therefore, it may be wise to check the thyroid functions of all CKD patients regularly. In CKD patients, SCH is related to low serum albumin levels. The issues surrounding thyroxin replacement in CKD patients with SCH, particularly when accompanied by hypoalbuminemia, may require additional, more extensive randomised trials and long-term follow-up.

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Disclosure Statement

There are no conflicts of interest to disclose for the authors.

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