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THE ANALYSIS OF SUBCLINICAL HYPOTHYROIDISM PREVALENCE IN PATIENTS WITH CHRONIC KIDNEY DISEASE.

General Medicine

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KEYWORDS

INTRODUCTION:

Even in emerging countries, chronic diseases have emerged as a significant contributor to the worldwide morbidity and mortality rates. The incidence of end-stage renal disease (ESRD) is from 150–200 per million people, while the prevalence of chronic kidney disease (CKD) is approximately 800 per million people. 1

In South India, diabetic nephropathy accounts for 29.6% of all cases of chronic kidney disease, followed by chronic interstitial nephritis (20.4%), chronic glomerulonephritis (17.4%), and hypertension nephropathy (11%). 2

Among those who took part in the Third National Health and Nutrition Examination Survey, it was discovered that CKD was related with a higher frequency of both clinical and subclinical primary hypothyroidism. This finding was regarded to be quite interesting.

When the blood thyroid-stimulating hormone (TSH) level is high (range: 4.2–10 IU/ml), but the corresponding serum-free thyroxine (FT4) level is within normal limits (range: 0.93–1.7 ng/dl), a condition known as subclinical hypothyroidism (SCH) can be detected.3

Several studies have found an association between subclinical primary hypothyroidism and markers of cardiovascular risk and cardiac dysfunction. This association was found to be significant. 4

In addition, subclinical primary hypothyroidism has been recognised as a reliable indicator of death from any cause in patients undergoing continuous dialysis and as a risk factor for nephropathy and cardiovascular events in individuals afflicted with type 2 diabetes. 5

There is, however, a lack of sufficient quantitative evidence concerning the frequency of subclinical primary hypothyroidism in large populations of people, at varying degrees of estimated glomerular filtration rate (GFR). As a result, the purpose of this study is to determine the prevalence of SCH among ESRD patients in South India as well as the risk factors that are related with it.

MATERIALS AND METHODS:

This was an analytical study conducted at a tertiary-care center in DR.PSIMS AND RF. The study was conducted over 1 year.

Patients with overt hypothyroidism, SCH, and overt hyperthyroidism, as well as pregnant women, were not allowed to participate in the study. Also excluded from the study were patients who were taking medications that affected thyroid function, such as lithium and high-dose steroids (hydrocortisone 1100 mg or equivalent dose of other commonly used steroids).

As a result, the study cohort consisted of one hundred CKD patients who were consecutively examined.

All of 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, and serum levels of creatinine, albumin, phosphorus, and calcium.

All of the patients had an evaluation of their thyroid functions. TSH levels were determined with the help of a Roche Elecsys modular analytics E 170 equipped with electrochemiluminescence 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 (14.5 IU/ml; normal range: 0.27–4.5 IU/m) in order to diagnose SCH. The normal range for TSH is 0.27–4.5 IU/m. Patients who had high TSH levels (14.5 IU/ml) and low FT4 levels (0.93 ng/dl) were classed as having overt hypothyroidism, regardless of whether or not they exhibited symptoms of hypothyroidism. This was the case even if the patients did not have symptoms of hypothyroidism.

All study participants provided their informed consent, and the DR. PSIMS&RF 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. With respect to categorical and continuous variables, respectively, 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 the examination of 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 ESRD 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.

Variables that had a significant association with SCH in the unadjusted analysis were included in the adjusted model.

The association between selected variables and SCH was assessed using logistic regression analysis, and the results were reported as odds ratios.

After that, a multiple linear regression analysis was carried out in order to investigate the connection between SCH and serum albumin, with the additional factors of age and gender being taken into consideration. The selection of the variables for this logistic regression analysis was again very similar to what has been detailed for the previous study.

Through the use of multiple linear regression, we were able to obtain a 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:

Of the 100 CKD patients as shown in the table.1 (mean age: 53.45 ± 12.37 years).

In the whole sample, the mean values of estimated GFR, serum TSH, and serum creatinine concentrations were 12.392 ± 8.81 ml/min per 1.73 m (range, 3 to 54.4 ml/min per 1.73 m), 9.59 ± 13.11 mIU/L (range, 0.17 to 100.6 mIU/L), and 7.23 ± 3.73 mg/dl (range, 0.8 to 1.8 mg/dl), respectively.

The majority of participants (n = 45, 45.0%) had serum thyroid function test results that were within the reference range. This means that their TSH values ranged from 0.35 to 4.5 mIU/L while their FT levels were normal. On the other hand, 54% (n = 54) of the participants had subclinical biochemical hypothyroidism (i.e., TSH >4.5 mIU/L while their FT levels were normal).

Overall, 5 (5%) subjects had estimated GFR between 30 and 59 ml/min per 1.73 m and 19 subjects had estimated GFR <30 ml/min per 1.73 m, Most participants (*n* = 76, 76%) had an estimated GFR of 15 to 30 ml/min per 1.73 m.

In Table 1, we have provided the baseline characteristics.

Descriptive Statistics					
	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

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

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

As shown in table 4, the prevalence of subclinical primary hypothyroidismwas increased in persons with progressively lower kidney function, ranging from 53.9% for persons with estimated GFR ≤ 15 ml/min per 1.73 m in total stage 5 CKD to 63.2% in persons with estimated GFR below 29 ml/min per 1.73 m in total stage 4 CKD patients. Only 20% of total stage 3 CKD patients.

Table.4

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	

Correlation of variables with TSH **Table.5**

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
SALBUMIN	-0.015	0.9
SPHOSPHORUS	-0.07	0.5
CALCIUM	-0.08	0.2
ALP	-0.27	0.2
AC RATIO	0.9	1
SURIC ACID	0.008	0.9

DISCUSSION:

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

According to the National Kidney Foundation's CKD staging system, Lo et al [6].'s analysis of hypothyroidism and various levels of estimated GFR led to the conclusion that impaired kidney function was linked to a rise in the prevalence of SCH and overt hypothyroidism.

In agreement with our study, in their study prevalence of subclinical hypothyroidism amounted to 54 % in CKD patients with an estimated GFR ! of 30 ml/min/1.73 m2.

Similar findings were made by Chonchol et al. [7], who found that 20% of CKD patients who did not need dialysis also had SCH. According to Kang et al. [8], SCH may be related to cardiac dysfunction and is prevalent in ESRD patients receiving continuous ambulatory peritoneal dialysis.

The physiology of thyroid hormones is known to be changed in CKD patients. The baseline TSH rises, occasionally reaching values of 120 IU/ml, the response to exogenous thyrotropin-releasing hormone (TRH) is muted, the diurnal 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 [9].

Additionally, these patients' hypothyroidism may be brought on by prolonged metabolic acidosis. Brungger et al. [10] used their experimental model to illustrate the potential pathways. They demonstrated that hypothyroidism is caused by metabolic acidosis, which greatly lowers serum T3 and T4 levels and raises serum TSH levels in response.

A lower blood albumin concentration has been linked to an increased risk of SCH in ESRD patients, according to our study. Compared to patients with normal TSH, our SCH patients exhibited considerably decreased serum albumin levels (table 1).

Kang et al. [8] found that patients with SCH had significantly higher serum albumin levels compared to individuals with normal serum TSH levels in their study cohort of 51 ESRD patients on continuous ambulatory peritoneal dialysis. This is in contrast to what we observed, which was that patients with SCH had lower serum albumin levels. It is not understood what causes this discrepancy to exist.

The key distinctions between our study and their study, however, are that their study included patients undergoing continuous ambulatory peritoneal dialysis, whereas our study focused on hemodialysis patients, and that our study group was smaller than theirs. This makes it challenging to draw any conclusions.

The intriguing finding by Gilles et al. [11] that patients with proteinuria had higher TSH levels can be attributed to the potential loss of thyroid hormones in the urine. The relationship between hypoalbuminemia and other endocrine disorders in CKD has not been supported by evidence [12]. Hypoalbuminemia in CKD patients is a separate risk factor for cardiovascular mortality, albeit [13].

There have been disagreements regarding whether thyroxine supplementation is necessary for SCH in ESRD. Reduced thyroid function may serve as an adaptation for ESRD patients to reduce protein catabolism. Therefore, attempts to fix it might be harmful to the patient. The discovery that ESRD patients who had thyroxin replacement were observed to have a negative nitrogen balance and an enhanced leucine flow offer evidence for this statement [14].

The cardiovascular risk in people with ESRD, SCH, and

hypoalbuminemia has not yet been established. Future randomized trials will be necessary to determine the impact of thyroxine replacement in this subgroup.

Limitations:

We were unable to determine the temporality of the connection between SCH, serum albumin, and ESRD due to the cross-sectional study design. Another restriction that prevented us from assessing effect modification due to gender, age, and diabetes status was the small sample size.

There are questions about the accuracy of these estimations based on single measurements of all laboratory parameters. Additionally, because neither the etiology of SCH nor a measurement of anti-thyroid antibodies was done in our study, we are unable to determine if the SCH we found in our patients was linked to a decline in GFR or a primary thyroid pathology.

CONCLUSIONS:

In conclusion, our study revealed a 54.0% prevalence of SCH among a sample of CKD patients. Therefore, it may be wise to regularly check the thyroid functions of all ESRD patients. In ESRD patients, SCH is related to low serum albumin levels. The issues surrounding thyroxin replacement in ESRD patients with SCH, particularly when accompanied with hypoalbuminemia, may require additional, bigger randomised trials and long-term follow-up.

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

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