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ASSOCIATION OF THYROID STATUS IN PATIENTS WITH CHRONIC KIDNEY DISEASE IN A TERTIARY CARE HOSPITAL

General Medicine

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ABSTRACT

INTRODUCTION: The concept of subclinical primary hypothyroidism has emerged over the past several decades, as our ability to detect subtle changes in thyroid function tests is progressively improved. Although it is recognized that patients with subclinical primary hypothyroidism may have subtle symptoms of thyroid dysfunction, the definition is purely a biochemical one, defined as elevated serum thyrotropin (TSH) levels but normal free thyroxine (FT4) levels.[1]

AIMS AND OBJECTIVES: Proposed topic of research: Prevalence of Subclinical Hypothyroidism In Patients With Chronic Kidney Disease, Objective of Proposed Research: Prevalence of Subclinical Hypothyroidism In Patients With Chronic Kidney Disease, Broad objectives: To estimate TSH and Free T4 levels in Chronic Kidney Disease patients and calculate the eGFR using MDRD formula and classify the patients with CKD into 5 stages

METHODOLOGY: This Cross sectional Observational Study was single-centre study, which was take place at NRS Hospital Kolkata total time take April 2017 to March 2018.

RESULT AND ANALYSIS: We found 10(10.0%) patients had overt hypothyroidsm. 100(100.0%) patients had >3 month of illness. The mean TSH (mean± s.d.) of patients was 6.5200 ± 4.4210 micro IU/mL. The mean FT4 (mean± s.d.) of patients was 1.0509 ± .3960 ng/dL. The mean urea (mean± s.d.) of patients was 96.8830 ± 31.6749. The mean creatinine (mean± s.d.) of patients was 3.3010 ± 1.2648. The mean eGFR (MDRD) (mean± s.d.) of patients was 24.5080 ± 16.6236 ml/min /1#73m2. Association of age in years vs. subclinical hypothirodism was not statistically significant (p=0.1486).

CONCLUSION: We conclude that the prevalence of subclinical hypothyroidism is high among all the stages of CKD patients. Need for treatment depends on the patient's clinical scenario and decision of the clinician based on the presentation.

There is an increasing trend of decreased thyroid functional status along with decrease of estimated GFR (eGFR). Chronic kidney disease impairs thyroid functional status in different ways. Thyroid functional status evaluation is recommended in each and every patient of CKD.

KEYWORDS

Subclinical Hypothyroidism and Chronic Kidney Disease

INTRODUCTION

The concept of subclinical primary hypothyroidism has emerged over the past several decades, as our ability to detect subtle changes in thyroid function tests is progressively improved. Although it is recognized that patients with subclinical primary hypothyroidism may have subtle symptoms of thyroid dysfunction, the definition is purely a biochemical one, defined as elevated serum thyrotropin (TSH) levels but normal free thyroxine (FT4) levels.[1]

Subclinical primary hypothyroidism has been recognized in several studies to be associated with markers of cardiovascular risk and cardiac impairment). Even minor deviations from serum TSH normal range might accelerate the development of atherosclerosis and have adverse effects on cardiovascular performance in the general population. Moreover, subclinical primary hypothyroidism has been identified as a strong predictor of all-cause mortality in chronic dialysis patients and as a risk factor for nephropathy and cardiovascular events in type 2 diabetic patients.[2] There is, however, limited quantitative evidence regarding the prevalence of subclinical primary hypothyroidism in large samples of individuals, including large non-U.S. cohorts at different levels of estimated glomerular filtration rate (GFR).[3]

Chronic kidney disease is an increasing health problem throughout the world including Bangladesh. It is a long-standing, progressive deterioration of renal function. The kidney normally plays an important role in the metabolism, degradation and excretion of several thyroid hormones.[4] All levels of the hypothalamic-pituitary-thyroid axis may be involved, including alterations in hormone production, distribution, and excretion. As a result, abnormalities in thyroid function tests are frequently encountered in uremia. End-stage renal disease (ESRD) alters the hypothalamic-pituitary-thyroid hormone axis in addition to the peripheral thyroid hormone metabolism. Among thyroid hormones, triodothyronine (T3) is the most metabolically active thyroid hormone and can be reduced in ESRD patients even with a normal TSH level. In general, reduced T3 levels in ESRD patients are due to the decreased peripheral tissue conversion of T4 into T3, while thyroid gland production of T3 is normal and T3 clearance rates are normal or decreased, as in other non-thyroidal illnesses. Most patients with end-stage renal disease have decreased plasma levels of free triiodothyronine (FT3), which reflect diminished conversion of thyroxine (T4) to T3 in the periphery. This abnormality is not associated with increased conversion of T4 to the metabolically inactive reverse T3 (rT3), since plasma rT3 levels are typically normal. This finding differentiates the uremic patient from patients with chronic illness in which the conversion of T4 to T3 is similarly reduced, but the generation of rT3 from T4 is enhanced. In addition to decreased production, low levels of total T3 also may reflect reduced protein binding.[5] The kidney normally contributes to the clearance of iodide from the body. With advancing renal failure iodide excretion is diminished leading sequentially to an elevated plasma inorganic iodide concentration and an initial increment in thyroidal iodide uptake. The ensuing marked increase in the intrathyroidal iodide pool results in diminished uptake of radiolabeled iodide by the thyroid in uremic patients. Increases in total body inorganic iodide can potentially block thyroid hormone production (the Wolff Chaikoff effect). Chronic renal failure affects thyroid function in multiple ways, including low circulating thyroid hormone concentration, altered peripheral hormone metabolism, disturbed binding to carrier proteins, possible reduction in tissue thyroid hormone content, and increased iodine store in thyroid glands. [6]

AIMS AND OBJECTIVES

- **Proposed topic of research:** Prevalence of Subclinical Hypothyroidism In Patients With Chronic Kidney Disease
- **Objective of Proposed Research:** Prevalence of Subclinical Hypothyroidism In Patients With Chronic Kidney Disease
- **Broad objectives:** To estimate TSH and Free T4 levels in Chronic Kidney Disease patients.

METHODOLOGY

- **Study design:** Cross sectional Observational Study.
- **Study Setting:** This is a single-centre study, which was take place at IPGME&R and SSKM Hospital Kolkata.
- **Study Population:** CKD patients admitted in General Medicine ward at NRS Hospital Kolkata total time take April 2017 to March 2018.

EXCLUSION CRITERIA:- Patients with family history of thyroid disorder or past history of any medication for thyroid disease or history

of any surgery or any radiological intervention to thyroid gland were exclude from the study.

- **Sample Size:** 100
- **Sample Design:** Consecutive patients presenting with CKD are evaluated and submitted to following criteria;-
- eGFR: , ≤90 ml/min
- Control not required

RESULT AND ANALYSIS

Our study showed that 13(13.0%) patients had ≤40 years of age, 19(19.0%) patients had 41-50 years of age, 33(33.0%) patients had 51-60 years of age, 31(31.0%) patients had 61-70 years of age and 4(4.0%) patients had 71-80 years of age. The mean age (mean± s.d.) of patients was 54.2100 ± 11.1358 years. 42(42.0%) patients had female and 58(58.0%) patients had male. 40(40.0%) patients had DM history. 39(39.0%) patients had history of hypertension. 100(100.0%) patients had no past history of thyroid disorder. 25(25.0%) patients had subclinical hypothyroidism. 10(10.0%) patients had CKD stage II, 6(6.0%) patients had CKD stage IIIa, 10(10.0%) patients had CKD stage IIIb, 31(31.0%) patients had CKD stage IV and 43(43.0%) patients had CKD stage V.

We found 10(10.0%) patients had overt hypothyroidsm. 100(100.0%) patients had >3 month of illness. The mean TSH (mean± s.d.) of patients was 6.5200 ± 4.4210 micro IU/mL. The mean FT4 (mean± s.d.) of patients was 1.0509 ± .3960 ng/dL. The mean urea (mean± s.d.) of patients was 96.8830 ± 31.6749. The mean creatinine (mean± s.d.) of patients was 3.3010 ± 1.2648. The mean eGFR (MDRD) (mean± s.d.) of patients was 24.5080 ± 16.6236 ml/min /1#73m2. Association of age in years vs. subclinical hypothirodism was not statistically significant (p=0.1486).

Present study showed that in subclinical hypothirodism-no, 27(36.0%) patients had female and 48(64.0%) patients had male. In subclinical hypothirodism-yes, 15(60.0%) patients had female and 10(40.0%) patients had male. Association of sex vs. subclinical hypothirodism was statistically significant (p=0.0352). In subclinical hypothirodism-no, 26(34.7%) patients had DM. In subclinical hypothirodism-yes, 14(56.0%) patients had DM. Association of DM vs. subclinical hypothirodism was not statistically significant (p=0.0500). In subclinical hypothirodism-no, 27(36.0%) patients had history of hypertension. In subclinical hypothirodism-yes, 12(48.0%) patients had history of hypertension. Association of history of hypertension vs. subclinical hypothirodism was not statistically significant (p=0.2867). Also we found in subclinical hypothirodism-no, 75(100.0%) patients had past history of thyroid disorder. In subclinical hypothirodism-yes, 25(100.0%) patients had past history of thyroid disorder. In subclinical hypothirodism-no, 30(40.0%) patients had CKD stage V. In subclinical hypothirodism-yes, 13(52.0%) patients had CKD stage V. Association of CKD stage vs. subclinical hypothirodism was statistically significant (p=0.0401). In subclinical hypothirodism-no, the mean age (mean± s.d.) of patients was 53.6667 ± 11.1977 years. In subclinical hypothirodism-yes, the mean age (mean± s.d.) of patients was 55.8400 ± 11.0101 years. Distribution of mean age vs. subclinical hypothirodism was not statistically significant (p=0.4008).

We found in subclinical hypothirodism-no, the mean urea (mean± s.d.) of patients was 94.5507 ± 31.8171. In subclinical hypothirodism-yes, the mean urea (mean± s.d.) of patients was 103.8800 ± 30.8103. Distribution of mean urea vs. subclinical hypothirodism was statistically significant (p=0.0438). In subclinical hypothirodism-no, the mean creatinine (mean± s.d.) of patients was 3.2107 ± 1.2864. In subclinical hypothirodism-yes, the mean creatinine (mean± s.d.) of patients was 3.5720 ± 1.1809. Distribution of mean creatinine vs. subclinical hypothirodism was not statistically significant (p=0.2178). In subclinical hypothirodism-no, the mean eGFR (MDRD) (mean± s.d.) of patients was 26.1387 ± 17.4751 ml/min/1#73m2. In subclinical hypothirodism-yes, the mean eGFR (MDRD) (mean± s.d.) of patients was 19.6160 ± 12.8487 ml/min/1#73m2. Distribution of mean eGFR (MDRD) vs. subclinical hypothirodism was statistically significant (p=0.0494).

DISCUSSION

Chandra A et al [7] (2016) found that an increased prevalence of hypothyroidism was observed in patients with a reduction in the glomerular filtration rate. There is growing evidence of increased prevalence of subclinical hypothyroidism in non dialysis-independent CKD patients.

It was found that in subclinical hypothirodism-no, 26(34.7%) patients had DM. In subclinical hypothirodism-yes, 14(56.0%) patients had DM. Association of DM vs. subclinical hypothirodism was not statistically significant (p=0.0500).

It was found that in subclinical hypothirodism-no, the mean urea (mean± s.d.) of patients was 94.5507 ± 31.8171. In subclinical hypothirodism-yes, the mean urea (mean± s.d.) of patients was 103.8800 ± 30.8103. Distribution of mean urea vs. subclinical hypothirodism was statistically significant (p=0.0438).

Somana JS et al [8] (2017) found that Subclinical hypothyroidism was found to be 8%, 10%, 20% and 12% in the stages II, III, IV and V of CKD patients and it gradually increases as the stage of the CKD advances. As the eGFR falls, TSH starts increasing and it may be due to alteration in the hypothalamo-pituitary axis, TSH glycosylation and diurnal rhythm. It may also be due to altered metabolism of thyroid hormones and decreased peripheral conversion of T4 to T3. The exact mechanisms linking CKD and hypothyroidism are still unclear.

Naseem F et al [9] (2018) found that the percentage of patients above 40 years with SHT was much higher, but not statistically significant (P = 0.096). When stratified according to gender, 21.6% were male, and 46.2% were female (P = 0.03). The study shows a considerably high prevalence of SHT in CKD patients .

It was found that in subclinical hypothirodism-no, the mean creatinine (mean± s.d.) of patients was 3.2107 ± 1.2864. In subclinical hypothirodism-yes, the mean creatinine (mean± s.d.) of patients was 3.5720 ± 1.1809. Distribution of mean creatinine vs. subclinical hypothirodism was not statistically significant (p=0.2178).

It was found that in subclinical hypothirodism-no, the mean eGFR (MDRD) (mean± s.d.) of patients was 26.1387 ± 17.4751 ml/min/1#73m2. In subclinical hypothirodism-yes, the mean eGFR (MDRD) (mean± s.d.) of patients was 19.6160 ± 12.8487 ml/min/1#73m2. Distribution of mean eGFR (MDRD) vs. subclinical hypothirodism was statistically significant (p=0.0494).

Chonchol M et al [10](2008) found that the prevalence of subclinical primary hypothyroidism increased from 7% at an estimated GFR ≥90 ml/min per 1.73 m^2 to 17.9% at an estimated GFR <60 ml/min per 1.73 m^2 (P < 0.0001 for trend).

Khatiwada S et al [11](2015) found that Thyroid dysfunction was found in 38.6 % CKD patients,the most common being subclinical hypothyroidism(27.2 %), followed by overt hypothyroidism (8.1 %) .

Hossain MMet al [12](2015) found that subclinical hypothyroidism (5%) in chronic kidney disease patients.

Table: Distribution of History all parameters

		Frequency	Percent
Dm History	**No**	60	60.0%
	Yes	40	40.0%
	Total	100	100.0%
History Of Hypertension	**No**	61	61.0%
	Yes	39	39.0%
	Total	100	100.0%
Subclinical Hypothyroidism	**No**	75	75.0%
	Yes	25	25.0%
	Total	100	100.0%
Past History Of Thyroid Disorder	**NO**	100	100.0%
	Total	100	100.0%
Overt Hypothyroidsm	**NO**	90	90.0%
	YES	10	10.0%
	Total	100	100.0%
Duration Of Illness >3 Months	**YES**	100	100.0%
	Total	100	100.0%
CKD Stage	**II**	10	10.0%
	IIIa	6	6.0%
	IIIb	10	10.0%
	IV	31	31.0%
	V	43	43.0%
	Total	100	100.0%

CONCLUSION

Subclinical primary hypothyroidism is more common in persons with CKD not requiring chronic dialysis compared with those with normal kidney function. We found that overall prevalence of subclinical hypothyroidism was 25% in CKD patients.

They observed a high prevalence of thyroid dysfunction in our CKD patients and revealed significant association between CKD progression and thyroid dysfunction.

We conclude that the prevalence of subclinical hypothyroidism is high among all the stages of CKD patients. Need for treatment depends on the patient's clinical scenario and decision of the clinician based on the presentation.

There is an increasing trend of decreased thyroid functional status along with decrease of estimated GFR (eGFR). Chronic kidney disease impairs thyroid functional status in different ways. Thyroid functional status evaluation is recommended in each and every patient of CKD.

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