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Original Research Article

Thyroid status in patients undergoing maintenance haemodialysis: a South Indian cohort study

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ABSTRACT

Background: Hypothyroidism is common throughout the world and the prevalence of hypothyroidism is high in India. Ailment of thyroid function has been documented to occur at a higher rate in patients with chronic kidney disease (CKD), including those undergoing dialysis than in general population.
Methods: A prospective cross-sectional observational clinical study in real time was carried out to assess the thyroid status in eighty-nine adult patients undergoing a 4 h three times weekly haemodialysis schedule in a rural tertiary referral hospital in South India. The status of the thyroid was monitored via Free T3 Free T4 and Thyroid Stimulating Hormone levels.
Results: Subclinical hypothyroidism was common in patients undergoing haemodialysis. Although there was a negative correlation between the levels of thyroid hormones and other variables, it was clinically insignificant.
Conclusions: The present study showed that abnormalities in thyroid function are high in patients undergoing haemodialysis and that there were no clinically significant correlation between the levels of thyroid hormones and clinical or biochemical characteristics.

Keywords: Haemodialysis, Observational study, Subclinical hypothyroidism, Thyroid status

INTRODUCTION

Hypothyroidism is common throughout the world.[1] The prevalence of hypothyroidism is high in India - 11%, particularly in cities situated inside as related to seaside towns[2] and about 42 million people in India are estimated to suffer from thyroid disease.[3] Ailment of thyroid function has been documented to occur at a higher rate in patients with chronic kidney disease (CKD), including those undergoing dialysis[4] than in general population. A survey conducted to determine the prevalence of hypothyroidism in North India among non-dialysis dependent CKD patients found an increase of hypothyroidism in this population.[5]

Low levels of thyroid hormones in haemodialysis patients has emerged as a potent biomarker of not only End Stage Renal Disease (ESRD) but also for malnutrition and inflammation as well.[6,7] Thyroid disorders in haemodialysis patients have attracted less attention despite new growing evidence of a higher mortality in ESRD patients with thyroid disease, in particular

hypothyroidism. In spite of the growing volume of information, there is a dearth of Indian data with respect to thyroid status in patients undergoing haemodialysis. To extend additional understanding into this, we performed a survey of the haemodialysis population visiting our tertiary care centre to ascertain the prevalence of hypothyroidism in patients undergoing maintenance haemodialysis as part of routine care for their renal problems.

METHODS

This study was a prospective study of patients undergoing maintenance haemodialysis at the Dialysis Unit of our institution between March 2018 and March 2019. Studies were performed at no extra cost to the participants, and patients were not compensated. The study protocol and data extraction form were approved by the Institutional Ethics Committee. The study in general was conducted in accordance with GCP Guidelines and written informed consent was obtained from all participants.

Authors performed a prospective cross-sectional analysis on 89 adults (>18 year of age) undergoing maintenance haemodialysis at Melmaruvathur Adhi Parasakthi Institute of Medical Sciences and Research Hospital, Melmaruvathur. All patients were on a 4 hr three times weekly haemodialysis schedule. The dialysis modalities were on-line hemodiafiltration (OL-HDF) or conventional haemodialysis (C-HD) with high-flux or low-flux dialyzer membranes respectively. We used semisynthetic membranes (polyamide or polysulphone) with surface ranging from 1.6-2.1 m2. The dialysis solution consisted of standard bicarbonate preparations (HCO3-: 32-35 mmol/L, Na: 138 mmol/L, K: 1-3 mmol/L, Mg: 0.5-0.75 mmol/L, Ca: 1.25-1.75 mmol/L). Low-molecular-weight or unfractionated heparin were used as standard anticoagulation. The inclusion criteria were as broad as possible in order to maximize generalization and to reflect the real-world conditions.

The following data were extracted using a standardized data extraction form - Demographic data (Age, sex, Height, Weight, BMI Waist circumference), pulse rate, Blood pressure, Disease Characteristics (Cause and duration of dialysis), Biochemical Profile (Blood Urea, Serum Creatinine, protein, albumin, calcium phosphate eGFR) along with status of thyroid - Free T3 (FT3), Free T4 (FT4) and Thyroid Stimulating Hormone (TSH) levels. Kidney function was calculated by using the formula developed and validated in the Modification of Diet in Renal Disease study. The Modification of Diet in Renal Disease formula was as follows: estimated GFR = 175.0 X (serum creatinine-1.154) X (age-0.203) X 1.212 (if black) X 0.742 (if female).

TSH, FT4, and FT3 were estimated by Enzyme Linked Fluorescent Assay (ELFA) using a fully automated immunoassay analyser MINI VIDAS® of bioMérieux USA. The reference range followed in our laboratory for TSH is 0.40–6.2 μ IU/L, FT3 is 1.4–4.2 pg/ml, and FT4 is 0.8 –2.0 ng/dl. The subjects were divided into three groups based on the levels of TSH FT3 and FT4 as follows: Euthyroid (TSH, FT3 and FT4 levels in normal range); Sub Clinical Hypothyroidism (TSH levels High; FT3 and FT4 levels in the normal range); Overt Hypothyroidism (TSH levels high; FT3 and FT4 levels low).

Sample size calculation

The minimum required sample size for a multiple regression study was found to be 76 subjects with desired probability level at 0.05, the number of predictors in the model being 3, the anticipated effect size being 0.15 and the desired statistical power level of 0.8. Assuming 10% of the study subjects may drop out of the study, 89 subjects were enrolled for the study.

Statistical analysis

Data are presented as mean±SD values. All data were subjected to one-way analysis of variance (ANOVA) and individual comparisons were made using Dunnett's t-test or Tukey HSD Post-hoc Test, wherever appropriate to establish the statistical difference between groups. All tests were two-sided, and p-values <0.05 were considered significant. Statistical analyses were accomplished using Graph Pad Prism 5 (Graph Pad Software, San Diego, CAUSA) for Windows (Microsoft Corporation, USA).

RESULTS

A total of eighty nine patients undergoing maintenance haemodialysis were enrolled for the present study. Their subject and biochemical characteristics are shown in Table 1. As shown in Table 1 there were no significant differences with respect to demographic or disease characteristics.

Subjects with overt hypothyroidism tended to be slightly younger while subjects with SCH were slightly older; however, these differences did not reach levels of statistical significance. Although the urea levels were higher and creatinine levels were lower as compared to the other groups, the difference in levels did not reach levels of statistical significance.

The thyroid status of the patients undergoing haemodialysis is shown in Table 2. As shown in Table 2, the levels of TSH and FT3 were higher in patients with SCH which was statistically significant. Although technically a negative correlation with R value of (-) 0.3194 was found between the levels of the thyroid hormone and various clinical (age, sex, height or weight) and biochemical (blood urea, creatinine) parameters or eGFR, the relationship between the various variables is only weak.

Table 1: Subject and biochemical Characteristics of patients undergoing haemodialysis.

Characteristic	Euthyroid (n=38)	SCH (n=40)	Hypothyroidism (n=11)
Age (years)	51.5±12.8	56.0±12.2	48.8±14.6
Sex (Male, Female)	25,13	30,10	7,4
Height (cm)	157.5±8.4	155.1±11.5	153.8±8.6
Weight (kg)	56.5±9.9	56.7±11.0	53.5±11.9
Waist (cm)	78.4±12.7	77.2±20.8	82.6±10.4
Pulse (bpm)	82.7±10	82.9±7.5	83.6±6.8
Sys BP (mm Hg)	145.1±20.5	149.9±14.8	140±7.7
Diastolic BP (mm Hg)	86.4±8.3	88.4±6.5	84.2±4.9
Diabetes and Hypertension (n)	14	17	7
Hypertension (n)	22	23	4
No Diabetes/Hypertension	2	0	0
Duration of dialysis (years)	4±5	4.4±5.2	5.9±4.2
Hb (g%)	7.9±1.7	7.5±1.8	8.5±2.7
Platelet Count	2.0±0.6	2.1±0.8	2.2±0.7
Urea (mg/dL)	84.6±32.3	71.9±28.8	93.4±54.2
Creatinine (mg/dL)	9.1±6.8	7.1±2.9	7.5±2.3
Calcium (mg/dL)	8.6±2.1	10.5±12.3	8.2±2.6
Phosphate (mg/dL)	4.6±1.4	5.5±5.8	5.1±2.2
Uric acid (mg/dL)	6.0±2.0	5.8±1.7	6.4±1.4
Protein (g %)	6.1±0.8	6.2±0.7	6.7±0.7
Albumin (g %)	4.5±4.6	3.7±0.5	3.7±0.5
Ejection Fraction (%)	64.3±10.5	65.4±8.9	59.6±9.7

Table 2: Thyroid Profile of patients undergoing haemodialysis.

Characteristic	Euthyroid (n=38)	SCH (n=40)	Hypothyroidism (n=11)
TSH (μ IU/L)	2.6±1.0	8.69±5.25 ***	16.18±14.9 ***
FT3 (pg/ml)	1.96±0.6	3.6±1.1***	1.6±0.5
FT4 (ng/dl)	1.1±0.5	1.07±0.17	0.67±0.16**

** $p < 0.01$ as compared to Euthyroid group
*** $p < 0.001$ as compared to Euthyroid group

DISCUSSION

The present study carried out to evaluate the status of thyroid gland in patients undergoing maintenance dialysis as part of routine medical care indicated that the frequency of SCH is high. Rhee and co-workers while studying the relationship between thyroid function and estimated glomerular filtration rate in patients with chronic kidney disease, showed that impaired kidney function was associated with higher risk of hypothyroidism, independent of socio-demographics and comorbidities.[8] A large observational study of thyroid function and mortality conducted in dialysis patients showed that hypothyroidism as well as high-normal TSH levels were associated with higher risk of cardiovascular disease and death.[9] In several studies of ESRD, low T3 levels have been reported as an unfavourable prognostic factor for survival.[10-12] moreover, pretransplant low T3 levels may be associated with higher risk of kidney graft failure.[13] Our finding of SCH in the present study is in agreement with the above mentioned studies. Since thyroid functional disease is an under-recognised cardiovascular risk factor in kidney disease patients, measurement of TSH levels may be justified as a screening test for hypothyroidism in patients undergoing haemodialysis to improve early risk stratification and reduction of cardiovascular disease and death.

To our knowledge, this is the first prospective study that has assessed the thyroid status by measuring TSH and T3 and T4 levels in subjects undergoing maintenance haemodialysis. The greatest strength and limitation of this study is observational nature of the study. Because there were no exclusion criteria, with inclusion of all subjects undergoing haemodialysis, our study is a representation of the haemodialysis population of a tertiary care centre. This study might underestimate the prevalence of thyroid disorders in patients undergoing haemodialysis as our study is not a controlled study. However, the present has the following limitations: a) Cross sectional nature of the study with limited period and not able to establish the causal relationship; b) thyroid status was assessed only

once, which could lead to distorted classifications; c) the levels of reverse triiodothyronine were not assessed. Further our study requires replication since we cannot identify the reason for SCH.

CONCLUSION

The present study showed that abnormalities in thyroid function are high in patients undergoing haemodialysis and that there were no clinically significant correlation between the various clinical and biochemical characteristics. Since there is an overlap between the uremic syndrome and hypothyroidism, tests to assess thyroid status should be interpreted with caution and clinicians should be made aware of the challenge in clinical decision making and management. A large prospective study involving more number of patients with increased follow up may present a better picture of hypothyroidism in patients undergoing maintenance haemodialysis.

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