ORIGINAL ARTICLE

Thyroid Function Tests Abnormalities in Patients on Thrice Weekly Hemodialysis

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ABSTRACT

Background: The diagnosis of thyroid disorder is rather difficult in patients with chronic kidney disease on maintenance hemo-dialysis (HD) due to their overlapping clinical features. The overlooked thyroid problems can be a cause of increased morbidity and mortality among end-stage renal disease (ESRD) uremic patients. Both hypothyroidism and eu-thyroid sick syndrome are least addressed precipitating factors of all-cause and cardiovascular mortality in uremic patients. This study intends to fractionate the patients with thyroid dysfunction on maintenance hemo-dialysis.

Patients and Methods: Seventy patients of ESRD booked for thrice weekly HD, 3-4 hours per sessions in Dialysis center of Sir Ganga Ram Hospital, Lahore underwent blood sampling for measurement of serum free T3, free T4 & TSH during their active HD session. All patients were categorized to overt hypothyroidism, overt hyperthyroidism, subclinical hypothyroidism, subclinical hyperthyroidism and euthyroid sick syndrome and its subtypes according to their laboratory values.

Results: Male to female ratio was 1.9:1, with mean age of 47 years. Euthyroid status, hypothyroidism and euthyroid sick syndrome were observed in 32%, 12.9% and 57.1% patients respectively.

Conclusion: It is concluded that most of HD patients are either suffering from euthyroid sick syndrome or hypothyroidism. As euthyroid sick syndrome can be a causative factor for sudden cardiac death, regular assessment of thyroid function tests in patients on maintenance HD is recommended to determine cardiac risk of dialysis patients.

Keywords: thyroid function tests, thyroid stimulating hormone, euthyroid sick syndrome, end stage renal disease, hemodialysis

INTRODUCTION

Thyroid hormones are metabolized, degraded and excreted, mainly by the kidneys. Therefore, it is very frequent to have deranged thyroid functions tests in patients with renal impairment. However, there is a considerable degree of overlap in symptoms of impaired thyroid functions and symptoms of renal failure. Therefore, very careful interpretation of results is required while assessing any of these abnormalities. It is clear from epidemiological data that pre-dialysis patients with uremia are considerably at increased risk of developing hypothyroidism.[1,2] It is mainly because of raised iodide levels in plasma secondary to impaired renal excretion, which in turn lead to increased intra-thyroidal iodide concentration. Thyroid hormone synthesis is usually blocked by this inappropriately elevated level of iodide within thyroid gland. This is called as Wolff-Chaikoff effect. This is the reason that may be responsible for increase frequency of goiter and hypothyroidism in patients with renal impairment.[3] Low plasma levels of free tri-iodothyronine (T3) in uremic patients can be explained by decrease peripheral conversion of thyroxine (T4) to T3. [4-6] Metabolic acidosis and diminished protein binding can also be responsible for low levels of total T3 and T4.[7] While T4 binding to thyroid binding globulin can also be affected by the presence of free fatty acids and heparin in the blood. Therefore, transiently elevated T4 levels in hemodialysis patients can be better explained by the common use of heparin for prevention of blood clotting in dialysis tubing.[8] Low levels of T3 are found to be associated with decreased overall patient survival and the development of malnutrition-inflammation syndrome[(9,10)]. Malnutrition-inflammation syndrome is common in dialysis patients with markedly elevated cytokines levels. The plasma levels of thyroid stimulating hormone (TSH) are not usually affected by the renal impairment.[4,5,11] Initially it was considered that low plasma T3 levels are normal adaptation to

any chronic illness, however, now they are found to be associated with increased incidence of all cause and cardiovascular mortality in uremic patients.[10,12-14] Whether low T3 and T4 are markers for some other clinical process that associates more directly with mortality or have a causal role remains to be determined as does the pathophysiologic basis for this association. Symptoms of hypothyroidism mimic uremic symptoms, therefore, it is difficult to suspect hypothyroidism in dialysis patients and most of these patients remain undiagnosed. These undiagnosed thyroid abnormalities remain a cause of increased morbidity and mortality among dialysis patients. This study is conducted to find out how many percentages of patients on thrice weekly dialysis are having abnormal thyroid functions tests in our setup and are not getting management accordingly.

PATIENTS AND METHODS

Cross-sectional study was conducted at the dialysis center of Sir Ganga Ram hospital, Lahore employing convenient sampling technique. Seventy patients of end stage renal disease undergoing thrice weekly maintenance hemodialysis were included. Each dialysis session constitutes 3-4 hours duration. Patients were assessed via a designed questionnaire before the start of dialysis as per their age, gender, cause of ESRD, vital signs including body temperature, heart rate, respiratory rate, systolic and diastolic blood pressure, associated comorbidities (IHD, HTN, DM), active medication history, and duration of renal replacement therapy. Blood sample were collected for Thyroid profile including free T3, free T4 and TSH, during active dialysis session, and sent to laboratory immediately. Patients were labeled as overt hypothyroidism with low FT4 and high TSH levels, Subclinical hypothyroidism with high TSH and normal FT4, overt hyperthyroidism with high FT4 and/or FT3 and low TSH, subclinical hyperthyroidism with low TSH and normal FT4 and T3. Euthyroid sick syndrome was defined according to the accepted criteria and further divided into 7 types,[8,15] four of them with low FT3 (type 1= normal TSH and FT4, type 2= low TSH and normal FT4, type 3= low TSH and low FT4, type 4= normal TSH and low FT4) and 2 with high FT4 and (type 5= normal TSH and normal FT3, type 6= normal TSH and Low T3) type 7 = normal FT3, TSH and low FT4).

RESULTS

A total of 70 patients with end-stage renal disease on regular hemodialysis were enrolled in the current study. Their thyroid profile with mean frequencies are shown in Table 1.

Table 1: Means frequencies of thyroid hormones

Parameter	Mean±SD
Free T3	2.52 +0.35
Free T4	0.68 +0.18
TSH	4.41 +12.2

Table 2: Ratio of thyroid hormones

Parameter	Low (%)	Normal (%)	High (%)
Free T3	39 (55.7)	31(44.3)	0
Free T4	23(32.9)	46 (65.7)	1 (1.4)
TSH	0	61 (87.1)	9 (12.9)

Table 3: Thyroid status of patients

Thyroid status	Frequency (%)
Euthyroid	21 (30)
Overt Hypothyroidism	9 (12.9)
Euthyroid sick syndrome	40 (57.1%)
Type 1	22 (31.4)
Type 4	9 (12.9)
Type 6	1(1.4)
Type 7	18 (25.7)

Percentage of patients having low, normal and high free T3, free T4 and TSH are shown in Table 2. Table 3 summarizes the thyroid status of the study patients. It is noteworthy that most of the patients (57.1%) in our study were found to have sick euthyroid syndrome and none of the patient found to be hyperthyroid.

DISCUSSION

Patient with euthyroid sick syndrome have almost 3-fold higher risk of death in the first year when compared with patients with euthyroidism according to a study conducted in past.[14] In this study, 57.1% of patient had euthyroid sick syndrome, so its clinically significant, as almost sixty percent of patients are considered at higher risk of death. These results are comparable to the study conducted in Spain in 2009, where they found 68.6% of patients with euthyroid sick syndrome.[15] These patients with euthyroid sick syndrome need to be followed up to compare their mortality with that in euthyroid patients. This study found overt hypothyroidism in 12.9% of patients that have not been tested before and on no treatment for thyroid disorder. As there is considerable degree of clinical overlap between chronic kidney disease and hypothyroidism, it is hard to detect hypothyroidism clinically in patients with renal impairment. In addition to low total and free T3 levels, there are a number of symptoms that are common to both conditions. Such as, cold intolerance, puffy appearance, dry skin, lethargy, fatigability, and constipation. Furthermore, the frequency of goiter is markedly increased in end-stage renal disease.[4,16] Hypothyroidism can occur in patients with renal disease, with a frequency that may be slightly greater than that in the general population.[4,17] To diagnose hypothyroidism, patient should have elevated serum TSH levels with low serum free T4 and normal thyroid binding globulins levels.[4] Delayed deep tendon relaxation and depressed metabolic rate may be confirmatory clinical findings. This clinical finding of delayed deep tendon reflexes proved to be very beneficial as it can be used to diagnosed hypothyroidism in patients with impaired renal functions. These hypothyroid patients (12.9%) were not aware of their hypothyroidism. After getting results these patients were put on adequate dose of thyroxine and planned to keep in long term follow up. Study conducted in India have almost similar results with 16% of patients suffering from overt hypothyroidism.[18] Despite these findings, most uremic patients are found to be euthyroid as proven by their normal plasma concentrations of TSH and free T4, and tendon relaxation time.[4,5,11,19] In this study 30% of patients were euthyroid. Despite the euthyroid status of most uremic patients, there is some evidence for blunted tissue responsiveness of T3(11). Although basal oxygen utilization is normal in renal failure, the expected increase following the administration of T3 is not seen. Reduce T3 levels are believed to be protective by decreasing protein catabolism.[20] In this study none of the patients was found to have hyperthyroidism, sub-clinical hypo- or hyperthyroidism. This may be due the smaller sample size of our study. So, further studies need to be conducted on larger scale to get more elaborated results.

CONCLUSION

This is concluded that most of hemodialysis patients may be either suffering from euthyroid sick syndrome or hypothyroidism. Euthyroid sick syndrome can lead to sudden cardiac death and increase mortality in renal patients undergoing hemodialysis. So, cardiac risk of dialysis patients can be estimated by regular monitoring of their thyroid function tests. Further studies with increased sample size are recommended to find out more cases of thyroid disorder in hemodialysis patients.

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