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Euthyroid Sick Syndrome in Chronic Hemodialysis Patients: Prevalence and Associated Factors

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Abstract **Original Research Article**

Introduction: Thyroid diseases in chronic hemodialysis patients (CHP) are often underdiagnosed, primarily manifesting as Euthyroid Sick Syndrome (ESS), which is characterized by clinical euthyroidism associated with biological hypothyroidism. Our study aims to determine the thyroid profile in our CHP to clarify the prevalence and associated factors of ESS. ***Material and Methods:*** This is a cross-sectional, analytical study including CHP at our center. We examined clinical data and performed hormone assays (free triiodothyronine (T3), free thyroxine (T4), and ultra-sensitive thyrotropin (U-TSH)). We performed an analysis of independence using the Chi-square test between clinical and biological factors and ESS. ***Results:*** 36 patients were included, with a sex ratio of 1.4. The mean age was 44 years (17-85). The mean duration of hemodialysis was 94 months (4-408). The average hormone levels were: T3 at 2.21 ± 1.01 ng/l, T4 at 0.98 ± 0.55 ng/dl, and U-TSH at 2.4 ± 2.1 mUI/l. The prevalence of ESS was 36.11%, representing 76.47% of thyroid diseases, while hyperthyroidism was found in 11,11% of cases. The mean C-reactive protein level was 14 mg/l, mean hemoglobin was 8.02 g/dl, and mean parathyroid hormone was 688 pg/ml. The threshold of acceptability is 3.84 for a degree of freedom equal to 1 and was consulted on the table of the Chi-square with a risk of 5%. The deviation of the Chi-square for our study is 5,66 for inflammatory syndrome and hyperparathyroidism which exceeds the threshold of acceptability 3.84. Consequently, we identified inflammatory syndrome and hyperparathyroidism as significant factors associated with ESS. ***Conclusion:*** ESS affects more than one-third of the CHP in our study, highlighting the importance of systematic screening. Inflammatory syndrome and hyperparathyroidism appear as associated factors.

Keywords: Euthyroid sick syndrome, chronic hemodialysis patients, inflammatory syndrome, hyperparathyroidism, thyroid diseases.

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INTRODUCTION

Chronic kidney disease (CKD) exposes patients, due to the endocrine and exocrine dysfunction of the kidneys, to alterations in various organs and systems, particularly the endocrine system. In addition to the well-documented parathyroid complications that are systematically assessed in chronic hemodialysis patients, the thyroid gland also experiences functional and morphological changes because of its close relationship with the kidneys.

Thyroid diseases are common and often underdiagnosed in chronic hemodialysis patients, primarily manifesting as euthyroid sick syndrome (ESS), which features clinical euthyroidism alongside biological hypothyroidism. ESS is serious, as epidemiological studies have identified it as an independent cardiovascular risk factor. Its pathophysiology is still not fully understood. Additionally, other thyroid disorders, such as hyperthyroidism and nodular goiter, may further complicate end-stage renal disease.

Our study aims to assess the thyroid profile in our chronic hemodialysis patients and clarify the prevalence and associated factors of euthyroid sick syndrome.

MATERIAL AND METHODS

We conducted a cross-sectional analytical study at the nephrology, dialysis, and renal transplantation department of Ibn Rochd University Hospital in Casablanca, Morocco, in January 2025. We excluded any patient receiving treatment that could interfere with thyroid function (antithyroid drugs, amiodarone, rifampicin). For each patient, we studied: anthropometric

and clinical data (age, sex ,the cause of end-stage renal disease (ESRD) , duration of hemodialysis, clinical signs of thyroid diseases).We collected blood samples before connecting the patients to dialysis, including thyroid hormone assays (free triiodothyronine (T3), free thyroxine (T4), and ultra-sensitive thyrotropin (U-TSH)), as well as hemoglobin, C-reactive protein (CRP), albumin, calcium, phosphate, vitamin D, and parathyroid hormone (PTH).

Euthyroid sick syndrome (ESS) is defined by abnormalities in peripheral thyroid hormones T3 and/or T4, with normal TSH and clinical euthyroidism.

We performed a Chi-squared independence analysis on various factors (sex, age, duration of hemodialysis, anemia, phosphocalcic balance, hyperparathyroidism, and inflammatory syndrome with high CRP level) in relation to ESS. Following this analysis, we identified the factors associated with euthyroid sick syndrome (ESS)**.**

RESULTS

36 chronic hemodialysis patients were included, with a mean age of 44 years (17 to 85 years). Patients aged 65 years or older represented 13.88% of the sample (n = 5). The sex ratio was 1.4, with 21 men and 15 women. **(Figure 1)**

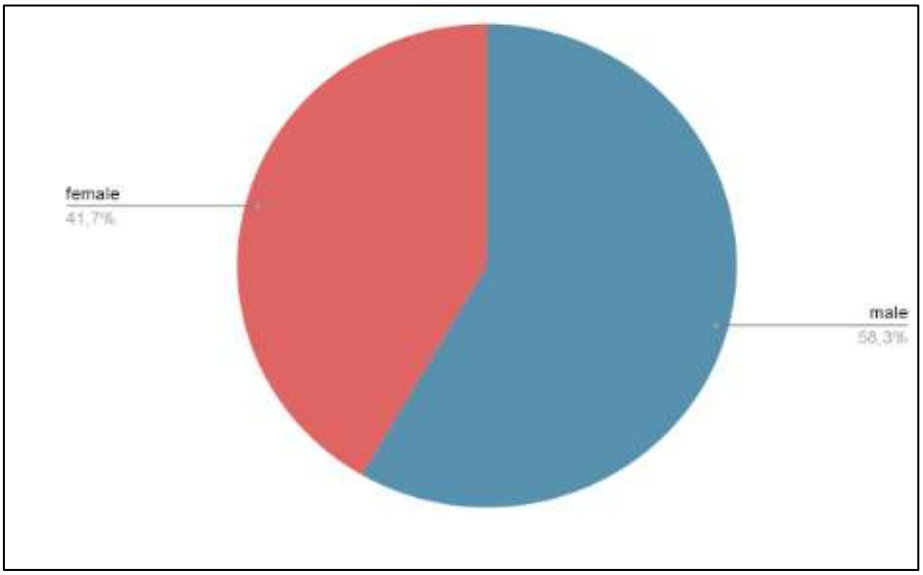

Figure 1: Distribution of patients by gender

The average duration of hemodialysis was 94 months (4 to 408 months). The causes of end-stage renal disease (ESRD) were as follows: undetermined nephropathy (30.56%, n = 11), vascular nephropathy (38.89%, n = 14), diabetic nephropathy (11.11%, n = 4), polycystic kidney disease (2.78%, n = 1), lupus (8.33%, n = 3), and focal segmental glomerulosclerosis (8.33%, n = 3). **(Table 1).**

Table 1: Causes of End-Stage Renal Disease (ESRD)

Cause of ESRD	Percentage (%)	Number of patients (n)
Undetermined nephropathy	30.56	11
Vascular nephropathy	38.89	14
Diabetic nephropathy	11.11	4
Polycystic kidney disease	2.78	1
Lupus	8.33	3
Focal segmental glomerulosclerosis	8.33	3

Three of our patients underwent 2 sessions of 5 hours of dialysis per week, while 33 patients were dialyzed 3 times a week for 4 hours per session. The average interdialytic weight gain (IWG) was 2.4 kg (0.5 to 4.5 kg). 10 patients had heart disease of various types, confirmed by transthoracic echocardiography. The mean Body Mass Index (BMI) was 22.9 kg/m² (16.97 to 29.32 kg/m²).

All patients were clinically euthyroid. The mean hormone levels were: T3 at 2.21 ± 1.01 ng/l, T4 at 0.98 ± 0.55 ng/dl, and U-TSH at 2.4 ± 2.1 mUI/l. The prevalence of euthyroid sick syndrome (ESS) was 36.11% (n=13), representing 76.47% of thyroid diseases. (n=17), while hyperthyroidism was found in 11.11% of cases (n=4), representing 23.53% of thyroid diseases. **(Table 2).**

Table 2: The frequency of various thyroid disorders

Thyroid disorder	Number of cases	Percentage among all patients % (n=36)	Percentage among patients with thyroid disorder % (n=17)
Eutyhroid sick syndrome (ESS)	13	36,11 %	76,47 %
Hyperthyroidism	4	11,11 %	23,53 %

The mean C-reactive protein level was 14 mg/l, the mean hemoglobin level was 8.02 g/dl, and the mean parathyroid hormone level was 688 pg/ml.

Statistical analysis revealed that inflammatory syndrome with high CRP level and hyperparathyroidism were significantly associated with ESS, with a Chi-squared value of 5,66 exceeding the acceptable threshold of 3.84 at a 5% risk level. **(Table 3).** At the top of every case in the **table 3**, we find the observed frequencies. At the bottom of every case in the table, we find the theoretical frequencies for the Chi-Square Test. E= 5,66 >3.84 ⇒ Dependence. The same results have been found for inflammatory syndrome.

Table 3: Factors associated with Eutyhroid sick syndrome (ESS): Chi-Square Test

ESS Parathyroid hormone (PTH)	Presence of ESS	Absence of ESS	Total
Hyperparathyroidism	8 4,69	5 8,3	13
Normal level of Parathyroid hormone	5 8,3	18 14,7	23
Total	13	23	36

The Chi-square values for sex, age, duration of hemodialysis, calcium levels, phosphorus levels and hemoglobin were all below the acceptability threshold of 3.84. Therefore, we did not consider these factors as dependent on ESS.

DISCUSSION

In the embryonic stage, there is a close relationship between the thyroid gland and the kidneys. Thyroid hormones play an important role in the development, structure, and hemodynamics of the kidneys. The kidneys, in turn, are necessary for the secretion, metabolism, and excretion of thyroid hormones [1,2]. Any thyroid dysfunction is likely to cause vascular disturbances in the glomerulus and tubular function. [1,3,4]. On the other hand, the impairment of renal function in various kidney pathologies, particularly chronic kidney disease, also impacts both the hypothalamic-pituitary axis and the peripheral metabolism of thyroid hormones. [1,5,6].

The plasma concentration of TSH is usually normal during chronic kidney disease. [7-10]. In chronic kidney disease, abnormally elevated uremic toxins such as urea, creatinine, metabolic acidosis, and certain medications used, notably furosemide and per-dialytic anticoagulation with heparin, can interfere with and inhibit binding and transport proteins, consequently leading to a decrease in the concentration of thyroid hormones. [1,11-15].

The most common thyroid disorder in chronic hemodialysis patients is euthyroid sick syndrome [1,16,17]. The prevalence of euthyroid sick syndrome varies between 9% and 25%.[18]. In our study, the frequency was 36.11% (13 cases), representing 76.47% of thyroid diseases. Other studies have reported similar results. **(Table 4)**

Table 4: Prevalence of euthyroid sick syndrome in our study and in the literature

Country	Study	n	Prevalence of euthyroid sick syndrome (ESS) %
Italy	Zoccali [20]	n=200	20 %
USA	Lim [3]	—	25 %
Czech Republic	Horaceck [19]	n=167	56,3 %
Casablanca Morocco	Our study	n=36	36,11 %

Hyperthyroidism is rarely found in hemodialysis patients. It is considered a cause of resistance to recombinant erythropoietin in anemia. In our study, it was found in 11.11% of patients.

Several prospective studies [19-22] have demonstrated a significant difference between chronic kidney patients with and without euthyroid sick syndrome, concluding that the latter constitutes an independent poor prognostic factor [23-26].

Studies have identified factors associated with euthyroid sick syndrome (ESS), which include long duration of hemodialysis, advanced age, inflammatory

syndrome, and hyperparathyroidism [27,28]. The results of our work align with the literature, highlighting inflammatory syndrome and hyperparathyroidism as factors associated with ESS. However, we did not find a correlation between advanced age, duration of hemodialysis and ESS.

CONCLUSION

Euthyroid sick syndrome affects more than one-third of chronic hemodialysis patients in our study and represents a significant risk factor for cardiovascular morbidity and mortality, highlighting the importance of systematic screening, particularly through assessments that include T3, T4, and TSH levels. Our study found that inflammatory syndrome and hyperparathyroidism are factors associated with ESS. Addressing these conditions could reduce the prevalence of ESS.

Conflict of Interest: No conflict of interest declared by the authors.

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