Graves’ disease is the most common cause of severe hyperthyroidism that is accompanied by greater than usual clinical signs and symptoms and laboratory abnormalities


RESULTS A total of 107 patients with overt hyperthyroidism were evaluated during the study period, 81 of whom were women (76%) with a mean age (±SD) of 46.9±16.1 years.

Clinical Features (Figure 1) Of the 107 patients, 49 were classified as having mH (46%), 41 of whom were women (84%) 49±15 years of age; 37 were classified as MH (36%), 26 of whom were women (84%) 47±17 years of age; and 21 were classified as SH (20%), 41 of whom were women (84%) 41±17 years of age. Hyperthyroidism was regarded as de novo disease in 33 of 49 patients with mH (67%), 33 of 37 with MH (89%), and 19 of 21 with SH (90%). Hyperthyroidism was considered to be a relapse in 16 of 49 patients with mH (33%), 41 of 32 with MH (13%), and 2 of 21 with SH (10%). The SH group was significantly younger than the other groups, and a greater proportion of SH patients had their first (de novo) episode of hyperthyroidism (P<0.05 for both age and de novo episode as compared with patients who had mH and MH). The clinical features of the patients according to the severity of hyperthyroidism are shown in Figure 1. Here and elsewhere, percentages are rounded to an integer.

Causes of Hyperthyroidism (Figure 2) Graves’ disease was the cause of hyperthyroidism in 79 of the 107 patients (74%), and was significantly more frequent in patients with SH (n = 18, 86%) as compared with Graves’ disease in the mH group (n = 31, 63%) and MH group (n = 30,
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81%). None of the patients with SH had toxic multinodular goiter or thyroid adenoma. The other causes of hyperthyroidism are shown in Figure 2.

Signs and Symptoms (Figure 3)
The most common symptoms in the SH group were weakness, nervousness, dyspnea, and weight loss. Weight loss was 15.6±17, 5.8±11.7, and 8.6±9.7 lb (7.1±7.7, 5.8±5.3, and 3.9±4.4 kg) in the SH, MH, and mH groups, respectively. The heart rate and goiter grade were greater in the SH group as compared with the mH and MH groups (P<0.01). Atrial fibrillation was significantly more frequent in the SH group (16%) as compared with the mH (5%) and MH (0%) groups. However, there were no significant differences in the frequency of exophthalmos, goiter, or tremor in the SH group as compared with the mH and MH groups. Logistic-regression analysis found that the following three features were independently associated with SH: younger age (odds ratio [OR], 0.958 [95% confidence interval 95%CI, 0.923 to 0.995] P = 0.026), higher heart rate (OR, 1.03 [95% CI, 1.01 to 1.06, P = 0.013), and overall weakness (OR, 4.35 [95% CI, 1.48 to 12.78, P = 0.008]).

Laboratory Data (Figure 4)
The only laboratory findings that were significantly different were TSH levels in the SH versus the mild hyperthyroidism group. The SH group had higher serum aminotransferase (AST) (P<0.01) and calcium (P<0.05) levels, and lower serum cholesterol and albumin concentrations (both P<0.05) as compared with the mH and MH groups. There was a positive association between serum FT4 concentrations and heart rate (r = 0.309, P<0.05), alanine aminotransferase (r = 0.275, P<0.01), and TSH-receptor antibodies (r = 0.238, P<0.01), and a negative correlation with cholesterol (r = 0.313, P<0.01).

Treatment and Outcome (Figure 5)
Follow-up of more than 6 months was performed in 80 patients, 18 with SH (95%), 35 with mH (71%), and 27 with MH (73%). The duration of follow-up was 28.7±18.7 months for SH, 42.7±31.1 months for mH, and 49.8±43.3 months for MH (P = not significant). There were no significant differences in the therapy administered to the three study groups, including antithyroid drugs, radioiodine and surgery, nor were there differences in the subsequent rates of hypothyroidism following therapy.
the administration of antithyroid drugs, radiiodine, and surgery, nor were there differences in the subsequent rates of hypothyroidism following therapy in the three groups. However, patients with SH had a slightly lower cure rate as compared with the other two study groups. The only variable that was an independent predictor of cure was the serum FT₄ concentration (OR, 0.98 [95% CI, 0.97 to 0.99] P<0.05); however, at the conclusion of the analysis, the thyroid functional status was similar among the three groups.

CONCLUSION Graves’ disease is the most common cause of severe hyperthyroidism and is accompanied by more clinical signs and symptoms and laboratory abnormalities as compared with milder forms of hyperthyroidism.

COMMENTARY

In this study, several features characterized the SH group: the majority had de novo hyperthyroidism (90%) as compared with 33% of patients with mH and 13% with MH who had de novo disease. The remaining patients had a relapse of hyperthyroidism. In addition, heart rates were higher and atrial fibrillation was more common in patients with SH as compared with patients who had less severe hyperthyroidism. Still, there were no differences in the type of therapy, cure rate, and time to achieve a cure. Logistic regression found that FT₄ was the only independent predictor of cure. The study was unable to find a difference in treatment, time to achieve a cure, and remission rate among patients in the three groups of hyperthyroidism. Although the symptoms of hyperthyroidism were more severe in patients with SH and MH, symptomatology was not used as a criterion for the diagnosis of severe disease.

The study by Iglesias based the severity of disease on the serum FT₄ levels, which are likely to provide one of the best criteria for severe hyperthyroidism, although the patient’s presenting symptoms and cardiovascular manifestations generally provide a reliable set of features to identify patients with severe disease. Moreover severe myopathy and severe asthenia are also harbingers of severe disease. Still, as compared with younger patients, older patients with severe hyperthyroidism, are generally less likely to have tachycardia and tremor, and present with more weight loss (1). Moreover, cardiovascular manifestations of Graves’ disease, especially atrial fibrillation, are common presenting symptoms in patients over 50 years of age (1-4).

In a comprehensive review Brent (1) advised antithyroid drugs, β-blockers, and propylthiouracil to block the conversion of T₄ to T₃. Most experienced endocrinologists rely on the symptoms of hyperthyroidism to provide an assessment of the severity of disease. Omitting the clinical presentations of signs and symptoms seems to be an important omission in stratifying the severity of disease.

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References