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*Thyroid function in patients with amyotrophic lateral sclerosis*

Amyotrophic lateral sclerosis (ALS) is a severe disease characterized by neurogenic amyotrophy and degeneration of upper and lower motor neurons (3). The etiopathogenesis of this disease is unknown. Disturbances of thyroid gland function and association motor neurone disease with hyperthyroid Graves' disease was suspected (8). The aim of this study was to evaluate serum triiodothyronine (T3), thyroxine (T4), and thyroid stimulating hormone (TSH) in serum of ALS patients and to find out whether there is a relationship between thyroid hormones level in ALS and the clinical parameters of the disease (the clinical state of patients and the duration of the disease).

MATERIAL AND METHODS

Thirty one (16 ALS and 15 controls) patients with an average age of 60 (range 28–71 years) took part in the study. The ALS patients were diagnosed according to the El Escorial criteria of ALS (2). They were divided into 2 groups according to the clinical state scale (10) (with mild and severe symptoms). The average duration of ALS was 18 months (6–48 months). The ALS patients were also divided into 2 groups according to duration of ALS (short and long duration). The control group consisted of 15 patients, of equal age, with lumbosacral disc disease, which was confirmed by MRI. Samples of blood from ALS and control group patients were taken during the diagnosis. The characteristics of the patients are presented in Table 1.

Table 1. The characteristics of patients

Group	N	Male/female
Control	15	9/6
ALS (total)	16	9/7
ALS short duration ( $\leq 12$ months)	11	6/5
ALS long duration ( $> 12$ months)	5	3/2
ALS mild clinical state	8	5/3
ALS severe clinical state	8	3/5

N – number of patients

The study was approved by the Ethics Committee of Medical University in Lublin. Each ALS patient and control subject gave consent to enter the study.

The serum levels of total T3, total T4, and TSH were measured by radioimmunoassay. The Mann-Whitney U test was used to examine the differences between the groups;  $p$  values  $< 0.05$  were considered significant.

## RESULTS

The mean serum T3, T4 and TSH levels are presented in Table 2. The median serum T3, T4 and TSH levels and range of their values in ALS patients are presented in Fig. 1, Fig. 2 and Fig. 3.

Table 2. Serum thyroid hormone levels

Group	T3 (ng/ml) mean $\pm$ SD	T4 ( $\mu$ g/dl) mean $\pm$ SD	TSH ( $\mu$ IU/ml) mean $\pm$ SD
Control	0.91 $\pm$ 0.19	7.30 $\pm$ 1.35	1.48 $\pm$ 1.16
ALS	0.88 $\pm$ 0.51	7.44 $\pm$ 1.49	1.17 $\pm$ 0.63
ALS short duration	1.02 $\pm$ 0.57	8.09 $\pm$ 1.75	0.89 $\pm$ 0.46
ALS long duration	0.83 $\pm$ 0.15	7.18 $\pm$ 1.38	1.39 $\pm$ 0.68
ALS mild clinical state	0.89 $\pm$ 0.20	7.37 $\pm$ 0.73	1.46 $\pm$ 0.76
ALS severe clinical state	1.14 $\pm$ 0.81	7.50 $\pm$ 2.06	0.96 $\pm$ 0.45

The values are expressed as mean  $\pm$  SD

Table 3. Comparative analysis of thyroid hormones level between the group of ALS patients and controls

Hormone	Significance
T3	$p = 0.58$
T4	$p = 0.81$
TSH	$p = 0.59$

Mann-Whitney U test; statistical significance  $p < 0.05$

Table 4. Comparative analysis of thyroid hormones level between the groups of ALS patients

Comparison	T3	T4	TSH
Short versus long duration of ALS	$p = 0.39$	$p = 0.32$	$p = 1.00$
Mild versus severe clinical state	$p = 0.56$	$p = 0.42$	$p = 0.29$

Mann-Whitney U test; statistical significance  $p < 0.05$

The results showed that serum T3, T4 and TSH levels in ALS patients were not different from those of the controls ( $p > 0.05$ ) – Table 3. There were also no significant differences in serum T3, T4 and TSH levels between the groups of ALS patients depending on the duration of the disease and the clinical state of patients (Tab. 4).

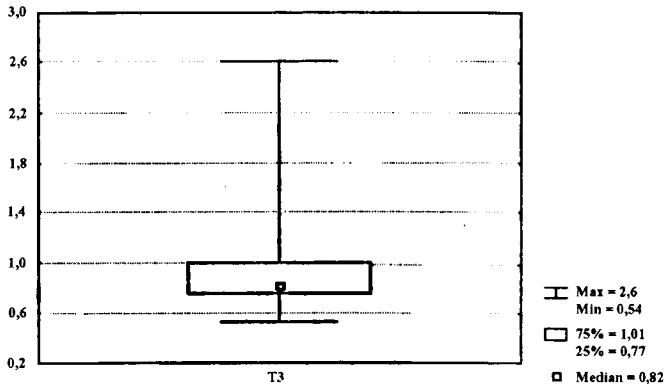


Fig. 1. T3 level in ALS patients

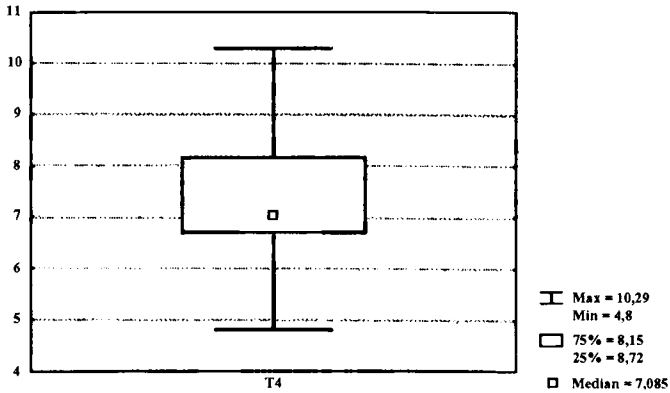


Fig. 2. T4 level in ALS patients

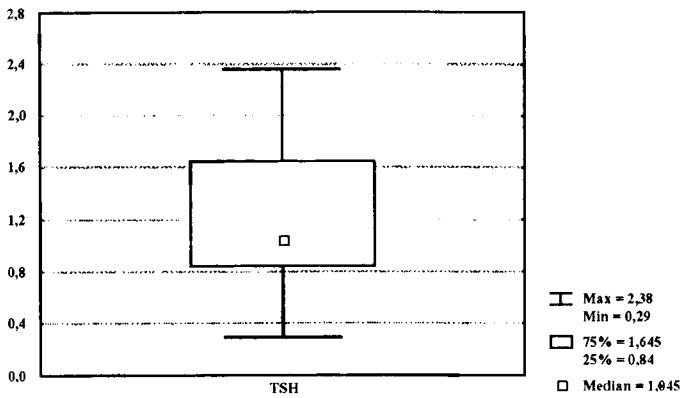


Fig. 3. TSH level in ALS patients

## DISCUSSION

Our results showed that serum T3, T4 and TSH levels were not different from those in the controls, and their level did not depend on the clinical state of ALS patients or the duration of the disease.

Previously, the normal serum T3, T4 and TSH levels were also reported by different authors (5-7). However, there are some data in the literature indicating the association of ALS with hyperthyroidism and Graves' disease (immunogenic thyrotoxicosis). In patients presented by Pou et al. (9) the neurological symptoms disappeared after the treatment of hyperthyroidism. Appel et al. (1) observed a family history of thyroid disease in 19 %, and other autoimmune disorders in 21 % of patients with ALS. Past or present thyroid disease in 19 % of ALS patients was found. Some patients had a marked increase in microsomal and/or thyroglobulin antibody levels. It suggests that autoimmunity may play an important role in the etiopathogenesis of ALS. Fishman et al. (4) observed the presence of antibodies to gangliosides in the serum of ALS patients with association of thyroid gland adenoma. Yoshino et al. (11) measured triiodothyronine receptors (NT3R) in the precentral gyrus of the brain from people who died of ALS, and observed a significantly decreased density of NT3R compared to controls that could suggest a tendency to hypothyroidism in ALS. In the light of literature data it seems that disturbances of thyroid gland function might influence motor neurons.

Our results referring to the serum of ALS patients do not indicate that changes in thyroid gland hormone exist in this disease. However, the coexistence of ALS with autoimmune diseases, including immunogenic thyrotoxicosis, reducing the density of T3R in the central nervous system may suggest their unclear role in the etiopathogenesis of motor neuron disease. Moreover, it seems that recovery of motor neuron symptoms after hyperthyroidism treatment can give a hope that ALS may also be a reversible disorder.

## CONCLUSIONS

1. The study demonstrated that serum T3, T4 and TSH levels in ALS patients did not differ from those of the controls.

2. The clinical parameters of ALS did not influence serum T3, T4 and TSH levels.

## REFERENCES

1. Appel S.H. et al.: Amyotrophic lateral sclerosis. Associated clinical disorders and immunological evaluations. *Arch. Neurol.*, 43, 234, 1986.
2. Brooks B.R.: El Escorial World Federation of Neurology criteria for the diagnosis of amyotrophic lateral sclerosis. *J. Neurol. Sci.*, 124 (Suppl), 96, 1994.
3. Desport J.C. et al.: Factors correlated with hypermetabolism in patients with amyotrophic lateral sclerosis. *Am. J. Clin. Nutr.*, 74, 328, 2001.
4. Fishman P.S. et al.: Antibodies to the ganglioside GD1 b in a patient with motor neuron disease and thyroid adenoma. *Arch. Neurol.*, 48, 1188, 1991.
5. Iwasaki Y., Kinoshita M.: Normal thyroid function in 32 patients with amyotrophic lateral sclerosis. *Jpn. J. Med.*, 28, 309, 1989.
6. Kiessling W.R.: Thyroid function in 44 patients with amyotrophic lateral sclerosis. *Arch. Neurol.*, 39, 241, 1982.
7. Malin J.P. et al.: T4, T3 and rT3 levels in serum and cerebrospinal fluid of patients with amyotrophic lateral sclerosis. *J. Neurol.*, 236, 57, 1989.
8. McMenamin J., Croxon M.: Motor neurone disease and hyperthyroid Graves' disease: an association? *J. Neurol. Neurosurg. Psychiatry*, 43, 46, 1980.

9. Pou Serradell A. et al.: Amyotrophic lateral sclerosis syndrome and hyperthyroidism. Cure with antithyroid drugs. *Rev. Neurol. (Paris)*, 146, 219, 1990.
10. Riviere M. et al.: An analysis of extended survival in patients with amyotrophic lateral sclerosis treated with riluzole. *Arch. Neurol.*, 55, 526, 1998.
11. Yoshino Y. et al.: Assay of nuclear triiodothyronine receptors in the precentral gyrus in patients with amyotrophic lateral sclerosis. *Rinsho. Shinkeigaku*, 30, 45, 1990.

#### SUMMARY

Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disease affecting motor neurons. Etiopathogenesis of the disease is not known. It is supposed that immunological disturbances play a role, which is among others confirmed by coexistence of ALS with autoimmunological disorders, including thyroid diseases. The aim of the study was to investigate the thyroid function in ALS through the measurement of triiodothyronine (T3), thyroxine (T4), and thyroid stimulating hormone (TSH) in the serum of ALS patients. The hormones level was measured by radioimmunoassay method. The study showed that the hormones level in ALS patients was not different from controls, and the clinical parameters of the disease did not influence the measured hormones level.

#### Funkcja tarczycy u chorych na stwardnienie boczne zanikowe

Stwardnienie boczne zanikowe (SLA) jest chorobą neurodegeneracyjną, charakteryzującą się uszkodzeniem neuronów ruchowych. Etiopatogeneza SLA nie jest znana. Przypuszcza się, że pewną rolę odgrywają zaburzenia immunologiczne, czego dowodem może być między innymi występowanie SLA łącznie z chorobami autoimmunologicznymi, w tym chorobami tarczycy. Celem pracy była ocena funkcji tarczycy u chorych na SLA poprzez pomiar we krwi poziomu trójiodotyroniny (T3), tyroksyny (T4) i hormonu stymulującego tyreotropinę (TSH). Poziom wymienionych hormonów oznaczano metodą radioimmunologiczną. Badanie wykazało, że poziomy hormonów we krwi osób chorych na SLA nie różniły się istotnie od poziomów w grupie kontrolnej. Również parametry kliniczne choroby nie miały wpływu na poziom badanych hormonów.