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Thyroid function hormones profile in acute stroke patients

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Abstract

Objectives: This study carried out to estimate the correlation of serum thyroid hormones concentration with clinical characteristic and effective short term outcome in patient following severe ischemic stroke. Outcome in a tertiary care hospital in Cairo.

Methods: n the current descriptive (cross-sectional) investigation we tried to demonstrate the correlation between the difference in thyroid pattern and acute ischemic stroke in 101 cases that were approved to Nasser Institute Hospital within two days of the event between from May 2019 to November 2019 with follow up after 30 days of discharge from hospital. Inclusion and exclusion criteria were strictly exercised. National Institute of Health Stroke Scale (NIHSS) and modified Rankin scale (mRS) score was noted. Thyroid function hormones (TSH, T3, T4) were estimated from blood. Patients were stratified into 6 groups: euthyroid, nonthyroidal illness syndrome (NTIS), subclinical hyperthyroid, hyperthyroid, subclinical hypothyroid, and hypothyroid. Clinical, functional, and radiological evaluation were done for the patients. Statistical SPSS 20.0 software and Microsoft excel were used for statistical analysis ($P \leq 0.05$).

Results: A total of 101 stroke cases were thus included in the study comprising 57 males and 44 females. The mean age of patients was 18-80 [63.6 ± 12.4] years. Of the 101 patients 75.2% were euthyroid, 16.8% were nonthyroidal illness syndrome (NTIS),3.96% were subclinical hyperthyroid,0.99%were hyperthyroid, 0.99% were subclinical hypothyroid, and 1.98%were hypothyroid. Univariate analysis shows serum T3 was inversely associated with NIHS score after 30 days of discharge from hospital. Multivariate analysis shows significant correlation between nonthyroidal illness syndrome and NIHS score and mRS on day o of onset and after 30 days of discharge and also shows inversely association between T3 and NIHS score and mRs after 30 days of discharge from hospital.

Conclusion: Non thyroidal illness syndrome had influence to degree of stroke severity, degree of disability and functional outcome. Serum T3 levels had a negatively correlation with NIHSS score and modified Rankin scale. Low serum T3 levels associated with poor prognosis in acute ischemic stroke patients.

Key words: Acute ischemic stroke, thyroid dysfunction, non thyroidal illness syndrome patient outcome

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Introduction

Cerebrovascular Stroke is the third most common reason of death worldwide and a leading reason of long-term disability. According the WHO, stroke is known as the clinical syndrome of fast beginning (commonly seconds or minutes) of centric (or worldwide, as in subarachnoid haemorrhage) cerebral deficit, enduring more than 24 hours or causing death, with no obvious reason other than a vascular one **(Al-Mahdawi et al., 2013)**.

The appearance of high blood pressure, atherosclerosis, diabetes and thyroid dysfunction are known as hazard conditions for stroke. So far, the extent to which any of these pathophysiological risk factors share in a cerebrovascular stroke has not been known. **(pande et al., 2017).**

Disorders of thyroid gland may include: hyperthyroidism, hypothyroidism and thyroid disease syndrome. Thyroid disease syndrome can be represented as unusual results on thyroid function tests that occur in the absence of a thyroid gland. Changes in thyroid function test results may reflect alternations in the production of thyroid hormones through effects on the thyroid gland itself, on the thyroid axis, pituitary gland, or thyroid gland, on peripheral tissue metabolism of hormones, or by incorporation of all these Effects **(Al-Mahdawi et al., 2013).**

Disturbances in the hypothalamus pituitary-thyroid (HPT) axis impact stroke risk and stroke finddings **(Gao et al., 2010).** Hypothyroidism is the cause of high blood pressure, hypercholesterolemia, heart failure, hypo and hypercoagulability, all of which are risk factors for stroke. **(Chen et al., 2014).** Furthermore, Hyperthyroidism may relate to atrial fibrillation, which is a major reason of cardioembolic stroke **(Alevizaki et al., 2007).**

The correlation between thyroid hormones and functional findings post-stroke is complicated. The present results has appeared that the low T3 levels directly after severe ischemic stroke (AIS) are related with higher stroke acuteness and mortality, and lower functional findings **(Q'keefe et al., 2015)**.

This is also right in critically ill hospitalized cases who have non-thyroidal illness syndrome(NTIS; or 'euthyroid sick syndrome'), where T3 levels are low, but TSH is normal, NTIS cases have lower short-term prediction and greater mortality rates at 12 months in comparison with non-NTIS cases **(Q'keefe et al., 2015)**.

Objectives of the Study

This study carried out to estimate the correlation of serum thyroid hormones concentration with clinical characteristic and effective short term outcome in patient following severe ischemic stroke.

Study setting and population

The present study is a cross sectional analytical study performed in neurology inpatient department in Nasser Institute Hospital and Treatment from May 2019 to October 2019 and included 101 patients within 48 hours of ischemic stroke onset.

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Study protocol

Patients with radiologically confirmed acute ischemic stroke according to the World Health Organization criteria with symptoms onset within 48 hours on admission, from both sexes, with age ranges from 18 to 80 years old patients with head injury, subarachnoid hemorrhage, tumors, and central nervous system infections; and history of thyroid dysfunctions were excluded.

Methods:

In addition to regular stroke protocol at the stroke unit of Nasser Institute Hospital, the patients were subjected to the following:

1- Full personal & medical history including:

Age, sex, risk factors of ischemic stroke; diabetes mellitus (DM), systemic hypertension (HTN), dyslipidemia, atrial fibrillation (AF), ischemic heart disease (IHD), valve replacement, other cardiac diseases, old history of cerebrovascular accidents including infarction.

2-Detailed examination including:

1- General Examination.

2- Neurological examination: include a measure of National Institutes of Health Stroke Scale (NIHSS) **(NIH Stroke Scale; Lyden et al, 1994)** at day0 and 30 days after discharge and Modified Rankin Scale (mRS) **(Bonita et al, 1988)** 30days after discharge.

3-Laboratory investigations:

Thyroid function was evaluated by measuring serum T3, T4, and TSH; at Nasser institute laboratory.

On the basis of thyroid pattern, the participants were classified into: euthyroid, NTIS/non thyroidal illness syndrome, subclinical hyper thyroid, hyperthyroid, subclinical hypothyroid and hypothyroid.

- Euthyroid state was identified as normal T3, T4, and TSH
- NTIS was identified as a low T3 with low or normal TSH and low or normal T4 Or high T4 syndrome
- Subclinical hyperthyroid was diagnosed as low or normal T3, normal T4, and low TSH
- Hyperthyroid was identified as high T3, high T4, and low TSH
- Subclinical hypothyroid was identified as low or normal T3, normal T4, and high TSH
- Hypothyroid was identified as low T3, low T4, and high TSH

Ethical Considerations:

Written consent from each patient or relatives for the research study and ethical approval was obtained from the ethical committee faculty of Ain Shams of medicine prior to the data collection.

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Statistical analysis

IBM SPSS statistics (V. 26.0, IBM Corp., USA, 2019) was applied for results analysis. Results were demonstrated as mean ± SD for quantitative parametric records and median (IQR) for quantitative nonparametric records as well both number and percentage for classified results.

Results

Demographics

101 patients with age (18-80) years old, mean equals 63.6 years ± 12.4. Male patients were 57 (56.4%), while female patients were 44 (43.6%), the most prevalent risk factors in the present study results were hypertension in 74 patients (73.3%), diabetes mellitus in 54 patients (53.5%), cardiac abnormalities in 44 patients (43.6%), old ischemic Stroke in 24 patients (23.8%), dyslipidemia in 29 patients (28.7%) and atrial fibrillation (AF) was found in 23 patients (22.8%).

Table (1): shows baseline thyroid function screening of the study patients at the time of the stroke onset

Thyroid function	Number	Percentage
Euthyroid	76	75.2
Abnormal thyroid	25	24.75
Non thyroidal illness syndrome	17	16.8
Subclinical Hyperthyroid	4	3.96
Hyperthyroid	1	0.99
subclinical hypothyroid	1	0.99
Hypothyroid	2	1.98
TSH	Number	Percentage
Normal	93	92.1
Low	5	4.95
High	3	2.97
T3	Number	Percentage
Normal	82	81.2
Low	18	17.8
High	1	0.99
T4	Number	Percentage
Normal	97	96.03
Low	2	1.98
High	2	1.98
Total	101	100

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Study groups comparison:

The differences between normal and abnormal thyroid groups in their demographic and baseline clinical factors data didn't have significant differences ($P > 0.05$) except in the distribution of HTN , AF and sex.

Univariate analysis

Thyroid with NIHSS and mRS

Association between stroke severity according to NIHSS and base line thyroid functions at the time of the stroke onset or at 30 days follow up among patients with different baseline thyroid functions wasn't significance (P>0.05)

The univariate analysis showed that the association between baseline thyroid function and modified Rankin scale at one month of the follow up time was significant ($P \leq 0.05$) **Table (2) and Table 3**

Table (2): Thyroid function

Variable		MRS after one month of stroke onset n (%)		χ^2	*P*
		Favorable	Unfavorable		
Thyroid function	Normal	71(93.4)	5 (6.6.)	3.8	0.05*
	Abnormal	20 (80)	5 (20)		

Favorable MRS: 0 – 3, unfavorable MRS: 4 – 6. Tests of significance was conducted with Chi-Square test, *: Significant difference at 0.05 level of significance

Table (3): Association between the baseline thyroid functions and modified Rankin scale at the follow up time

		MRS		Test value¥	*P*
		Median (IQR)	Range		
Thyroid	Euthyroid	1 (1 - 2)	0 - 5	6.1	0.3
	Nonthyroidal illness syndrome	2 (1 - 4)	1 - 6		
	subclinical hyperthyroidism	1.5 (1 - 2)	1 - 2		
	Hyperthyroid	1 (1 - 1)	1 - 1		
	subclinical hypothyroidism	1 (1 - 1)	1 - 1		
	Hypothyroid	1.5 (1 - NA)	1 - 2		
TSH	Normal	1 (1 - 2)	0 - 6	0.88	0.65
	Low	1 (1 - 2)	1 - 2		
	High	1 (1 - NA)	1 - 2		
T3	Normal	1 (1 - 2)	0 - 5	5.9	0.05*
	Low	2 (1 - 4)	1 - 6		
	High	1 (1 - 1)	1 - 1		
T4	Normal	1 (1 - 2)	0 - 6	1.5	0.47
	Low	1.5 (1 - NA)	1 – 2		
	High	1 (1 – 1)	1 – 1		

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¥: Kruskal-Wallis test. *: Significant difference at 0.05 level of significance

Correlation was carried between stroke outcome measured by difference in mRS and NIHSS after 30 days of discharge from hospital and results of baseline laboratory investigation of thyroid hormones level there were an inverse correlation between NIHSS 30 and mRS and baseline T3 level (p=0.008 , p=0.009) respectively, Other (T4 and TSH) correlations weren't significant (*P*> 0.05).

Multivariate analysis was performed

Prediction of NIHSS after 30 days follow up depending on its independent variables is shown in Table 4. As the Relationship between NIHSS after 30 days of the stroke onset and multiple risk factors including baseline thyroid function using linear regression was significant for each of thyroid function (NTIS), AF and dyslipidemia (*P*< 0.05).

Table (4): Prediction of NIHSS after 30 days follow up depending on its independent variables

	Beta	SE	t	*P*
(Constant)	3.480	2.256	1.543	.127
Age	.026	.039	.676	.501
Female	-1.658	.940	-1.763	.082
DM	-.946	.894	-1.059	.293
HTN	-.135	1.223	-.111	.912
cardiac	.378	.983	.385	.701
previous stroke	-2.577	1.639	-2.793	.126
Dyslipidemia	4.586	1.536	2.985	.004*
AF	3.275	1.190	2.753	.007*
Nonthyroidal illness	3.861	1.140	3.385	.001*

Beta: regression coefficient, SE: standard error. *: Significant difference at 0.05 level of significance. Assumption of linear regression were met including normally distributed, non-auto-dependent (Durbin-Watson = 2.2), homoscedastic and without outliers (standardized values = -1.8 & 3.5) residuals.

Table (5): Relationship between modified Rankin scale 30 days after stroke onset and multiple risk factors including baseline thyroid function using ordinal logistic regression was significant for each of thyroid function, baseline NIHSS, dyslipidemia (*P*< 0.05).

Table (5)**:** Relationship between modified Rankin scales 30 days after stroke onset

Independent variables	Beta	SE	P	Adjusted OR
Baseline NIHSS	.572	.081	.000*	1.771807124
Age	.011	.013	.429	1.011060722
Male	-.575	.342	.093	0.562704869
Female	0 [a]	.		

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Non-DM	.432	.322	.180	1.540335115
DM	0 [a]	.		
Non-HTN	.325	.407	.424	1.384030646
HTN	0 [a]	.		
cardiac normal	-.361	.349	.301	0.696978998
cardiac abnormal	0 [a]	.		
No previous stroke	.463	.323	.191	1.318896803
previous stroke	0 [a]	.		
No dyslipidemia	-1.442	.592	.015*	0.236454377
Dyslipidemia	0 [a]	.		
Nonthyroidal illness syndrome	1.194	.451	.008*	3.300255864
Euthyroid	0 [a]	.		
No AF	-.123	.422	.770	0.884264
AF	0 [a]	.		

Beta: regression coefficient, SE: standard error, df: degree of freedom, CI: confidence interval, LL: lower limit, UL: upper limit. *: Significant difference at 0.05 level of significance. [a]: Reference value for each variable. The ordinal logistic regression model is fit (parallel line test = 8.6, $P = 1$) using Negative log-log function

Discussion

According to our study patients distribution of baseline and 30 days follow up thyroid function and hormones level, the study found that 25 patients (24.75%) of 101 study stroke patients had abnormal thyroid functions, of whom, 17 patients (16.8%) had non-thyroidal illness syndrome (NTIS), 4 patients(3.96%) were with subclinical hyperthyroid, 2 patients(1.98%) were hypothyroidism and (0.99%) of patients in hyperthyroid and subclinical hypothyroid (one patient in each group). About baseline hormones level abnormalities in our patients, Serum TSH level was low in 5 patients (4.95 %), and high in 3 patients (2.97 %). Serum T3 level was low in 18 patients (17.8 %), and high in one patient (0.99%). Serum T4 level was low in 2 patients (1.98 %) and high in 2 patients (1.98 %).

The proportions of thyroid disturbances in the present study agreed with a study conducted on 382 ischemic stroke patients with normal thyroid function (77.0%) and abnormal thyroid profile (23.0%). Among them (4.5%) had subclinical hypothyroidism and 1.6% had subclinical hyperthyroidism **(Jeong et al., 2010).**

It disagreed with a study conducted on 105 ischemic stroke patient and 105 control normal group; 8.6% of the ischemic stroke cases cleared hypothyroid profile, 8.6% had hyperthyroid profile and 3.8% had sick euthyroid profile and these data were statistically significant in comparison to control patients**. (Al-Mahdawi et al., 2013)**, and also disagreed with a study of 75 stroke patients, of them 43(57.3%) had nonthyroidal illness syndrome (NTIS), 13 (17.3%) were euthyroid, 6 (8%) were hyperthyroid, 9 (12%) were subclinical hypothyroid, and 4 (5.3%) were hypothyroid. **(pande et al., 2017).**

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Univariate analysis

The current study found that there was significant associations between normal and abnormal group with mRS 30 days follow up ($P < 0.05$) as (20%) of patients in abnormal group had unfavorable mRS ranged from(4-6) to (6.6%) in normal group univariate analysis showed the association of T3 and NIHSS 30 as there was significant difference between low T3 and NIHSS at 30 day follow up which represented by negative correlation and the correlation between baseline T3 and the 30 days follow up mRS was significant ($P< 0.05$) (negative correlation) but the correlation with other hormones TSH and T4 were not significant. The present findings agreed with a prospective study conducted by **Ambrosius et al. (2011)** included 387 acute ischemic stroke patients and found that patients with low baseline T3 had a higher NIHSS (P = 0.006), also a study of **Zhang and Meyer (2010)** reported that low T3 had poor neurological outcomes, increased stroke severity indicated by NIHSS.

A study done by **Ambrosius et al. (2011)** which investigated the relationship between thyroid hormones and stroke outcomes and found that the 30th day and one-year mRS scores were significantly higher in patients with initial low free T3 (P = 0.001, 0.03 respectively).

The present study findings were in a disagreement with a study conducted by **Neidert et al. (2011)** that investigated the predictive value of thyroid hormones to stroke outcomes and found minor values.

Multivariate analysis

There was no risk factor had a significant relationship with the initial severity (NIHSS), while on the 30th day, patients with AF, dyslipidemia, nonthyroidal illness, were more likely to get more severe stroke (P < 0.05).. According to disability with mRS the multivariate analysis showed that patients with nonthyroidal illness syndrome, dyslipidemia, or high baseline NIHSS score had a significant higher mRS score on the 30th day from the stroke onset.

Our study agreed with **Hama et al., (2005)** study which reported post-stroke nonthyroidal illness syndrome in 51 stroke patients was associated with a difficult functional improvement. A study of 737 patients with acute first stroke found that the nonthyroidal illness syndrome was an independent predictor of early and late survival, and predicted handicap at 1 year **(Alevizaki et al., 2007**).

Conclusion

Non thyroidal illness syndrome (NTIS) has an influence on the degree of stroke severity, degree of disability and functional outcome.

Initial serum T3 levels have a negative correlation with the one-month NIHSS score and modified Rankin scale.

So, the low serum T3 levels are associated with poor short-term prognosis in acute ischemic stroke patients.

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