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ORIGINAL ARTICLE

Impact of Thyroid function on Stroke Severity and Functional Outcome in Acute Ischemic Stroke Patients

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ABSTRACT

Background: Acute ischemic stroke and thyroid conditions have complicated interactions. With mixed findings, earlier research has suggested a link between thyroid function and the severity and outcome of strokes.

Aim: Toevaluate the impact of thyroid function on acute ischemic stroke patient's functional outcome and stroke severity.

Patients and methods: This prospective cohort study, which comprised 70 patients admitted within 48 hours of the beginning of their first acute ischemic stroke, was carried out at the Stroke and Critical Care Units of the Neurology Department at Zagazig University Hospitals. On admission, routine laboratory tests and thyroid hormone levels were examined. Modified Rankin scales [mRS] and the National Institute of Health and Stroke scale [NIHSS] were used to measure the severity of the stroke and the functional outcome, respectively.

Results: In 41% of patients, abnormal thyroid function was found. Non-thyroid sickness syndrome was the thyroid anomaly that was most frequently noted [low FT3]. Stroke severity and a poor outcome were substantially correlated with high TSH and **low FT3**.

Conclusion: The severity and functional prognosis of an ischemic stroke may be predicted by abnormal thyroid hormone levels at presentation.

Keywords: Thyroid, thyroid function, stroke severity, and low FT3 all relate to acute ischemic stroke

INTRODUCTION

Stroke is one of the most widespread neurological conditions and is ranked as the third leading cause of death worldwide, with 42.7% of cases involving men and 46.1% involving women [1]. If either an ischemic or hemorrhagic stroke might result in physical impairments [2]. Thyroid gland is the One of the largest endocrine glands, the thyroid produces, stores, and secretes thyroid hormones. Several studies have shown that thyroid dysfunction, whether asymptomatic or severe, affects how stroke survivors fare after their attacks [3- 5].

Hypothalamus-pituitary-thyroid [HPT] axis disturbances influence stroke risk and stroke outcomes. Hypertension, hypercholesterolemia, cardiac dysfunction, hypo- and hypercoagulability, all of which are risk factors for stroke, can be brought on by hypothyroidism [6]. Atrial fibrillation, which is a prevalent cause of cardioembolic stroke, and hyperthyroidism are both connected [7, 8].

Thyroid hormones and functional outcomes after stroke have a complicated relationship. According to recent evidence, acute ischemic strokes with low T3 levels are more severe, have a higher death rate, and have worse functional outcomes [9, 10].

METHODS

Seventy patients, 33 men and 37 women, with a mean age of 63.2 ±12.1 years, participated in this prospective cohort study, which was conducted from July 2022 to January 2023 in the stroke and intensive care units of the neurology department of Zazazig University Hospitals. In this study,

patients who had their first acute ischemic stroke within 48 hours of admission were included.

Inclusion criteria: Individuals whose brain scans, including magnetic resonance imaging [MRI] and computed tomography [CT], revealed acute ischemic stroke, both sexes and participants older than 18 years old were included in the study if their symptoms began within 48 hours after their first acute ischemic stroke, as defined by the World Health Organization criteria.

Exclusion criteria: Individuals with a history of thyroid surgery, radioactive or thyroid hormone replacement therapy, hepatic or renal failure, pre-existing thyroid malfunction, or drug use known to affect thyroid function were excluded from the study.

Every patient underwent a thorough personal and medical history check, which included questions about age, sex, risk factors for ischemic stroke like diabetes [DM], systemic hypertension [HTN], dyslipidemia, and cardiac conditions, as well as a thorough physical examination that included general and neurological Examinations

Assessment of stroke severity and functional outcome were conducted using the following scales:

National Institutes of Health Stroke Scale [NIHSS]: measured on admission to intensive care units.Results of NIHSS ranged from 0 to 42 for measuring the severity of stroke. The NIHSS Classified to: mild stroke [1-4], moderate stroke [5-15] and severe stroke [>15] **[11].**

Modified Rankin Scale [mRS]: This scale is used to evaluate short-term outcome in patients with acute ischemic stroke and was applied to all patients at30days post stroke with score ranging from no symptoms [0] to death [6], patients with favorable outcome have a score≤ 2 and patients with unfavorable outcome have a score>2 [**12].**

Laboratory investigations included Complete blood count [CBC], Liver function test [LFT], kidney function test [KFT], Hemoglobin A1C [HbA1C], Fasting blood sugar [FBS], Postprandial sugar [PPS], lipid profile, creatinine kinase[CK], coagulation screen, highly sensitive c- reactive protein [CRP] , all as routine laboratory investigations for stroke patients.

Special Laboratory Investigations: Serum levels of FT3, FT4 were quantified by RIA [radioimmunoassay] and TSH by IRMA [immunoradiometric assay] at biochemistry laboratory of Zagazig University Hospitals. Normal range in our laboratory for; FT3 is 3.5-6.5 pmol/l, Normal range for FT4 is 11.9-26.0 pmol/l and Normal range for TSH is 0.3-5.0 miu/ml.

Blood samples for FT3, FT4, and TSH levels were collected within 48 hours of acute ischemic stroke onset. On the basis of thyroid profile, the abnormalities could be according to the following classification:

Euthyroid state was diagnosed as normal FT3, FT4, and TSH. Non thyroidal illness syndrome [NTIS] was diagnosed as a *low FT3 with normal TSH and FT4 [low FT3 syndrome]**[13].**Subclinical hyperthyroidism was diagnosed as normal FT3, normal FT4, and low TSH **[14].** Hyperthyroidism was diagnosed as high FT3, high FT4, and low TSH **[14].**Subclinical hypothyroidism was diagnosed as normal FT3, normal FT4, and high TSH **[15]**.Hypothyroidism was diagnosed as low FT3, low FT4, and high TSH **[15].**

Other Investigations:

Carotid duplex: The criteria for significant hemodynamic carotid stenosis is considered as 70% or greater reduction of the lumen. Echocardiogram and Electrocardiogram [ECG].

Ethical Considerations:

Prior to the data collection, each patient or a family member gave their consent for the research study, and the ethical approval was acquired from the Faculty of Medicine, Zagazig University ethical committee. The study was done according to The Code of Ethics of the World Medical Association [Declaration of Helsinki] for studies involving humans.

Statistical Analysis:

With SPSS software version 18, data were examined [USA]. The parametric data shown as mean SD or as a percentage. Unpaired statistics were used to compare the data from the various groups. For parametric data, use the Student's t-test; for categorical data, use the Fischer exact test and the Chi square test. To find relationships between variables, Pearson correlation was used. The degree of importance will be determined at $P<0.05$.

RESULTS

Seventy AIS patients were enrolled; their mean ages were 63.2±12.1, their stroke severity on the

NIHS scale was 13.6± 5.7, and their one-month outcomes were documented as good in 36% of patients and unfavorable in 64% of patients. In 29 patients [41%], abnormal thyroid function was noted. Low FT3 syndrome [34%], subclinical hyperthyroidism [3%] and subclinical hypothyroidism [4%], were the abnormalities that were noted. There was evidence of an inverse association between TSH and FT3, on the one hand, and NIHSS and mRS, on the other.

Table (1): Demographic data of the studied groups

Parameter	Patients (N=70)
Age	63.2 ± 12.1
Gender :	
Male	36 (51%)
Female	34 (49%)
Risk factors:	
DM	37 (53%)
HTN	53 (76%)
Dyslipidemia	36 (51%)
Smoking	30 (42%)
Cardiac disease	39 (56%)
Stroke severity at admission (NIHSS):	
Mild ≤ 7	15 (21.4 %)
Moderate 8- 14	36 (51.4 %)
Severe ≥ 15	19 (27.2 %)
NIHSS at admission (mean ±SD)	13.6 ± 5.7
GCS at admission	13.2 ± 2.1
Stroke outcome at 1 month (mRS) :	
Favorable	25 (36%)
Unfavorable	45 (64%)

Table 2: Thyroid function profile in the studied cohort.

Variables	Patients (N=70)
Thyroid function:	
Normal	**41 (59%)**
Abnormal	**29 (41%)**
Classes of abnormal thyroid :	
Non-thyroid illness syndrome	**24 (34 %)**
Subclinical hypothyroidism	**3 (4 %)**
Subclinical hyperthyroidism	**2 (3 %)**
TSH (mean ± SD)	2.58 ± 2.06
FT3 (mean ± SD)	6.08 ± 5.4
FT4 (mean ± SD)	24.6 ± 21.3

Table (3): Comparison between patients with favorable and unfavorable outcome regarding thyroid function.

	Favorable (N=25)	Unfavorable (N=45)	T	P
TSH	3.12 ± 1.9	1.8 ± 2.4	2.52	<0.05
FT3	10.1 ± 8.4	3.9 ± 1.4	1.5	<0.001
FT4	16.9 ± 5.4	28.9 ± 18.3	-1.5	0.12

Table (4): Correlation between stroke severity at admission using NIHSS and thyroid hormones.

variable	R	p
TSH	-0.42	0.02
FT3	-0.78	0.001
FT4	+0.23	0.34

Table (5): Correlation between modified Rankin scale results and thyroid hormones

variable	R	p
TSH	-0.53	0.01
FT3	-0.59	0.001
FT4	+0.13	0.65

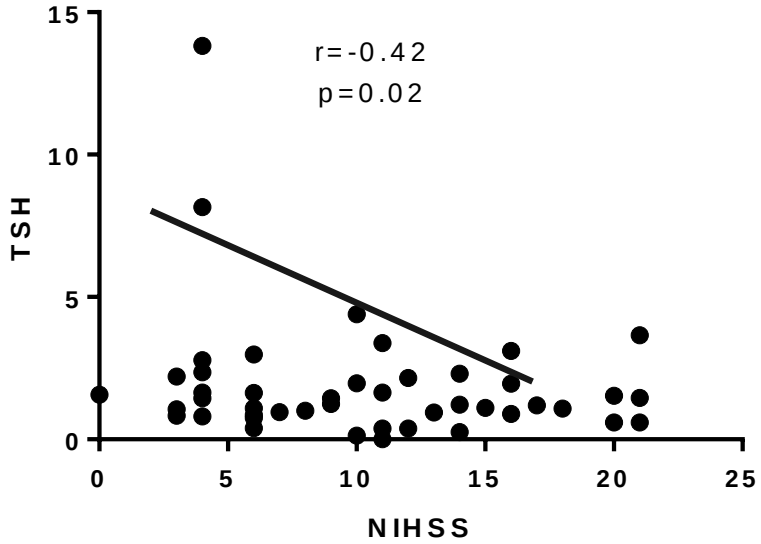

Figure (1): correlation between NIHSS and TSH

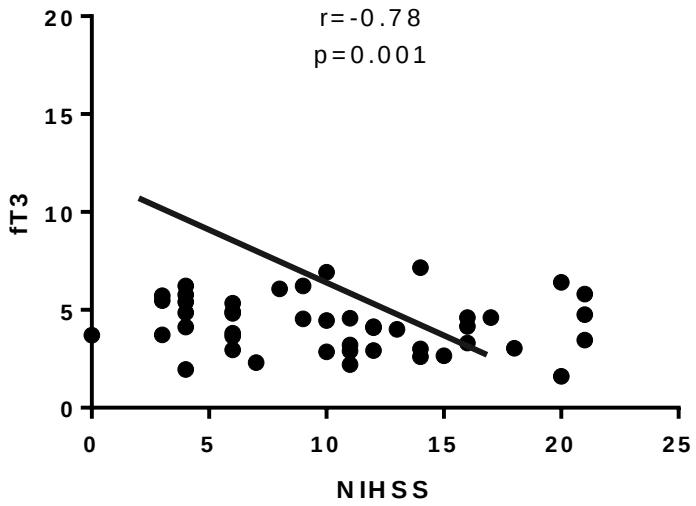

Figure (2): correlation between NIHSS and FT3

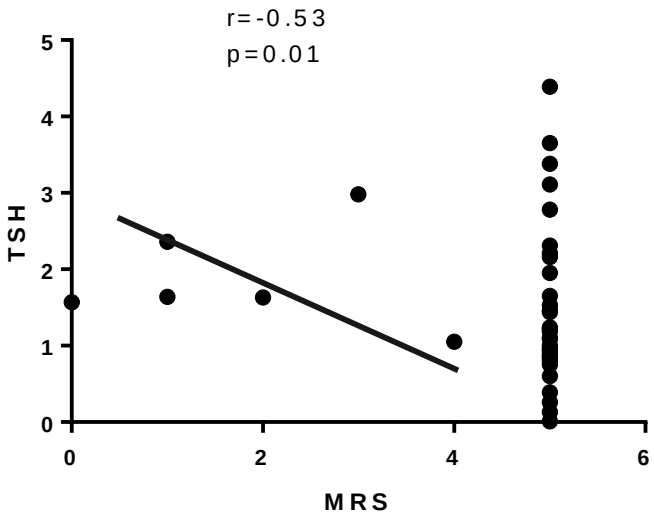

Figure (3): correlation between modified Rankin scale (mRS) and TSH

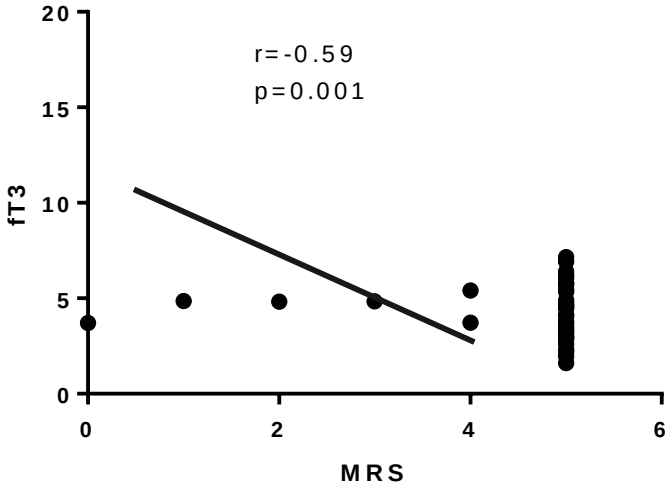

Figure (4): correlation between modified Rankin scale (mRS) and FT3

DISCUSSION

One of the most prevalent neurological conditions and the third leading cause of mortality globally is ischemic stroke. To reduce stroke morbidity and mortality, it is crucial to identify, manage, and treat the poor prognostic variables as soon as possible. According to earlier studies, problems with the hypothalamo-pituitary-thyroid [HPT] axis and thyroid disorders may affect stroke risk and outcome **[16].**

In the current study, we assessed thyroid function in a sample of patients with acute ischemic stroke [AIS] who were admitted to our critical care units for neurology. Also, the relationship between the severity of the stroke and the outcome was examined. 41% of AIS patients had abnormal thyroid function, with non-thyroid disease syndrome [low T3] accounting for 34% of the cohort under study as the most commonly seen anomaly. 4% of the participants in the current study exhibited subclinical hypothyroidism, however. This was consistent with a number of earlier investigations [**16- 18**]. **Wang et al., [17]** found that in their study, 30% of the patients had thyroid abnormalities, with the most common anomaly being low FT3 syndrome.**Nageeb et al. [18]**demonstrated that 46 [33%] of the stroke patients had subclinical thyroid impairment. Subclinical hypothyroidism and subclinical hyperthyroidism were both present in 10% and 23% of individuals, respectively.

The correlation between thyroid function and functional result was shown to be complex. We found that higher levels of TSH were associated with a favorable outcome while lower levels of FT3 were associated with an unfavorable outcome in patients**,** demonstrating that there was a significant difference between patients with and without a favorable mRS regarding thyroid hormone levels in the current study. Additionally, when we used the modified Rankin Scale to correlate thyroid hormones with short-term outcomes, we discovered no relationship between FT4 and stroke outcome but an inverse relationship between TSH and FT3 and the modified Rankin Scale.

In agreement with our study, a met analysis was conducted by **Dhital et al. [19]**greater TSH levels were shown to be associated with better mRS scores, demonstrating that subclinical hypothyroidism was associated with beneficial outcomes. The opposite, **Nageeb et al. [18]** demonstrated that functional prognosis in patients with acute stroke was associated with subclinical hyperthyroidism rather than hypothyroidism.

In the present investigation, increased TSH was not only linked to a favorable outcome but also to a less severe stroke as measured by the NIHS scale. This was consistent with a number of earlier investigations [**20-24**]. Many theories were considered to explain the relationship between subclinical hypothyroidism and functional outcome, including the following: patients with subclinical hypothyroidism have impaired response to stressful conditions due to reduced sensitivity to adrenergic stimulation and a state of hypometabolism that protects neurons from damage **[25].** Additionally, in the presence of high TSH, accelerated atherosclerosis causes an

increase in systemic vascular resistance, which in turn causes sublethal ischemia. With time, this sublethal ischemia causes neuronal preconditioning, which results in the development of collateral vessels that help the affected tissue withstand subsequent and protracted ischemic attacks **[26].**

Triiodothyronine [T3] was said to have the power to promote hypothermia, have an anti-edema effect, have an anti-apoptotic factor, reduce neuroinflammation, and cause vascular dilatation. Moreover, T3, particularly the free molecule, plays a crucial role in neurogenesis throughout the formation of the nervous system. According to reports, AIS and other dangerous illnesses, such as non-thyroid sickness syndrome or low T3 syndrome, frequently have this consequence **[27].** According to reports, poor peripheral thyroid hormone deiodination and abrupt hypothalamic-pituitary-thyroid [HPT] axis dysfunction are the fundamental processes of the Low-T3 syndrome in critical illness **[28].** Several investigations have shown that patients with ischemic stroke frequently experience low T3 syndrome. This condition is closely linked to poor functional outcomes, increased disability, and mortality in these individuals, as well as a considerable increase in stroke severity at presentation **[28-30].**

In this study, we showed that patients with low [FT3] levels had higher NIHS scale scores, which indicate a more severe first stroke. Moreover, low FT3 was seen in patients with high mRS scores, which indicates poor functional results.

Similarly, **Ambrosiusand collegues [31]** reported low free T3 levels at the time of admission in patients with acute ischemic stroke, and they revealed a link between low FT3 and higher NIHSS and mRS scores. Additionally, **Zhang and colleagues [32]** showed in their investigation that low free T3 levels were associated with poor clinical outcomes, and they came to the conclusion that FT3 is a standalone predictor of 3-month functional result.

Non-thyroid sickness syndrome was linked to worse NIHSS scores at admission and smaller improvements in both NIHSS scores and mRS scores at follow-up, according to other earlier research **[33, 34].** Although low FT3 is a characteristic seen in various acute situations, our investigation supported a relationship between low FT3 and stroke severity but did not infer causation.

Earlier studies suggested that the low FT3 levels in these patients could be explained by the inflammatory response brought on by a stroke. It has been hypothesised that elevated levels of IL-6 during inflammatory situations may cause elevated CRP as well as suppression of the hypothalamic-pituitary axis [HPA]. In turn, IL-6's suppression of the HPA axis reduces thyroid activation and hinders peripheral T4 to T3 conversion. Moreover, hunger, which has been linked to stroke patients experiencing it, could be another mechanism causing thyroid axis depression **[35].**

CONCLUSION AND RECOMMENDATION

FT3 and TSH were inversely correlated with stroke severity and functional outcome in patients with acute ischemic stroke. It is recommended that more research be done to see whether treating these thyroid anomalies may enhance the functional prognosis of ischemic stroke patients.

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