Acta Scientific Neurology (ISSN: 2582-1121)

Volume 7 Issue 1 January 2024

Research Article

Impact of Thyroid Disease on Functional Outcome in Ischemic Stroke Secondary to Large Vessel Occlusion

Adel Mabrook AlSefari MD[1], Omar Khaled Ameen MD[2], Hanan AlHazmi MBBS[2] MD[1], Ali Mahmoud AlBalawi MD[2], Fahmi AlSenani MBBS[2], Jamal Muthana MD[2], Mohammed Ahmed Melibari MD[1] and Manhal N Redwan MD[1]

[1]Diabetic and Endocrine Center, AlNoor Specialist hospital, Makkah, Kingdom of Saudi Arabia

[2]Stroke Program, Neurology Department, National Neuroscience Institute, King Fahad Medical City, Riyadh, Kingdom of Saudi Arabia

***Corresponding Author:** Omar Khaled Ameen, Stroke Program, Neurology Department, National Neuroscience Institute, King Fahad Medical City, Riyadh, Kingdom of Saudi Arabia.

DOI: 10.31080/ASNE.2024.07.0695

Received: November 13, 2023

Published: December 12, 2023

Abstract

Background: Hypothyroidism can cause hypertension, hypercholesterolemia, cardiac dysfunction, and both hypo- and hypercoagulability; all of which are risk factors for stroke.

Objectives: To explore the association between thyroid disease and occlusion of large vessels as well as functional outcome in patients with ischemic stroke.

Material and Methods: A retrospective study was conducted among all acute ischemic stroke patients, secondary to large vessel occlusion, admitted to King Fahad Medical City (KFMC), Riyadh, Kingdom of Saudi Arabia, provided that thyroid hormones were measured for those patients. The electronic charts of all eligible patients admitted between January 2021 and June 2022 were reviewed. Severity of stroke was measured through the National Institute of Heath Stroke scale (NIHSS). Functional disability one month after discharge was assessed using the modified Rankin scale (mRS). Levels of thyroid hormones (thyroxine "T4", Triiodothyronine "T3" and thyroid stimulating hormone "TSH"), low density lipoprotein (LDL) as well as glycated hemoglobin (HbA1c) were extracted from patients` electronic files.

Results: A total of 177 patients included in the study. Their age ranged between 17 and 100 years (60.74 ± 15.55). Males represented 56.3% of patients. Almost half (47.1%) of cases were categorized as severe stroke while 39.1% were mild to moderate. None of the studied patients` characteristics (age, gender, TSH, T3, T4, LDL, HbA1c) was significantly associated with stroke severity. Concerning functional disability one month after discharge, moderately severe and severe disabilities were observed among 27.7% and 21.5% of patients, respectively whereas death was reported in 15.8% of cases. Patients` age was highest in patients of category 5 (severe disability) (69.0 ± 14.6 years) and lowest among those of category 0 (no disability), p = 0.001. LDL level was highest among patients of category 2 (slight disability) and lowest among those of category 6 (dead) (3.2 ± 1.4 and 2.2 ± 1.1, respectively), p = 0.031. There was a statistically significant association between severity of stroke based on NIHSS scale and impact on functional outcome based on modified ranking scale, p<0.001.

Conclusion: Thyroid disorders were not associated with severity of stroke. Older patients had more severe functional disability while LDL was lowest among dead patients. Stroke severity was associated with functional disability.

Keywords: Stroke; Thyroid Diseases; Functional Disability

Introduction

Stroke is the second leading cause of death and the third leading cause of disability worldwide [1,2]. Perturbations in the hypothalamus-pituitary-thyroid (HPT) axis affect stroke risk and stroke outcomes. Hypothyroidism can cause hypertension, hypercholesterolemia, cardiac dysfunction, and both hypo- and hypercoagulability; all of which are risk factors for stroke [2-4].

Hyperthyroidism is also associated with atrial fibrillation, which is a common cause of cardioembolic stroke [5]. Previous studies showed that stroke patients with subclinicalhyperthyroidism (decreased TSH and normal FT3 and FT4) were at a high risk of death and disability [6,7].

Only one study was done in ischemic stroke secondary to large vessel occlusion showed that reduction in TSH levels is an independent predictor of unfavorable outcomes after mechanical thrombectomy [8].

The objective of this study is to investigate possible associations of thyroid hormone status with clinical severity using National Institutes of Health Stroke Scale (NIHSS) and outcome in patients admitted for acute ischemic stroke secondary to large vessel occlusion.

Patients and Methods

A retrospective study was conducted among all acute ischemic stroke patients, secondary to large vessel occlusion, admitted to King Fahad Medical City (KFMC), Riyadh, Kingdom of Saudi Arabia, provided that thyroid hormones were measured for those patients. KFMC is non-profit tertiary, clinical and research hospital. The electronic charts of all eligible patients admitted between January 2021 and June 2022 were reviewed. Demographic data for patients were also collected. Severity of stroke was measured through the National Institute of Heath Stroke scale (NIHSS). Functional disability one month after discharge was assessed using the modified Rankin scale (mRS). Levels of thyroid hormones (thyroxine "T4", Triiodothyronine "T3" and thyroid stimulating hormone "TSH"), low density lipoprotein (LDL) as well as glycated hemoglobin (HbA1c) were extracted from patients` electronic files. The (NIHSS) is a tool applied to assess stroke-related neurological deficit [9]. It has been approved to be a determinant of both short- and long-term outcomes among stroke patients [10,11]. A trained person rates the ability of the patent to answer questions and do activities, without providing assumptions about what the patient can perform [12]. Items were scored on a 3- to 5-point scale, with 0 as normal. Total score ranges from 0 to 42, with higher the score suggesting higher severity. The total score was categorized as follows; 1-5 (mild), 6-14 (mild to moderate), 15-24 (severe) and >25 (very severe) [13].

The modified Rankin Scale (mRS) is a widely applied valid functional status outcome measure in stroke interventions [14,15]. It has 7 categories ranging from independent and free of disability (0) to death (6) [16].

Study protocol has been approved by the Research and Ethics committee at King Fahad Medical City, Riyadh, Kingdom of Saudi Arabia.

Data entry and statistical analysis were performed using Statistical Package for Social Sciences (SPSS software), version 28 (version 28.0.1.1, IBM, Armonk, NY). One-way analysis of variance (ANOVA) test was applied to compare means of a continuous variable between more than two groups and chi-square test was applied to test for the difference and/or association between two categorical variables. P-value <0.05 was considered as a cut-off value for statistical significance.

Results

A total of 177 patients included in the study. Age and gender were available for 174 patients. The age ranged between 17 and 100 years (60.74 ± 15.55). Males represented 56.3% of patients table 1.

Age (years)	
Range	17-100
Mean ± SD	60.74 ± 15.55
Gender [No. (%)]	
Males	98 (56.3%)
Females	76 (43.7%)

Table 1: Age and gender distribution of the participants (n = 174).

Severity of the stroke severity, based on the score of the National Institute of Health stroke scale is summarized in figure 1 as 47.1% of cases are categorized as severe while 39.1% were mild to moderate.

As demonstrated in table 2, none of the studied patients` characteristics (age, gender, TSH, T3, T4, LDL, and HbA1c) was significantly associated with stroke severity based on NIHSS stroke scale.

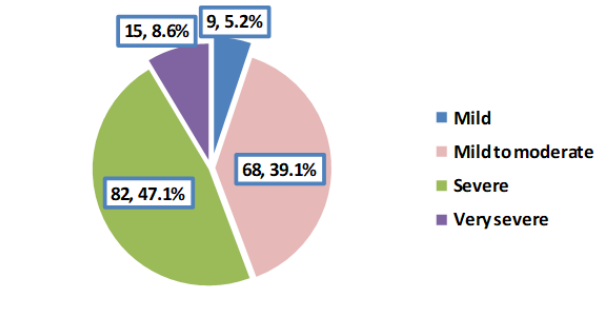

Figure 1: Stroke severity based on the score of the National Institute of Health stroke scale.

	NIHSS stroke severity				p-value
	Mild N = 9 Mean ± SD	**Mild to moderate N = 68 Mean ± SD**	**Severe N = 82 Mean ± SD**	**Very severe N = 15 Mean ± SD**	
Age (years)	50.8 ± 13.1	59.2 ± 14.5	63.1 ± 15.9	60.7 ± 17.6	0.098*
Gender [No. (%)]					
Males (n = 98)	5 (5.1)	45 (45.9)	41 (41.8)	7 (7.1)	
Females (n = 76)	4 (5.3)	23 (30.3)	41 (53.9)	8 (10.5)	0.205˚
TSH	N = 5 2.6 ± 2.0	N = 45 1.7 ± 1.4	N = 59 1.7 ± 1.5	N = 9 1.6 ± 1.4	0.534*
T4	N = 5 13.0 ± 1.2	N = 40 13.5 ± 2.6	N = 56 12.9 ± 3.1	N = 8 12.8 ± 1.7	0.729*
T3	N = 2 3.0 ± 0.6	N = 5 2.9 ± 0.8	N = 10 4.1 ± 3.0	N = 3 2.9 ± 1.1	0.755*
LDL	N = 9 2.4 ± 0.7	N = 67 2.8 ± 1.1	N = 79 2.7 ± 1.1	N = 13 2.4 ± 0.6	0.446*
HbA1c	N = 9 6.3 ± 1.5	N = 64 7.4 ± 2.4	N = 77 7.0 ± 1.9	N = 13 7.5 ± 2.4	0.394*

Table 2: Patients characteristics associated with stroke severity based on the score of the National Institute of Health stroke scale.

*One-way analysis of variance (ANOVA) test

˚Chi-square test

Concerning functional disability one month after discharge, moderately severe and severe disabilities were observed among 27.7% and 21.5% of patients, respectively whereas death was reported in 15.8% of cases. table 3.

	Frequency	Percentage
No symptoms	16	9.0
No significant disability	23	13.0
Slight disability	10	5.6
Moderate disability	13	7.3
Moderately severe disability	49	27.7
Severe disability	38	21.5
Dead	28	15.8

Table 3: Degree of disability of stroke patients one month after discharge based on modified Rankin scale (mRS) (n = 177).

Patients` age was highest in patients of category 5 (severe disability) (69.0 ± 14.6 years) and lowest among those of category 0 (no disability), p = 0.001. LDL level was highest among patients of category 2 (slight disability) and lowest among those of category 6 (dead) (3.2 ± 1.4 and 2.2 ± 1.1, respectively), p = 0.031 table 4.

As shown in table 5, there was a statistically significant association between severity of stroke based on NIHSS scale and impact on functional outcome based on modified ranking scale where 55.6% of patients with mild severity had no disability whereas 28.6% of patients with very severe stroke had either severe disability or dead, p < 0.001.

There were no significant differences between male and female patients as regards the levels of thyroid hormones (Table 6). There was a negative significant correlation between TSH and HbA1c (Pearson's correlation coefficient (r) = 0.222, p = 0.017) table 7.

	Modified Rankin scale							p-value
	0 N = 16 Mean ± SD	1 N = 23 Mean ± SD	2 N = 10 Mean ± SD	3 N = 13 Mean ± SD	4 N = 49 Mean ± SD	5 N = 38 Mean ± SD	6 N = 28 Mean ± SD	
Age (years)	50.4 ± 14.8	59.0 ± 14.6	57.3 ± 10.1	64.2 ± 12.5	57.8 ± 14.9	69.0 ± 14.6	63.3 ± 17.2	0.001
Gender	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	
Males (n = 99)	11 (11.1)	13 (13.1)	5 (5.1)	10 (10.1)	27 (27.3)	15 (15.2)	18 (18.2)	0.202˚
Females (n = 78	5 (6.4)	10 (12.8)	5 (6.4)	3 (3.8)	22 (28.2)	23 (29.5)	10 (12.8)	
TSH	N = 11	N = 16	N = 7	N = 10	N = 35	N = 24	N = 18	0.847
	1.7 ± 1.3	1.6 ± 1.4	1.4 ± 0.8	2.0 ± 1.6	1.4 ± 1.1	1.9 ± 1.8	1.8 ± 1.8	
T4	N = 10	N = 14	N = 6	N = 7	N = 34	N = 23	N = 18	0.837
	13.3 ± 2.0	12.5 ± 4.0	12.9 ± 2.0	13.0 ± 1.4	13.8 ± 3.2	13.2 ± 1.9	12.8 ± 3.1	
T3	N = 2	N = 3	N = 1	N = 1	N = 8	N = 6	N = 2	0.915
	3.5 ± 0.1	3.3 ± 0.6	3.5	3.5	4.4 ± 3.4	3.1 ± 1.1	2.3 ± 1.0	
LDL	N = 19	N = 22	N = 9	N = 13	N = 48	N = 35	N = 27	0.031
	2.8 ± 0.8	2.4 ± 1.0	3.2 ± 1.4	2.4 ± 0.9	3.0 ± 1.2	2.7 ± 1.0	2.2 ± 1.1	
HbA1c	N = 15	N = 22	N = 9	N = 13	N = 48	N = 34	N = 24	0.172
	6.0 ± 1.2	6.8 ± 1.9	6.8 ± 2.2	7.9 ± 2.3	7.2 ± 2.3	7.2 ± 2.1	7.9 ± 2.6	

Table 4: Factors associated with the functional outcome among stroke patients.

0: No symptoms, 1: No significant disability, 2: Slight disability, 3: Moderate disability

4: Moderately severe disability, 5: Severe disability, 6: Dead

*One-way analysis of variance (ANOVA) test; ˚Chi-square test

NIHSS	Modified Rankin scale						
	0 N = 16 N (%)	1 N = 23 N (%)	2 N = 10 N (%)	3 N = 13 N (%)	4 N = 46 N (%)	5 N = 37 N (%)	6 N = 27 N (%)
Mild (n = 9)	5 (55.6)	3 (33.3)	0 (0.0)	0 (0.0)	1 (11.1)	0 (0.0)	0 (0.0)
Mild/moderate (n = 67	5 (7.5)	13 (19.4)	7 (10.7)	6 (9.0)	17 (25.4)	9 (13.4)	10 (14.9)
Severe (n = 82)	6 (7.3)	5 (6.1)	3 (3.7)	5 (6.1)	26 (31.7)	24 (29.3)	13 (15.9)
Very severe (n = 14)	0 (0.0)	2 (14.3)	0 (0.0)	2 (14.3)	2 (14.3)	4 (28.6)	4 (28.6)

Table 5: Association between stroke severity and impact on functional outcome.

P < 0.001 (Chi-square test).

0: No symptoms, 1: No significant disability, 2: Slight disability, 3: Moderate disability, 4: Moderately severe disability

5: Severe disability, 6: Dead

	Males		Females		p-value*
	N	Mean ± SD	N	Mean ± SD	
TSH	65	1.46 ± 1.32	59	1.90 ± 1.57	0.096
T4	56	12.79 ± 2.33	57	13.62 ± 3.19	0.114
T3	11	3.79 ± 2.98	12	3.37 ± 0.80	0.637

Table 6: Comparison of thyroid functions between male and female patients.

*Independent two-sample t-test

	TSH	T4	T3
HbA1c	r = -0.222 P = 0.017	r = 0.146 p = 0.135	r = -0.268 p = 0.243
LDL	r = -0.113 P = 0.223	r = 0.101 p = 0.295	r = -0.212 p = 0.345

Table 7: Correlation between HbA1c, LDL and thyroid function parameters.

r: Pearson`s correlation coefficient

Discussion

It is unknown whether hypothyroidism impacts stroke patients in the form of stroke severity and functional outcomes [17]. Thus; the present study is a trial to explore such association.

Results of the current study observed that thyroid hormones (TSH, T3, T4) were not associated with stroke severity, although, it has been observed by others that hypothyroidism is a determinant factor for stroke and attributed this to the neuroprotective role of hypothyroidism in acute stroke patients [18]. Some others found that low T3 was associated with severity and short-term outcome of stroke [19]. Authors also considered hypothyroidism as a possible cause of stroke of unknown etiology in young people [20,21].

In this study, moderately severe and severe disabilities (one month after patient`s discharge) were observed among 27.7% and 21.5% of patients, respectively whereas death was reported in 15.8% of them. In China, the prevalence of functional disability among stroke survivors was 45% [22]. The American Heart Association documented that most of stroke patients (75%) expressed dysfunction and between 15 and 30% of survivors had severe disability.[23] Thus, functional disability among ischemic stroke patients needs great caution.

The association between thyroid disorders and functional disability in stroke patients has conflicting results in the literature [6,7,18,24]. Some studies have reported that low T3 level was associated with greater stroke severity and mortality as well as poorer functional outcomes [19,25,26]. However, O'Keefe., *et al.* (2015), [27], although observed that lower level of free T3 was associated with poorer prognosis post-stroke at different follow-up periods in bivariate analysis, this disappeared after control for confounders in multivariate analysis. Thus, thyroid hormones are associated with other factors, mainly age that affect stroke outcomes. The association between thyroid disorders and functional disability in stroke patients secondary to large vessel occlusion was not proved in this study.

Furthermore, the present study revealed a significant association between severity of stroke based on NIHSS scale and impact on functional outcome based on modified ranking scale. The same has been confirmed in other studies [22,24,25].

As quite expected, older patients in the current study, were more likely to have severe disability. The same has been observed by others [28,29]. On the other hand, LDL level was highest among patients of category 2 (slight disability) and lowest among those of category 6 (dead); this finding could be partially attributed to the possible association between low LDL and risk of intracerebral hemorrhage, [30] which characterized by high mortality and disability rate [31-33]. This is explained by the fact that cholesterol has a vital role in the formation of cell membranes, thus, LDL level might considered as a risk factor for intracerebral hemorrhage [34].

In another study conducted by O'Keefe., *et al.* (2015) [27], it has been observed that low TSH and T3 were associated with lower function and higher rates of death at three months; however after controlling for stroke severity, this disappeared.

Important limitations of the present study include its retrospective nature, which depends on the quality of medical record. Thus the results might be subjected to bias. Additionally, generalizability of findings is questionable as the study was conducted in one healthcare center. Despite of those limitations, the study carries a clinical significance in exploring the impact of thyroid disease on functional outcome in ischemic stroke secondary to large vessel occlusion.

Conclusion

In conclusion, stroke severity was not associated with thyroid hormones (TST, T3, and T4). Older patients had more severe functional disability while LDL was lowest among dead patients. Stroke severity was associated with functional disability. Based on these findings, further multi-centric study with sufficient sample size I warranted exploring the possible impact of thyroid disorders on stroke severity and on functional outcomes of stroke patients.

Bibliography

1. GBD. "Stroke Collaborators. Global, regional, and national burden of stroke, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016". *The Lancet Neurology* 18.5 (2019): 439-458.

2. Gao N., *et al*. "Carotid intima-media thickness in patients with subclinical hypothyroidism: a meta-analysis". *Atherosclerosis* 227 (2013): 18-25.

3. Iwen KA., *et al*. "Thyroid Hormones and the Metabolic Syndrome". *European Thyroid Journal* 2 (2013): 83-92.

4. Bai M-F., *et al*. "Effects of thyroid dysfunction on the severity of coronary artery lesions and its prognosis". *Journal of Cardiology* 64.6 (2014): 496-500.

5. Chen Q., *et al*. "Effect of hyperthyroidism on the hypercoagulable state and thromboembolic events in patients with atrial fibrillation". *Journal of Cardiology* 127 (2014): 176-82.

6. Akhoundi FH., *et al*. "Favorable functional outcomes in acute ischemic stroke patients with subclinical hypothyroidism". *Neurology* 77.4 (2014): 349-354.

7. Wollenweber FA., *et al*. "Subclinical hyperthyroidism is a risk factor for poor functional outcome after ischemic stroke". *Stroke* 44.5 (2013): 1446-1448.

8. Chen Z., *et al*. "Low TSH level predicts a poor clinical outcome in patients with anterior circulation ischemic stroke after endovascular thrombectomy". *Neurological Sciences* 41.7 (2020): 1821-1828.

9. NIH Stroke Scale. Approach to Human Subject Protection and Patient Safety.

10. Adams HP., *et al*. "Baseline NIH Stroke Scale score strongly predicts outcome after stroke: A report of the Trial of Org 10172 in Acute Stroke Treatment (TOAST)". *Neurology* 53.1 (1999): 126.

11. Runde D. "Calculated Decisions: NIH stroke scale/score (NIHSS)". *Emergency Medicine Practice* 22.7 (2020): CD6-CD7.

12. Know Stroke. "NIH Stroke Scale.

13. Brott T., *et al*. "Measurements of acute cerebral infarction: a clinical examination scale". *Stroke* 20.7 (1989): 864-870.

14. Broderick JP., *et al*. "Evolution of the modified rankin scale and its use in future stroke trials". *Stroke* 48 (2017): 2007-2012.

15. Banks JL and Marotta CA. "Outcomes validity and reliability of the modified rankin scale: implications for stroke clinical trials - a literature review and synthesis". *Stroke* 38 (2007): 1091-1096.

16. Nunn A., *et al*. "Analysis of the modified Rankin scale in randomized controlled trials of acute ischaemic stroke: a systematic review". *Stroke Research and Treatment* (2016).

17. Bashyal S., *et al*. "Alteration of thyroid hormone among patients with ischemic stroke visiting a tertiary care hospital: A descriptive cross-sectional study". *Journal of Nepal Medical Association* 59.240 (2021): 779-782.

18. Alevizaki M., *et al*. "Hypothyroidism as a protective factor in acute stroke patients". *Clinical Endocrinology (Oxford)* 65.3 (2006): 369-372.

19. Zhang Y and Meyer MA. "Clinical analysis on alteration of thyroid hormones in the serum of patients with acute ischemic stroke". *Stroke Research and Treatment* 2010 (2010): 290678.

20. Sheu JJ., *et al*. "Hyperthyroidism and risk of ischemic stroke in young adults: a 5-year follow-up study". *Stroke* 41.5 (2010): 961-966.

21. Rasura M., *et al*. "A case series of young stroke in Rome". *European Journal of Neurology* 13.2 (2006): 146-152.

22. Yang Y., *et al*. "The disability rate of 5-year post-stroke and its correlation factors: a national survey in China". *PLoS ONE* 11 (2016): e0165341.

23. Go AS., *et al*. "Heart disease and stroke statistics-2014 update: a report from the American Heart Association". *Circulation* 129 (2014): e28-292.

24. Leonards CO., *et al*. "Thyroid-stimulating hormone, white matter hyperintensities, and functional outcome in acute ischemic stroke patients". *Cerebrovascular Diseases Extra* 4 (2014): 61-68.

25. Alevizaki M., *et al*. "Low triiodothyronine: A strong predictor of outcome in acute stroke patients". *European Journal of Clinical Investigation* 37 (2007): 651-657.

26. Bunevicius A., *et al*. "Neuroprotective actions of thyroid hormones and low-T3 syndrome as a biomarker in acute cerebrovascular disorders". *Expert Review of Neurotherapeutics* 15.3 (2015): 315-326.

27. O'Keefe LM., *et al*. "Thyroid hormones and functional outcomes after ischemic stroke". *Thyroid Research* 8 (2015): 9.

28. Astuti P., *et al*. "Depression and functional disability in stroke patients". *Journal of Public Health Research* 9.2 (2020): 1835.

29. Wang S., *et al*. "The Disability Rte of 5- Year Post Stroke and Its Correlation Factors: A National Survey in China". *PLoS One* 11 (2016): e0165341.

30. Ma C., *et al*. "Low-density lipoprotein cholesterol and risk of intracerebral hemorrhage: A prospective study". *Neurology* 93.5 (2019): e445-e457.

31. Feigin VL., *et al*. "Global Burden of Disease Lifetime Risk of Stroke Collaborators: global, regional, and country-specific lifetime risks of stroke, 1990 and 2016". *The New England Journal of Medicine* 379 (2018): 2429-2437.

32. Feigin VL., *et al*. "Global burden of stroke and risk factors in 188 countries, during 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013". *The Lancet Neurology* 15 (2016): 913-924.

33. Krishnamurthi RV., *et al*. "The global burden of hemorrhagic stroke: a summary of findings from the GBD 2010 study". *Global Heart* 9 (2014): 101-106.

34. Bruckdorfer KR., *et al*. "The effect of partial replacements of membrane cholesterol by other steroids on the osmotic fragility and glycerol permeability of erythrocytes". *Biochimica et Biophysica Acta* 183 (1969): 334-345.