



“Association of Low Free T3 Levels with Stroke Pattern, Severity and Outcome in Patients with Acute Ischemic Stroke”

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KEYWORDS

Free T3, Acute Ischemic Stroke, Stroke Severity, NIHSS, Modified Rankin Scale, Stroke Outcome

ABSTRACT:

Background: Acute ischemic stroke (AIS) is a major global health burden, leading to significant morbidity and mortality. Recent studies indicate a potential link between free triiodothyronine (fT3) levels and stroke prognosis, with the "low T3 syndrome" emerging as a possible marker of poor outcomes in critically ill patients. However, its specific role in AIS remains underexplored, warranting further investigation into its impact on stroke severity, recovery, and long-term neurological function. This study aimed to investigate the association between low fT3 levels and stroke pattern, severity, and functional outcome in patients with AIS.

Material & Method: A prospective cohort study was conducted at Aarupadai Veedu Medical College & Hospital over 18 months, including 100 patients diagnosed with AIS. Stroke severity was assessed using the National Institutes of Health Stroke Scale (NIHSS), and functional outcomes were evaluated using the Modified Rankin Scale (mRS). Free T3 levels were measured within 48 hours of admission. Statistical analysis included correlation and regression models to assess associations between fT3 levels, stroke severity, and outcomes.

Results: The study population had a mean age of 59.66 ± 11.8 years, with a male predominance (59%). Anterior circulation stroke was more prevalent (75%) than posterior stroke (25%). A significant negative correlation was observed between fT3 levels and NIHSS scores ($r = -0.317$, $p < 0.05$), as well as fT3 levels and mRS scores ($r = -0.314$, $p < 0.05$), indicating that lower fT3 levels were associated with greater stroke severity and poorer functional outcomes. Additionally, NIHSS and mRS scores showed a strong positive correlation ($r = 0.878$, $p < 0.05$).

Conclusion: Low fT3 levels were significantly associated with more severe strokes and worse functional outcomes in AIS patients. These findings suggest that fT3 may serve as a prognostic biomarker in stroke management. Further studies are required to explore potential therapeutic interventions targeting thyroid hormone modulation in AIS.

Introduction:

Stroke is characterized by the sudden onset of focal or global neurological deficits, persisting for more than 24 hours or resulting in death, with no identifiable cause other than a vascular origin.(1–3) Stroke is a major global health challenge, ranking as the second leading cause of death and a significant contributor to long-term

disability. Key risk factors include lifestyle changes, poor dietary habits, hypertension, diabetes, and abnormal lipid profiles. Among the two main types of stroke, ischemic stroke is the most prevalent, accounting for approximately 68% of cases. Acute ischemic stroke (AIS) occurs due to an obstruction of blood flow to the brain, often caused by thrombosis or embolism, leading to rapid neurological deficits. The prognosis and severity



of AIS depend on multiple factors, including the size of the infarct, assessed through CT or MRI imaging, and the patient's initial neurological status, commonly measured using the National Institutes of Health Stroke Scale (NIHSS). (4,5)

The NIHSS score is a 42-point scale consisting of 11 parameters, used to assess the severity of acute ischemic stroke (AIS). Patients with minor strokes typically have an NIHSS score of less than 5, while higher scores indicate greater stroke severity. Additionally, infarct size, measured using MRI imaging, plays a crucial role in determining stroke severity—larger infarcts correlate with more severe ischemic strokes.(6–8)

Triiodothyronine (T3), the active form of thyroid hormone, is crucial for metabolism, neuroprotection, and cerebrovascular health. Emerging research suggests a strong link between free T3 (fT3) levels and stroke outcomes, particularly in acute ischemic stroke (AIS). The "low T3 syndrome," characterized by reduced fT3 with normal or low TSH and T4 levels, is frequently observed in critically ill patients and is associated with poor prognosis in conditions such as cardiovascular disease and sepsis. In AIS, low fT3 levels may indicate greater disease severity and worse functional outcomes. Studies suggest that reduced fT3 correlates with larger infarct volumes, more severe neurological deficits, and increased mortality rates. This association likely stems from the neuroprotective and anti-inflammatory properties of T3, which may be diminished in individuals with lower circulating levels. Additionally, thyroid hormones regulate cerebral perfusion, endothelial function, and oxidative stress, all of which are crucial in stroke progression and recovery.

There is limited literature available among the Indian population, hence this study aimed to investigate the association between free T3 levels and stroke pattern, severity and outcome in patients with acute ischemic stroke.

Result:

This study included total of 100 cases with mean age of 59.66±11.8yrs

Material & Method:

This prospective cohort study was conducted at the General Medicine department (OPD/IPD & MICU) of Aarupadai Veedu Medical College and Hospital. The study included 100 patients diagnosed with acute ischemic stroke (AIS), confirmed through imaging studies, with free T3 levels measured within 48 hours of hospital admission. Patients aged 18 years or older were eligible, while those with a history of thyroid disease, prior thyroid hormone therapy, hemorrhagic stroke, subarachnoid hemorrhage, severe comorbidities, or inability to provide consent were excluded. The study spanned 18 months, using a convenience sampling technique.

The primary independent variable was low free T3 levels, while outcome variables included stroke pattern (Anterior vs. Posterior), stroke severity (NIHSS score), and stroke outcome (Modified Rankin Score). The study aimed to enhance understanding of the association between thyroid hormone dysregulation and AIS, potentially guiding future therapeutic strategies.

Statistical analysis involved logistic regression to estimate odds ratios and confidence intervals for the association between free T3 levels and stroke characteristics. Descriptive statistics (mean, standard deviation, frequency distribution) assessed the prevalence of low free T3 levels in AIS patients. Linear regression and correlation analyses evaluated the relationship between free T3 levels, NIHSS score, and Modified Rankin Score, while chi-square or logistic regression examined differences in stroke outcomes based on stroke pattern.

Ethical considerations included minimal risks, such as slight discomfort from blood collection and low radiation exposure from imaging, with the benefit of improved stroke severity and outcome assessment to aid therapeutic decisions.

Table 1: Gender and stroke pattern distribution among patients

		Count	N %
Gender	Female	41	41.0%



	Male	59	59.0%
Stroke pattern	Anterior	75	75.0%
	Posterior	25	25.0%

Among them 59% were male patients and 41% were female with male preponderance in the study. The most common pattern was found to be anterior stroke in 75% and posterior in 25% of the cases.

Table 2: Showing Pearson's correlation of ft3 with MRS and NIHSS scores

Correlations		Ft3	MRS
ft3	r	-	-.317**
	p value		.001
NIHSS	r	-.314**	.878**
	p value	.001	.001

** . Correlation is significant at the 0.01 level (2-tailed).

There is significant negative association of ft3 with NIHS score (r-0.317, p<0.05*) and MRS score (r-0.314, p<0.05*). Also there is significant strong association between the NIHS score with MRS score among the patients (r-0.878, p<0.05*).

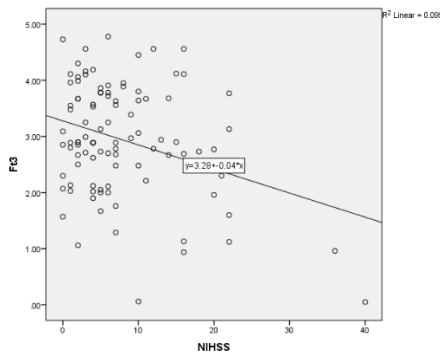


Figure 1: Correlation of ft3 with NIHSS

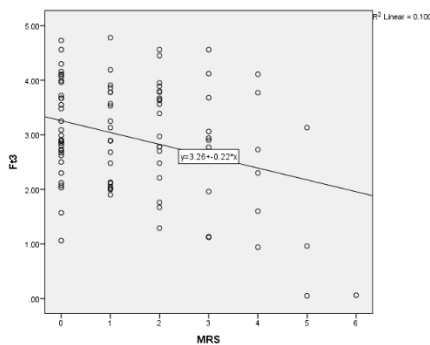


Figure 2: Correlation of ft3 with MRS

Discussion:

Several studies have highlighted that lower ft3 levels correlate with more severe stroke presentations, as assessed by the National Institutes of Health Stroke Scale (NIHSS), and poorer prognosis based on the modified Rankin Scale (mRS). Additionally, stroke pattern analysis suggests that patients with lower ft3 levels may be more likely to experience large-vessel occlusions and more extensive ischemic damage, potentially due to impaired cerebrovascular autoregulation and endothelial dysfunction associated with thyroid hormone deficiency.

This study included total of 100 cases with mean age of 59.66±11.8yrs. Among them 59% were male patients and 41% were female with male preponderance in the study. In study by Bhandal NS et al., the mean age of patients was found to be 68.4yrs with 38% female and 62% male with male preponderance in their study similar to present study.(9) Another study by Li QL et al., the mean age of patients was found to be 57.6yrs with 66.4% male.(10) Another study by Song Y et al., the mean age in good outcome was 64.53yrs and poor outcome it was 70.11yrs, with majority of male patients in their study.(11)



The most common pattern was found to be anterior stroke in 75% and posterior in 25% of the cases. There is significant negative association of fT3 with NIHSS score ($r=0.317$, $p<0.05^*$) and MRS score ($r=0.314$, $p<0.05^*$). Also there is significant strong association between the NIHSS score with MRS score among the patients ($r=0.878$, $p<0.05^*$). In concordance to present study Lamba B et al., found a negative correlation was found between FT3 levels and both the NIHSS score at admission and the mRS score during follow-up. The study concluded that reduced T3 levels were linked to greater clinical severity and poorer functional outcomes in AIS patients.(12) Also Zhang S et al., suggest that low FT3 levels at admission correlate with stroke severity, subtype, and prognosis, while bioinformatics analysis of DEGs may offer insights into clinical outcomes and potential therapeutic targets for improving stroke prognosis.(13) Also, Aly Ghonemy MH et al., documented with High TSH and low FT3 levels were significantly associated with greater stroke severity and poorer outcomes. Abnormal thyroid hormone levels at presentation may serve as predictors of ischemic stroke severity and functional prognosis.(14) Also in study by Natarajan B et al., the fT3 showing significant association with severity of the stroke. (15)

Also in study by Bhandal NS et al., found a significant correlation was found between alterations in the thyroid profile and ischemic stroke outcomes. Suggested that these findings highlight the need for further large-scale studies to explore potential therapeutic strategies for thyroid hormone replacement in managing ischemic stroke patients.(9)

Another study by Song Y et al., the patients with poor outcomes at three months exhibited significantly lower FT3 levels at admission compared to those with good outcomes (3.53 ± 0.70 pmol/L vs. 4.04 ± 0.68 pmol/L; $P < 0.001$). The findings suggest that lower FT3 levels at admission may serve as an independent prognostic biomarker for poor outcomes following ischemic stroke.(11) Multiple logistic regression confirmed that higher NIHSS scores (OR = 1.95; 95% CI, 1.66–2.30; $P \leq .001$) and lower total T3 (OR = 0.06; 95% CI, 0.01–0.68; $P = .024$) independently predicted poor functional outcomes in older patients, whereas total T3 was not an independent predictor in the younger group in study by Li L et al.”(10) These findings suggest that low serum triiodothyronine may serve as a predictive marker of short-term ischemic stroke outcomes, and a combined

model incorporating triiodothyronine, age, and NIHSS score could provide more accurate prognostic information.(16)

Conclusion: This study establishes a significant link between low free T3 (fT3) levels and stroke severity, pattern, and outcomes in acute ischemic stroke (AIS) patients. Among the 100 cases analyzed, the majority were male (59%), with a mean age of 59.66 ± 11.8 years. Anterior circulation stroke was the most common (75%), and lower fT3 levels showed a strong negative correlation with NIHSS and mRS scores, indicating greater stroke severity and poorer recovery. Additionally, the strong association between NIHSS and mRS scores reinforces the predictive value of stroke severity on functional outcomes. These findings suggest that thyroid hormone dysregulation, particularly low fT3, could serve as a potential biomarker for stroke prognosis. Further research is necessary to confirm these results and explore the therapeutic potential of thyroid hormone modulation in AIS management.

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Conflict of interest: Nil

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