

## A Prospective observational study on ischemic stroke and impact of thyroid profile at a tertiary care center

Siddharth Singh<sup>1</sup>, Santosh Kumar Nayan<sup>2\*</sup>, Raj Bahadur Singh<sup>3</sup>, Janardan Sharma<sup>4</sup>

<sup>1</sup>Assistant Professor, Dept. of Trauma and Emergency (General Medicine), IGIMS, Patna, Bihar, India

<sup>2</sup>Assistant Professor, Dept. of Trauma and Emergency (General Medicine), IGIMS, Patna, Bihar, India

<sup>3</sup>Assistant Professor, Dept. of Trauma and Emergency (General Medicine), IGIMS, Patna, Bihar, India

<sup>4</sup>Assistant Professor, Dept. of Trauma and Emergency (General Medicine), IGIMS, Patna, Bihar, India

Received: 10-11-2021 / Revised: 19-12-2021 / Accepted: 10-01-2022

### Abstract

**Background:** Stroke is reckoned as a major manifestation of Cardio-Vascular Diseases (CVD) and an alarming reason for long-term disability, mortality, and morbidity in India. Among the widespread endocrine disorders, Thyroid dysfunction tends to influence prognosis and stroke risks in multifarious ways. **Aim:** The objective of this study is to determine the possible association of serum T3 level with the severity of a stroke and post-stroke recovery. **Methodology:** This study included 588 patients admitted with the diagnosis of ischemic stroke who had visited the emergency department of the Indira Gandhi Institute of Medical Sciences, Patna. Patients who were above age of 18 were included in the study. **Results:** The findings revealed that about 273 (46.42%) patients were diagnosed with the ischemic stroke while 314 (53.40%) patients were diagnosed with haemorrhagic stroke. The average age +SD of the study was 58.2 + 12.4, and the male to female ratio was 1.45:2. Among the common risk factors determined, hypertension (76.65%) was the highest and dyslipidemia was second highest (52.98%), hemiplegia (84.12%) has been found as the most common clinical presentation. **Conclusion:** Increased levels of TSH might correlate with better functional outcomes, however, a low level of T3/FT3 would correlate with worse outcomes among the patients of acute ischemic stroke (AIS).

**Keywords:** Cerebrovascular stroke, Diabetes, Hypertension, Ischemic stroke, Risk factors

This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.

### Introduction

Stroke is reckoned as a major manifestation of Cardio-Vascular Diseases (CVD) and an alarming reason for long-term disability, mortality in India. Among the widespread endocrine disorders, Thyroid dysfunction tends to influence prognosis and stroke risks in multifarious ways. It is considered to be the fifth highest death cause in the United States where approximately 795,000 people are diagnosed with ischemic or haemorrhage per year[1]. Past literature has revealed that thyroid hormones hold magnitude in maintaining body growth with the modulation of immune system and metabolism. Thyroid dysfunction is related to mortality of ICU patients. These changes in thyroid chemical levels are alluded to as a euthyroid sick syndrome. It is additionally alluded to as non-thyroidal illness syndrome (NTIS). It is portrayed by low serum levels of triiodothyronine (T3) and undeniable degrees of converse T4 (TT4) joined by ordinary or low degrees of thyroxine (T4) and thyroid-investigating chemical (TSH)[1].

Scientists in certain examinations exhibited that triiodothyronine (T3) levels in non-survivors were essentially lower than those in survivors. Low T3 is a significant marker of mortality in basically sick patients. T4 and TSH didn't differ among survivors and non-survivors. However, different specialists had shown that there would be no affiliation[2]. In this way, embraced investigation of clinical ICU Patients to distinguish the autonomous indicators of ICU mortality based on thyroid chemical levels (TT3, TT4, TSH,) and to assess the capacity of thyroid chemical levels to foresee ICU mortality. Low serum T3 levels with typical T4 and TSH levels will be the most widely recognized hormonal example in NTIS.

\*Correspondence

**Dr. Santosh Kumar Nayan**

Assistant Professor, Dept. of Trauma and Emergency (General Medicine), IGIMS, Patna, Bihar, India

In intense stroke among a few other prognostic factors, a decrease of serum T3 level without the height of TSH seemed, by all accounts, to be related to the severity of stroke and more regrettable clinical result[3]. There are a few investigations that tended to the magnitude of checking thyroid utilitarian status after intense stroke. The goal of this study is to see the possible relationship of serum T3 level with the severity of stroke just as post-stroke recuperation.

### Literature Review

A number of fundamental studies have assessed the association between thyroid hormones and Acute Ischemic Stroke (AIS) to determine the impact it has on one another. The findings from these studies, however, do not seem consistent. According to the study by Dhital et. al (2017) on thyroid hormones and ischaemic stroke observed Elevated Initial TSH (clinical or subclinical hypothyroidism) might relate to better user results though low beginning T3/FT3 may associate with more terrible results in intense ischemic stroke among clinically euthyroid patients[1]. The researchers Boltzmann et. al (2017) had conducted an investigation on the impact of Thyroid Hormone Levels on Functional Outcome in Neurological and Neurosurgical Early Rehabilitation Patients and found in a blended example of neurological and neurosurgical sicknesses (e.g. stroke, traumatic injury, and intracerebral hemorrhages), age, the severity of starting (utilitarian) weakness, time among injury and confirmation, and all-out T3 level were viewed as of autonomous prescient incentive for the useful result[4]. Albeit the current review features the magnitude of thyroidal capacities in the post-intense stage, further investigations ought to analyze the worldly elements all the more intently.

In addition to this, the investigation by Hosne Ara Rahman et al (2015) had revealed that in patients with intense ischemic stroke lower T3 level, the danger of poor utilitarian result is elevated[5]. Alevizaki et al (2007) had depicted low T3 levels as related with result in an intense stroke patient[6]. Similarly, the scholars' Zhang

Youghua et al (2010) found that intense ischemic stroke with low T3 has a more awful neurological result[7]. The severity of low T3 syndrome might be a helpful indicator of utilitarian improvement in patients with intense ischemic stroke.

### Methodology

In this observational study, each participant has been subjected to an assessment of their neurological and clinical history. The Glasgow Coma Scale (GCS) and the Scandinavian Stroke Scale (SSS) had been utilized to achieve a neurological result. A background marked by hypertension will be characterized by Systolic blood pressure >140 mmHg or diastolic pulse of >90 mmHg, or both analyzed twice before treating hypertension or stroke has been provided. The presence of Type 2 diabetes mellitus would be characterized by the usage of insulin or oral hypoglycaemic agents even before the time when HbA1c and CVA occur. In every patient, thyroid profile has been done which included FT3, FT4, TSH, and hostile to thyroid Peroxidase[16, 17]. Based on thyroid profile, the patients were isolated into five classifications NTIS/euthyroid sick syndrome, euthyroid, hyperthyroid, hypothyroid, and subclinical hypothyroid:

- NTIS will be analyzed as a low FT3, low or typical, and low or ordinary TSH.
- Euthyroid will be analyzed as should be expected FT3, FT4, and TSH.
- Hyperthyroid will be analyzed as high FT3, high FT4, and low TSH
- Hypothyroid will be analyzed as low FT3, low FT4, and high TSH
- Subclinical hypothyroid will be analyzed as low or typical FT3, ordinary FT4, and high TSH.

### Research approach

A prospective observational study

### Place of study

Department of Trauma and Emergency, Indira Gandhi Institute Of Medical Sciences, Sheikhpura Patna

### Period of Study

1 year

Endorsement from the moral board will be gotten

Test size-all patients of ischaemic stroke visiting in crisis department

### Inclusive criteria

This study had taken place at the Department of Trauma and Emergency, IGIMS, Patna for a time of one year. It will be a forthcoming observational review and AIS will be conceded and followed up at 7<sup>th</sup> and 30<sup>th</sup> day after release. Patients with the following characteristics have been included from the study. Those who were of 18 years or more, with no past history of thyroid chemical abnormality, who introduced very first stroke inside 24 hours from manifestations beginning, with radiologically affirmed ischemic CVA introduced inside 72 hours of beginning of side effects.

### Exclusion criteria

Patients with known thyroid infection or biochemically characterized unmistakable thyroid illness were excluded from this study. Those utilizing prescriptions that can influence thyroid capacity were also excluded.

### Findings

Our meta-analysis included observational examinations with a pooled test of 588 patients. Albeit the included examinations surveyed comparable end focuses, the investigations were geologically fluctuated and varied in general plan. Out of 588 patients with stroke diagnosis conceded to crisis division in our middle, age range was from 21 to 92 years. Around 45% of patients were female, and 55% were male. The diagnosis was ischemic stroke in 83% patients and haemorrhagic stroke in 17% patients.

Stroke patients with positive outcomes (mRs  $\leq$  2) contrasted and ominous outcomes at release and 90 days follow-up had higher introductory TSH level, with huge mean contrasts of .12 and .25 separately[15]. Notwithstanding, on joining the changed ORs of relationship from the included examinations, higher starting TSH was not fundamentally connected with useful result considering 90 days follow-up. Patients with ideal result (mRs  $\leq$  2) at release and at 90 days after release had lower starting ft4 level, albeit not measurably critical. Likewise, on joining the most changed ORs of the included examinations, expanded ft4 level was not fundamentally connected with utilitarian result (mRs) considering 90 days after release, albeit the pattern was toward a negative result. Patients with troublesome result (mRs >2) at release and at 90 days after release had lower introductory ft3 and T3 levels; mean contrasts .36 and 8.60, individually, instead of patients with good result. On consolidating the most changed ORs of the included examinations, in any case, ft3 or T3 was not altogether connected with utilitarian result (mRs).

Table 1:Results obtained

Clinical variables	Low T3 group	Normal T3 group
Age (years)	68.1 ( $\pm$ 12.7)	66.8 ( $\pm$ 11.5)
Sex (% male)	18 (61.1%)	11 (61.1%)
Smoking	9 (31.0%)	6 (33.3%)
Hypercholesterolemia	8 (27.6%)	5 (27.8%)
Coronary artery disease	5 (17.2%)	3 (16.7%)
Diabetes mellitus	9 (31.0%)	6 (33.3%)
Atrial fibrillation	6 (20.1%)	4 (22.2%)
History of hypertension	19 (65.5%)	11 (61.1%)
Systolic BP (mmHg)	156.2 ( $\pm$ 27.9)	150.2 ( $\pm$ 29.5)
Diastolic BP (mmHg)	89.7 ( $\pm$ 11.4)	87.8 ( $\pm$ 14.2)
Baseline NIHSS scores	11.5 ( $\pm$ 3.5)	6.6 ( $\pm$ 4.3)
Mild (<8)	2 (6.9%)	15 (83.3%)
Moderate (8–14)	17 (58.6%)	2 (11.1%)
Severe ( $\geq$ 14)	10 (34.5%)	1 (5.6%)

From Figure 1, there was a critical negative connection between T3 levels and NIHSS scores among all patients ( $n = 588$ ,  $r = -0.758$ ,  $r^2 = 0.575$ , 95% Confidence Interval 0.40 to 0.75). This suggests, after intense stroke, that the lower T3 esteems are, the more terrible neurological debilitation will be.

### Discussion

Our investigation led us to a perplexing inference that albeit the result after intense ischemic stroke is better among patients with subclinical hypothyroidism, low starting ft3 level might connect to more terrible

useful result[8]. Patients with subclinical hypothyroidism (raised TSH with ordinary ft4 levels) have phenomenal useful outcomes (mRs 0-1) at 1 and 90 days after intense ischemic stroke, contrasted and euthyroid patients. Likewise, raised serum TSH levels at show were

related with better utilitarian outcomes at release and considering 90 days, and consolidated OR of relationship of TSH with practical result considering 90 days after stroke, albeit genuinely immaterial, showed a pattern toward lower mRS. High beginning TSH was related with a superior useful result, yet in addition with low severity score at affirmation and less mortality[9].

In the current study, low T3 had all the marks of being related with severe stroke and transient result; besides, there is a critical negative relationship identified between T3 levels and NIHSS scores on affirmation among all patients. The last option is an original observing which has not been accounted for somewhere else, it shows that a more terrible neurological debilitation is identified with the level of an abatement in T3 level, consequently T3 levels checking might actually fill in as a simple, fast, and plausible prognostic boundary for clinicians later on whenever affirmed by additional investigation[10, 11]. Our finding is predictable with Alevizaki et al. who expressed that low-T3 is a potential free indicator for stroke result. As in a few examinations acted in serious consideration units, intense stroke patients with low T3 or the blend of T3 and T4 gave off an impression of being related with more regrettable anticipation. Likewise, curiously the changes of T3 levels don't give off an impression of being identified with the area impacted by stroke[8, 14]. This proposes that the adjustment is more identified with an aggravation of thyroid chemical digestion rather than a blood supply irregularity instigated primary unsettling influence of the hypothalamic-pituitary-thyroid axis.

#### Conclusion

Subclinical hypothyroidism at affirmation is related with better utilitarian result, though low T3 might associate with more regrettable result in intense ischemic stroke among clinically euthyroid patients. This complicated connection justifies further examination. Regardless of whether revising thyroid profile with chemical supplementation or threat might prompt further developed outcomes require huge, all around planned forthcoming, interventional studies.

Limitations in the current review incorporate determination inclinations, little example size, single standard estimation of thyroid capacity, absence of long haul follow-up, and connections from any medications known to influence thyroid capacities which should be generally considered later on study[12]. Among the above things, the puzzling impacts from a couple of determination inclinations, for example, regardless of whether patients had accessible research center outcomes for thyroid capacity tests and whether they introduced to the medical clinic merit perusers' consideration while evaluating or utilizing these information.

Following investigations are required later on: (1) to screen over and over TSH, T3, and T4 levels at explicit occasions comparative with beginning of stir up (i.e., at beginning, first day, first week, multi month, 90 days); (2) to play out a changed examination, for example, calculated relapse and Mantel-Haenszel test to test in case T3 is to be sure an autonomous indicator alongside different elements and regardless of whether the relationship between low T3 disorder and more awful neurologic hindrance is really huge. Since there is still no convincing reply as to treatment of low T3 with regards to intense stroke, it would be additionally possible to plan a review on persuasive impact by giving appropriate thyroid chemical substitution.

#### References

1. Dhital, R., Poudel, D. R., Tachamo, N., Gyawali, B., Basnet, S., Shrestha, P., & Karmacharya, P. (2017). Ischemic stroke and impact of thyroid profile at presentation: a systematic review and meta-analysis of observational studies. *Journal of Stroke and Cerebrovascular Diseases*, 26(12), 2926-2934.
2. Go, A. S., Mozaffarian, D., Roger, V. L., Benjamin, E. J., Berry, J. D., Blaha, M. J., ... & Turner, M. B. (2014). Heart disease and

stroke statistics—2014 update: a report from the American Heart Association. *circulation*, 129(3), e28-e292.

3. Jiang, S., Xie, S., Lv, D., Wang, P., He, H., Zhang, T., ... & Chen, Y. (2017). Alteration of the gut microbiota in Chinese population with chronic kidney disease. *Scientific Reports*, 7(1), 1-10.
4. Sekhar, T. S., Appalaneni, R., Jada, A., & Pinnamaneni, S. (2018). Study of thyroid function in patients admitted in intensive care unit in a tertiary care centre. *International Journal of Research in Medical Sciences*, 6(8), 2717.
5. Bello, G., Pennisi, M. A., Montini, L., Silva, S., Maviglia, R., Cavallaro, F., ... & Antonelli, M. (2009). Nonthyroidal illness syndrome and prolonged mechanical ventilation in patients admitted to the ICU. *Chest*, 135(6), 1448-1454.
6. Kumar, K. H., Kapoor, U., Kalia, R., Chandra, N. A., Singh, P., & Nangia, R. (2013). Low triiodothyronine predicts mortality in critically ill patients. *Indian journal of endocrinology and metabolism*, 17(2), 285.
7. Ray, D. C., Macduff, A., Drummond, G. B., Wilkinson, E., Adams, B., & Beckett, G. J. (2002). Endocrine measurements in survivors and non-survivors from critical illness. *Intensive care medicine*, 28(9), 1301-1308.
8. Angelousi, A. G., Karageorgopoulos, D. E., Kapaskelis, A. M., & Falagas, M. E. (2011). Association between thyroid function tests at baseline and the outcome of patients with sepsis or septic shock: a systematic review. *European journal of endocrinology*, 164(2), 147.
9. Van Der Poll, T., Romijn, J. A., Endert, E. R. I. K., Borm, J. J., Buller, H. R., & Sauerwein, H. P. (1991). Tumor necrosis factor mimics the metabolic response to acute infection in healthy humans. *American Journal of Physiology-Endocrinology and Metabolism*, 261(4), E457-E465.
10. McIver, B., & Gorman, C. A. (1997). Euthyroid sick syndrome: an overview. *Thyroid*, 7(1), 125-132.
11. Casey, L. C., Balk, R. A., & Bone, R. C. (1993). Plasma cytokine and endotoxin levels correlate with survival in patients with the sepsis syndrome. *Annals of internal medicine*, 119(8), 771-778.
12. Neidert, S., Katan, M., Schuetz, P., Fluri, F., Ernst, A., Bingisser, R., ... & Christ-Crain, M. (2011). Anterior pituitary axis hormones and outcome in acute ischaemic stroke. *Journal of internal medicine*, 269(4), 420-432.
13. Hama, S., Kitaoka, T., Shigenobu, M., Watanabe, A., Imura, I., Seno, H., ... & Kurisu, K. (2005). Malnutrition and nonthyroidal illness syndrome after stroke. *Metabolism*, 54(6), 699-704.
14. Alevizaki, M., Synetou, M., Xynos, K., Pappa, T., & Vemmos, K. N. (2007). Low triiodothyronine: a strong predictor of outcome in acute stroke patients. *European journal of clinical investigation*, 37(8), 651-657.
15. Boltzmann, M., Schmidt, S. B., & Rollnik, J. D. (2017). Impact of thyroid hormone levels on functional outcome in neurological and neurosurgical early rehabilitation patients. *BioMed research international*, 2017.
16. Rahman, H. A., ur Rahman, M., Haque, J. A., Sharmin, S., & Saha, A. K. (2015). Low T3 Level and Prognosis of Acute Ischemic Stroke: A Comparative Analysis. *Bangladesh Journal of Nuclear Medicine*, 18(2), 145-148.
17. Zhang, Y., & Meyer, M. A. (2010). Clinical analysis on alteration of thyroid hormones in the serum of patients with acute ischemic stroke. *Stroke Research and Treatment*, 2010.

**Conflict of Interest: Nil Source of support: Nil**