International Journal of Science and Healthcare Research
Vol.9; Issue: 4; October-December 2024
Website: ijshr.com
Original Research Article *ISSN: 2455-7587*

Study of Thyroid Disorders in Patients of Stroke

Dr. A. K. Shadani[1], Dr. Anand Yadao[2], Dr. Akash Nema[3], Dr. Vigneswar T [4]

[1]Department of Medicine,
Shri Rawatpura Sarkar Institute of Medical Science and Research, Nava Raipur, India.

Corresponding Author: Dr. A. K. Shadani

DOI: https://doi.org/10.52403/ijshr.20240444

ABSTRACT

To study the prevalence of thyroid disorders among patients of ischemic stroke and to correlate it with the severity of stroke on basis of NIHSS score and functional outcome after 3 months on basis of modified Rankin Scale (mRS).[1]

Method: This hospital based descriptive, randomized, single blinded, analytical study was done in the department of Medicine, SRIMSR hospital, Raipur from September 2023 to Dec2024. A total of 82 patients above 18 years of age who had ischemic stroke were included. Every patient was subjected to detailed clinical history and neurological examination. Two neurological scores, namely NIHSS (National Institutes of Health Stroke Scale) and modified Rankin Scale (mRS) was used.

The severity distribution of NIHSS score on admission was divided into 3 categories, mild: NIHSS <8; moderate: 8-14; severe: >14. Neurological impairment and improvement were assessed using NIHSS, together with modified Rankin Scale (mRS)[1,2] from follow up OPD visits. Favorable outcome is defined as mRS≤2[3]. The first OPD follow up usually occurs 2-4 weeks after discharge from hospital and we have assessed clinically after 3 months of discharge. Basic and clinical characteristics including demographic data such as sex, age, concurrent illness, medication was collected and categorized.

We have divided patients into 5 group on the basis of serum free T3 (FT3), free T4 (FT4) and TSH; NTIS, Euthyroid, Hyperthyroid, Overt hypothyroid & Subclinical hypothyroid (SCH) [4].

Results: Among 82 patients with available laboratory data and relatively complete neurological impairment documentations met all inclusion criteria, 59 men and 23 women. Patients with subclinical hypothyroid had significantly mild neurological impairment at presentation on basis of NIHSS score (P = < .05) and have good functional outcome on follow up after 3 months on basis of mRS score.

Conclusion: On the basis of this study, it can be concluded that ischemic stroke patients with subclinical hypothyroid (SCH) at presentation has less stroke severity and these group of patients have better functional outcome at 3 months of follow up but further studies with large sample size are needed to validate our findings.

Keywords: Thyroid disorder, stroke, cerebrovascular accident, modified Rankin Scale (mRS), National Institutes of Health Stroke Scale (NIHSS)

INTRODUCTION

A stroke, or cerebrovascular accident, is defined as an abrupt onset of a neurologic deficit that is attributable to a focal vascular cause. Thus, the definition of stroke is clinical, and laboratory studies including brain imaging are used to support the diagnosis [5]. Stroke is the fifth leading cause of death and the primary cause of long-term adult disability in the United States [6]. A

stroke is a serious medical condition that requires emergency care. A stroke can cause lasting brain damage, long-term disability, or even death. Strokes can be classified into two major categories: ischemic and hemorrhagic. Ischemic strokes occurs if an artery that supplies oxygen-rich blood to the brain becomes blocked & hemorrhagic strokes occurs if an artery in the brain leaks blood or ruptures (breaks open). The pressure from the leaked blood damages brain cells [7].

Stroke is a form of acute stress and has detrimental effect on various neurophysiological pathways. Perturbations in the hypothalamus-pituitary-thyroid (HPT) axis affect stroke risk and stroke outcomes. Hypothyroidism can cause hypertension, hypercholesterolemia, cardiac dysfunction, and both hypo & hypercoagulability, all of which are risk factors for stroke [8, 9,10]. Hyperthyroidism is also associated with atrial fibrillation, which is a common cause of cardio embolic stroke [11]. Thyroid dysfunction has been associated with cerebrovascular accidents and is an area of active research in the present time. During critical illness, changes in circulating hormone levels are a common phenomenon.

These alterations are correlated with the severity of morbidity and the outcomes of patients in ICU. Thyroid hormone has an important role in regulating cellular metabolic activity and neural development. Circulating thyroid hormone levels seems to modulate the outcome of ischemic reperfusion injury [12]. A number of comorbidities have been associated with increased mortality in acute stroke patients. Hypothyroidism is a possible risk factor for stroke although there are very few studies to prove this. It is not known whether hypothyroidism (either clinical or subclinical) affects outcome in patients with acute cerebrovascular disease. The relationship between thyroid hormone and functional outcome post-stroke is complex. A neuroprotective role of hypothyroidism has been shown in acute stroke patients [13] The probable correlation between the decrease of thyroid hormones and the severity of stroke as well as the post stroke recovery needs further investigation.

AIM: To study the prevalence of thyroid disorders in patients of ischemic stroke.

OBJECTIVES: To determine the effect of deranged thyroid function on stroke severity at the time of presentation. To study effect of deranged thyroid function on functional outcome based on mRS score after 3 months. The World Health Organization (WHO) definition of stroke is: “rapidly developing clinical signs of focal or global disturbance of cerebral function, with symptoms lasting 24 hours or longer or leading to death, with no apparent cause other than of vascular origin”. Types of stroke: Stroke can either be ischemic (with or without infarction) or hemorrhagic (intracerebral or subarachnoid). stroke: Ischemic stroke results from occlusion of the cerebral arteries by an atherosclerotic thrombus or from an embolus arising from the proximal part of the arterial system or the heart. Cardiac rhythm disturbances like atrial fibrillation which results in stasis and blood clot formation, forms an important source of embolic stroke. This is to be differentiated from Transient Ischemic Attack (TIA) which resolves in less than 24 hours in spite of evidence of permanent brain injury on neuroimaging.

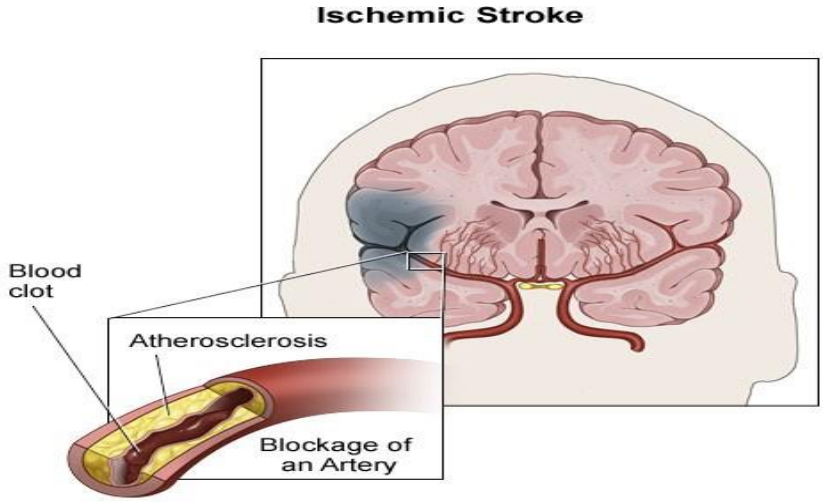

Figure 1: Atherosclerosis and acute ischemic stroke

Hemorrhagic stroke besides trauma as an etiology, spontaneous intracerebral hemorrhages are mainly due to arteriolar hypertensive disease, and rarely due to coagulation disorders and vascular malformation within the brain. **Intra parenchymal hemorrhage** due to hypertension and subarachnoid hemorrhage due to aneurysmal rupture are the two most common causes of hemorrhagic stroke. Hemorrhagic stroke either by its mass effect on the surrounding structures or by raising the intracranial pressure produces significant neurological deficit. **In intracerebral hemorrhage**, blood leaks from the vessel directly into the brain and hematoma occurs which causes mass effect on the surrounding brain and physical disruption of the nerve tissue. As the leakage gets arrested, the blood slowly disintegrates and is absorbed over a period of weeks and months.

Subarachnoid hemorrhage results from rupture of aneurysms present at the branching points of the large arteries of the circle of Willis, the blood is contained within the subarachnoid spaces and therefore, causes little focal effect on the brain. However, when there is severe bleeding it causes a delayed cerebral ischemia through a mechanism of constriction of the vessels of the circle of Willis and their primary branches (vasospasm).

The Stroke Syndrome: Stroke in its mildest form may consist of a trivial and transient neurologic disorder insufficient for the patient even to seek medical attention whilst in the most severe form the patient becomes hemiplegic or even comatose. However, the essential feature in all forms of stroke is the temporal profile of neurologic events irrespective of the grading of severity between these two extremes. The abruptness with which the neurologic deficit develops usually in a matter of seconds helps in making a diagnosis of vascular origin. **Based on Time of onset:** Most embolic strokes characteristically have a sudden onset and the deficit reaches its peak almost at once. Thrombotic strokes also have an abrupt onset, but they evolve somewhat more slowly over a period of several minutes or hours and sometimes progresses in a salutatory fashion, i.e., in a series of steps. Hypertensive cerebral hemorrhage is sudden in onset but the deficit may be either static or steadily progressive over a period of minutes or hours whilst in subarachnoid hemorrhage it is almost instantaneous.

Based on pattern of involvement: The second essential feature is the focal signature of stroke. The neurologic deficit helps in localizing the anatomical site involved and also in estimating the size of the infarct or hemorrhage. Hemiplegia stands as the classic sign of all cerebrovascular diseases, whether the lesion is restricted to the cerebral hemisphere or when it also involves the

brainstem with accompanying other diverse manifestations but in highly recognizable patterns. These include paralysis, numbness and sensory deficits on one side of the body, aphasia, visual field defects, diplopia, dizziness and dysarthria. The different patterns of involvement enable the physician to localize the lesion at times so precisely to even specify the culprit artery involved. The territory of any artery, large or small, deep or superficial, may be involved. When an infarct involves the territory of a carotid artery, unilateral signs predominate: hemiplegia, hemi anesthesia, hemianopia, aphasia, and agnosia are the common manifestations. In lesions involving the basilar artery territory, the signs of infarction are frequently bilateral and occur in association with cranial nerve palsies and other segmental brainstem and cerebellar signs; quadriparesis, hemiparesis, and unilateral or bilateral sensory impairment are present coupled with diplopia, dysarthria, ataxia, and vertigo in various combinations.

Based on sequence of resolution of neurological deficit: Excluding fatal strokes another important aspect in the temporal profile of stroke evolution is the arrest and then partial regression of the neurologic deficit in almost all cases. A focal syndrome of rapid regression that reverses itself entirely and dramatically over a period of minutes or up to an hour has been defined as the "transient ischemic attack" (TIA). Often, an extensive deficit from embolism also partially reverses itself within a few hours or days. In most cases of thrombotic strokes, improvement occurs gradually over weeks and months, and there is considerable residual disability. So a gradual downhill course over a period of several days or weeks helps in making an alternative diagnosis of non-vascular etiology. However there are exceptions, as in patients with multiple vascular occlusions and progression of a focal deficit due to brain edema developing secondary to large infarctions or hemorrhage.

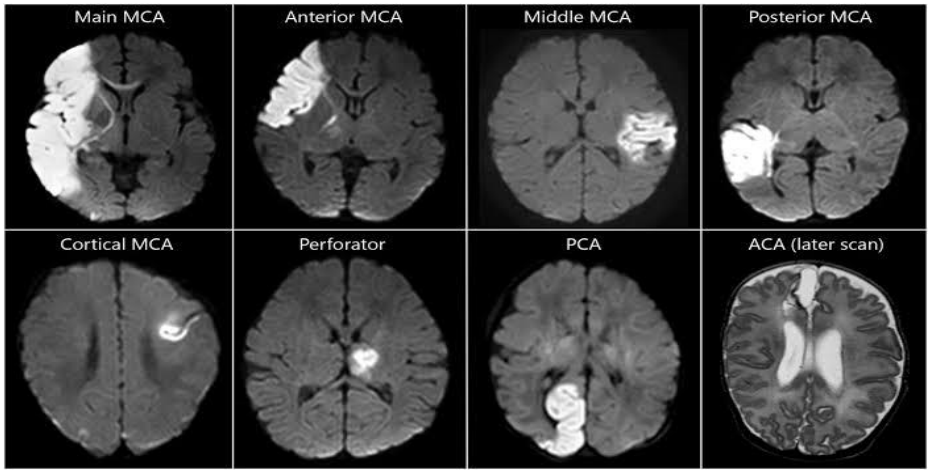

Figure 3: MRI Brain Showing Infarct

THYROID HARMONE AND CEREBROVASCULAR ACCIDENTS

Cerebrovascular Accidents (CVAs) are the leading cause of morbidity and mortality. It is a form of acute stress and has a detrimental effect on various neurophysiological pathways. Conditions such as hypertension, atherosclerosis, diabetes mellitus, and thyroid dysfunction are identified as risk factors in the etiology of stroke. It is not known till date as to what extent each one of these risk factors contribute to the pathophysiology of CVA. A number of comorbidities have been associated with increased mortality in acute stroke patients. It is not known whether hypothyroidism (either clinical or subclinical) affects outcome in patients with acute cerebrovascular disease. Subclinical hypothyroidism (SCH) is thought to have an influence on stroke outcomes. However, few reports demonstrate a favorable relationship

between the two. Although nonthyroidal illness syndrome [NTIS] is considered to be associated with adverse outcome in ICU patients, the performance of thyroid hormone levels in predicting clinical outcome in ICU patients is unimpressive. Few studies suggest addition of FT3 level to the APACHE II score could significantly improve the ability to predict ICU mortality. The nonthyroidal illness syndrome (NTIS or "euthyroid sick syndrome" or low triiodothyronine [T3] syndrome) is frequently encountered in hospitalized patients, especially those in Intensive Care Units (ICUs) and describes abnormalities in thyroid function tests in the absence of obvious thyroid disease. The most common abnormality is a decrease in T3 levels. In the presence of more severe illness, a fall in the level of thyroxin (T4) occurs while the thyroid-stimulating hormone (TSH) levels do not show the expected pituitary-thyroid axis reactivity. These changes are associated with disease severity and have been connected with poor short-term prognosis. The low-T3 syndrome is an independent predictor of early and late survival in patients with acute stroke, and predicts handicap at 1 year. Low T3 has been associated with increased short-term mortality in intensive care unit and long-term mortality
in cardiovascular disease. It is suggested that low T3 is associated with worse neurological outcome. The severity of low T3 may be a predictor of functional improvement in acute ischemic stroke. Acute cerebrovascular disorders are common causes of death and disability worldwide. Prognostication of stroke victims rests mainly on admission clinical and radiological indexes of disease severity. Preclinical studies strongly suggest that thyroid hormones have a capacity to exert neuroprotective actions in the central nervous system under ischemic conditions via genomic and nongenomic actions.

Age, male gender, blood glucose level, arterial fibrillation, dyslipidemia, smoking, NIHSS score, cardio embolic stroke type, and periventricular hyper intensities, but not FT4 or TSH, were significantly associated with poor functional outcome. Furthermore, poor functional outcome was independently associated with low FT3 (<2.29pg/mL). It was concluded that a lower FT3 value upon admission may predict a poor functional outcome in patients with acute ischemic stroke.

MATERIALS AND METHODS

STUDY POPULATION: All the newly diagnosed cases of ischemic stroke diagnosed by clinical evaluation and confirmed by Radiological investigation.

STUDY DESIGN: Hospital based Observational study.

After approval by the hospital ethics committee this study was carried out on adults above 18 years of age diagnosed with ischemic stroke. All the patients were selected randomly. A written informed consent was taken from all the patients.

SAMPLE SIZE: From previous study Pande A, Goel VK, Rastogi A, Gupta A[4]
Sample size formula by Cochran

Minimum Sample Size =**N =** $\frac{1.96^2 * p * (1-p)}{e^2}$

P = the incidence of mortality in ischemic stroke=30.67%=0.3067
1.96= z value for 5% confidence level
e= precision =10%

On calculation: = (3.8416*0.3067*0.6933)/ (0.10)2 = 82

STUDY DURATION: September 23 - Dec 24

INCLUSION CRITERIA FOR STUDY GROUP:

1) Patients who had a ischemic stroke.
2) Patients who presented to the hospital within 1 week of the event.
3) Patient above 18 years of age
4) No previous H/O thyroid disorder

EXCLUSION CRITERIA FOR STUDY GROUP:

1) Patients who presented to the hospital after 1 week of the event.
2) Patients who had head injury.
3) Patients who had tumors or central nervous system infections.

4) Patients with sepsis, renal and hepatic dysfunction.
5) Patients on drugs known to alter thyroid profile.
6) Patients with previous H/O thyroid disorder

METHODOLOGY

Patients of ischemic stroke who were admitted to SRIMSR Hospital, Raipur, were included in this study. 82 patients were studied who suffered from ischemic stroke and were admitted under Medicine department from September 2023 to December 2024.

All patients after fulfilling inclusion criteria were admitted under Medicine department, written informed consent was taken from all patients. Baseline demographic information including age, sex was recorded. Blood samples for thyroid were collected within 1 hour of admission and analyzed by Mind ray automated analyzer using dry chemistry by enzyme- linked fluorescent assay technique. The range, mean ± standard deviation (SD) of FT3, FT4, and TSH were 2.30- 4.52, 0.89- 1.76, 0.550- 4.780 respectively. Every patient was subjected to a detailed clinical history and neurological examination. Neurological score, namely, the National Institute of Health Stroke Scale (NIHSS) were used to access at the time of admission and after 3 months they were assessed by modified Rankin Scale (mRS). In each patient, a thyroid profile was done which included FT3, FT4, TSH. On the basis of thyroid profile, the patients were divided into five categories [4]:

1. NTIS/Euthyroid sick syndrome
2. Euthyroid
3. Hyperthyroid
4. Hypothyroid
5. Subclinical hypothyroid

Thyroid Disorder	**Blood Serum levels**		
	FT3	**FT4**	**TSH**
NTIS	Low	Low/Normal	Low/Normal
Euthyroid	Normal	Normal	Normal
Hyperthyroid	High/Normal	High/Normal	Low
Hypothyroid	Low/ Normal	Low	High
Subclinical Hypothyroid	Normal	Normal	High

TABLE 1: Distribution of thyroid disorders on basis of serum FT3, FT4, TSH levels

Stroke severity and functional outcome scoring system of both NIHSS and mRS respectively is shown below in table no.2, 3, 4 and 5.

National Institute of Health Stroke Scale (NIHSS)

CATEGORY	**SCORE/ DESCRIPTION**	**SCORE**
1a. Level of Consciousness (Alert, Drowsy, etc)	0 = Alert 1= Drowsy 2 = Stuporous3 =Coma	
1b. LOC Questions (Month, Age)	0 = Answers both correctly 1 =Answers one correctly 2 = Incorrect	
1c. LOC Commands (Open/ close eyes, make fist/let go)	0 = Obeys both correctly 1 = Obeys one correctly 2 = Incorrect	
2 Best Gaze (Eyes open - patient follows examiner's finger or face	0 = Normal 1 = Partial gaze palsy 2 = Forced deviation	
Visual Fields (Introduce visual stimulus/ threat to pt's visual fields Quadrants)	0 = No visual loss 1 = Partial Hemianopia 2 = Complete Hemianopia 3 = Bilateral Hemianopia	
Facial Paresis	0 = Normal 1 = Minor	

(Show teeth, raise eyebrows and squeeze eyes shut)	2 = Partial 3 = Complete	

Facial Paresis (Show teeth, raise eyebrows and squeeze eyes shut)	0 = Normal 1 = Minor 2 = Partial 3 = Complete	
5a. Motor Arm = Left 5b. Motor Arm = Right (Elevate to 90'if patient is sitting, 45' if supine)	0=No Drift 1 =drift 2 = Can't resist gravity 3 =No effort against gravity 4 =No Movement X = Untestable (Joint fusion or limb amputated	Left Right
6a. Motor Leg = Left 6b. Motor Leg = Right (Elevate Leg 30' with patient supine)	0=No Drift 1 =drift 2 = Can't resist gravity 3 =No effort against gravity 4 =No Movement X = Untestable (Joint fusion or limb amputated)	Left Right
Limp Ataxia (Finger - nose, heel down shin)	0 = No Ataxia 1 = Present in one limb 2 = Present in two limbs	
Sensory (Pin prick to face, arm, trunk and leg compare side to side)	0 = Normal 1 = Partial loss 2 = Severe loss	
Best Language (Name item, describe a picture and read sentence)	0 = No aphasia 1 = Mild to moderate aphasia 2 = Severe aphasia 3 = Mute	
Dysarthria (Evaluate speech clarity by patient and respecting listed words)	0 = Normal articulation 1= Mild to moderate slurring of words 2 = Near to unintelligible or worse X = Intubated or other physical barrier	
Extinction and Inattention (Use information from prior testing to define neglect or double stimuli testing)	0 = No neglect 1 = Partial 2 = Complete neglect	
	TOTAL SCORE	
Grading	Total Score	
Mild	<8	
Moderate	8 – 14	
Severe	> 14	

TABLE 4: Grading of stroke severity on basis of total score

Modified Rankin Scale:

The modified Rankin Scale (mRS) is a 6-point disability scale with possible scores ranging from 0 to 5. A separate category of 6 is usually added for patients who expire. The modified Rankin Scale (mRS) is the most widely used outcome measure in stroke clinical trials. Standardized interviews to obtain a mRS score are recommended at 3 months (90 days) following hospital discharge.

SCORE	DESCRIPTION
0	The patient has no symptoms at all.
1	The patient has no significant disability despite symptoms; able to carry out all usual duties and activities.
2	The patient has slight disability; unable to carry out all previous activities, but able to look after own affairs

	Without assistance.
3	The patient has moderate disability; requiring some help, but able to walk without assistance.
4	The patient has moderately severe disability; unable to walk without assistance and unable to attend to own bodily Needs without assistance.
5	The patient has severe disability; bedridden, incontinent and requiring constant nursing care and attention.
6	The patient has expired (during the hospital stay or after discharge from the hospital).

TABLE: 5[14, 15, 16]

Statistical Method

Continuous data were summarized as Mean ± SD (standard deviation) while discrete (categorical) in number and percentage.

Quantitative data were analyzed by, mean, SD, T TEST.

Qualitative data were analyzed by percentage, Chi square test, fisher Exact test. Statistical significance>0.05 is not significant<0.05 is significant<0.01 is highly significant .**Statistics software SPSS 20.0** Unpaired t-test was used for quantitative data and chi-square and Fisher's exact test was used for qualitative data analysis.

RESULTS AND OBSERVATION

Age and Sex wise distribution: In present study of 82 patients, age wise distribution of patients is shown below.

TABLE 6: Age wise distribution of patients with ischemic stroke

Age	N (%)
≤ 49 years	19(23.17%)
50-59 years	18(21.95%)
60-69 years	18(21.95%)
>70 years	27(32.92%)
Total	82(100%)

Age wise distribution of patients with ischemic stroke

In present study 19 patients (23.17 %) were under age group of 49 years, 18 patients (21.95 %) were under age group of 50-59 years, 18 patients (21.95 %) were under age group of 60-69 years and remaining 27 patients (32.92 %) were above 70 years of age group.

In present study of 82 patients, sex distribution among the patients of ischemic stroke is shown below

TABLE 7: sex distribution of ischemic stroke patients

Gender	N (%)
Male	59(71.95%)
Female	23(28.04%)
Total	82(100%)

In present study, 71.95 % patients were males and 28.04 % patients were females.

in present study of 82 patients, age & sex wise distribution and comparison is shown.

TABLE 8: Age and sex distribution among ischemic stroke patients.

Age	Gender		
	Male	Female	TOTAL
≤ 49 years	16(27.11%)	3(13.04%)	19
50-59 years	15(25.42%)	3(13.04%)	18
60-69 years	15(25.42%)	3(13.04%)	18
>70 years	13(22.03%)	14(60.86%)	27
Total	59	23	82
P VALUE	0.010		

In present study, most of the population was found to be among the age group of more than 70 years (males were 22.03 % and females were 60.86 %). Gender preponderance was seen in the occurrence of ischemic stroke among male patients below 70 years of age but in patients with age group above 70 years, females were affected more

(60.86%).In present study of 82 patients, distribution of thyroid disorders is shown below.

TABLE 9: Distribution of thyroid disorders among patients of ischemic stroke.

Thyroid Disorder	Number (%)
NTIS	45 (54.87 %)
EUTHYROID	15 (18.29 %)
SUBCLINICAL HYPOTHYROID	10 (12.19 %)
HYPERTHYROID	7 (8.53 %)
HYPOTHYROID	5 (6.09 %)
TOTAL	82 (100 %)

In present study depending upon serum free T3, free T4 and TSH levels,
Thyroid disorders were divided into **5 c**ategories namely
NTIS (Non Thyroid Illness Syndrome), Euthyroid, Subclinical Hypothyroid, Hyperthyroid and Hypothyroid. Among total number of 82 patients: NTIS was found in 54.87 % patients, Euthyroid was found in 18.29 % patients, Subclinical Hypothyroid was found in 12.19 % patients, Hyperthyroid was found in 8.53 % and hypothyroid was found in 6.09 % patients.
In present study of 82 patients, distribution of stroke severity on basis of NIHSS is shown below

TABLE 10: Distribution of stroke severity among patients of ischemic stroke.

NIHSS Score	
Stroke severity	**No. of patients**
Mild stroke	32 (39.02 %)
Moderate stroke	30 (36.58 %)
severe stroke	20 (24.39 %)
TOTAL	82 (100 %)

In present study, 39.02 % patients were having mild stroke, 36.58 % patients were having moderate stroke and 24.39 % patients were having severe stroke.
In present study of 82 patients, distribution of functional outcome after 3 months among patients of ischemic stroke on basis of mRS score is shown below

TABLE 11: Distribution of functional outcome after 3 months among patients of ischemic stroke.

Functional Outcome	Number of patients
Good (≤2)	33 (40.24 %)
Poor (≥3)	49 (59.75 %)
TOTAL	82 (100 %)

In present study, 59.75 % have poor functional outcome and 40.24% have good functional outcome on basis of mRs Score.
IN present study of 82 patients, distribution of thyroid disorder with stroke severity and comparison on basis of NIHSS score is shown below

TABLE 12: Distribution of thyroid disorder with stroke severity.

Thyroid Disorder	Mild stroke (<8)	Moderate stroke (8-14)	Severe Stroke (>14)	P value
NTIS	11 (34.37%)	21 (70%)	13 (65%)	0.12
Euthyroid	4 (12.5%)	6 (20%)	5 (25%)	0.58
Hypothyroid	4 (12.5%)	1 (3.33%)	0 (0%)	0.19
Subclinical hypothyroid	10 (31.25%)	0 (0%)	0 (0%)	0.001
Hyperthyroid	3 (9.37%)	2 (6.66%)	2 (10%)	0.66
Total	32 (100%)	30 (100%)	20 (100%)	

In present study majority 32 patients were having mild stroke. Among all thyroid disorder, patients with subclinical hypothyroidism had significant correlation with the stroke severity (P = 0.0011). In present study of 82 patients, distribution and

comparison of thyroid disorder among patients of ischemic stroke with functional outcome after 3 months on basis of modified Rankin Scale (mRS) is shown in next table

TABLE NO. 12: Distribution of thyroid disorder with functional outcome among patients of ischemic stroke.

THYROID DISORDER	modified Rankin Scale (mRS)		P value
	≤2	≥3	
NTIS	10 (30.30%)	35 (71.42%)	0.07
EUTHYROID	5 (15.15%)	10 (20.40%)	0.74
HYPOTHYROID	4 (12.12%)	1 (2.04%)	0.061
SUBCLINICAL HYPOTHYROID	10 (30.30%)	0 (0%)	0.002
HYPERTHYROID	4 (12.12%)	3 (6.12%)	0.31
TOTAL	33 (100%)	49 (100%)	

In present study, functional outcome was divided into 2 categories (good functional outcome with mRS ≤2 and poor functional outcome with mRS ≥3) and thyroid disorders was divided into 5 categories. Majority 49 (59.75%) patients had poor functional outcome and 33 (40.24%) patients had good functional outcome. Patients with subclinical hypothyroid had good functional outcome as compared to patients having other thyroid disorders and this data was statistically significant. (P = 0.002).

TABLE NO. 13: Distribution of presence or absence of diabetes and hypertension among patients of ischemic stroke.

DM	PRESENT	51 (62.19%)
	ABSENT	31(37.80%)
	TOTAL	82 (100%)
HTN	PRESENT	50 (60.97%)
	ABSENT	32 (39.02%)
	TOTAL	82 (100%)

In present study out of total 82 patients, 51 patients (62.19%) had type 2 DM and 50 patients (60.97%) had hypertension.

TABLE NO. 14: Distribution of stroke severity among patients with or without Type 2 DM.

		NIHSS				
		MILD (< 8)	**MODERATE (8-14)**	**SEVERE (>14)**	**TOTAL**	**P VALUE**
DM	PRESENT	19 (37.25%)	19 (37.25%)	13 (25.49%)	51 (100%)	
	ABSENT	12 (38.70%)	12 (38.70%)	7 (22.58%)	31 (100%)	0.95 NS

In present study, stroke severity was compared among patients with or without diabetes mellitus type 2 however it showed no correlation with the stroke severity on basis of NIHSS score and this data is statistically not significant (P = 0.95).

TABLE NO. 15: Distribution of stroke severity among patients with or without hypertension.

		NIHSS				
		MILD (< 8)	**MODERATE (8-14)**	**SEVERE (>14)**	**TOTAL**	**P VALUE**
HTN	PRESENT	21 (42%)	14 (28%)	15 (30%)	50 (100%)	
	ABSENT	11 (34.37%)	16 (50%)	5 (15.62%)	32 (100%)	0.10 NS

In present study, stroke severity was comparable in patients with or without hypertension. Patients with or without hypertension had no correlation with the stroke severity on basis of NIHSS score and this data is statistically not significant (P = 0.10).

TABLE NO. 16: Distribution of functional outcome after 3 months on basis of mRS scale among patients with or without Type 2 DM.

		MODIFIED RANKIN SCALE (mRS)			
		≤2 (GOOD)	**≥3 (POOR)**	**TOTAL**	**P VALUE**
DM	PRESENT	17 (33.33%)	34 (66.66%)	51 (100%)	
	ABSENT	16 (51.61%)	15 (48.38%)	31 (100%)	0.10 NS

In present study, diabetic patients had predominantly poor functional outcome (66.66%) but there was almost equal distribution among non-diabetic patients. However, patients with or without diabetes have no correlation with the functional outcome after 3 months on basis of mRS scale and this data is statistically not significant (P = 0.10).

Among poor functional outcome group, majority 33 patients had diabetes mellitus type 2 as compared to non-diabetic patients in which only 15 were affected.

TABLE NO. 17: Distribution of functional outcome after 3 months on basis of mRS scale among patients with or without hypertension.

		MODIFIED RANKIN SCALE (mRS)			
		≤2 (GOOD)	≥3 (POOR)	TOTAL	P VALUE
HTN	PRESENT	17 (34%)	33 (66%)	50 (100%)	0.14 NS
	ABSENT	16 (50%)	16 (50%)	32 (100%)	

In present study, hypertensive patients had predominantly poor functional outcome (66%) while there was equal distribution among non-hypertensive patients. However, patients with or without hypertension had no correlation with the functional outcome after 3 months on basis of mRS scale and this data is statistically not significant (P = 0.14). Among poor functional outcome group, majority 33 patients had hypertension as compared to non-hypertensive patients in which only 16 were affected.

DISCUSSION

Stroke is a form of acute stress and has detrimental effect on various neurophysiological pathways. Perturbations in the hypothalamus-pituitary-thyroid (HPT) axis affect stroke risk and stroke outcomes. During critical illness, changes in circulating hormone levels are a common phenomenon. Circulating thyroid hormone levels seems to modulate the outcome of ischemic reperfusion injury [12]. Thyroid dysfunction has been associated with cerebrovascular accidents and is an area of active research in the present time. This study is an endeavor to study this relationship.

Thyroid Disorder Distribution In this study, majority of patients (54.87%) had NTIS and 12% patients had subclinical hypothyroidism after stroke and these results were consistent with a study conducted by A Pande et al [4] in which out of 75, 43 patients (57.33 %) had Non-Thyroidal Illness Syndrome [NTIS], 13 patients (17.33 %) had Euthyroid, 6 patients (8 %) had hyperthyroid, 9 patients (12 %) had subclinical hypothyroid and 4 patients (5.33 %) had hypothyroid. In present study of 82 patients, 45 patients (54.87 %) had NTIS, 15 patients (18.29 %) had euthyroid, 10 patients (12.19 %) had subclinical hypothyroid, 7 patients (8.53 %) had hyperthyroid and 5 patients (6.09 %) had hypothyroid.

Thyroid disorders	A Pande et al [4]	Present Study
NTIS	43 (57.33 %)	45 (54.87 %)
Euthyroid	13 (17.33 %)	15 (18.29 %)
Hypothyroid	4 (5.33 %)	5 (6.09 %)
Subclinical hypothyroid	9 (12 %)	10 (12.19 %)
Hyperthyroid	6 (8 %)	7 (8.53 %)
TOTAL	75 (100 %)	82 (100%)

TABLE 18: Comparison among patients with different thyroid disorders

Severity of stroke at admission (NIHSS):

In this study various thyroid disorders were analyzed on admission and were compared with the stroke severity on basis of NIHSS score. It was found that among all thyroid disorders, patients with subclinical hypothyroid had significantly (P = 0.0011) milder stroke on admission as compared to patients with other thyroid disorders (NTIS, euthyroid, hypothyroid or hyperthyroid). The

above results showed that subclinical hypothyroidism have protective role in stroke severity and patients had milder neurological deficit on admission.

Functional outcome at 3 months after stroke (mRS):

In this study various thyroid disorders were analyzed and were compared with the functional outcome after 3 months on basis of mRS score. It was found that among all thyroid disorders, patients with subclinical hypothyroid had significantly better functional outcome after 3 months (P = 0.002), as compared to patients with other thyroid disorders (NTIS, euthyroid, hypothyroid or hyperthyroid). The above result showed that subclinical hypothyroidism has significant protective association of SCH with better outcomes after 3 months and lower mortality after cerebral ischemic stroke. Possible explanations for this association are ischemic preconditioning, reduced adrenergic tone, and hypo metabolic state.

Additional observations from this study:

In this study it was found that Type 2 DM and hypertension had no relation with the stroke severity on admission, however the proportion of patients in poor functional outcome group had more prevalence of T2DM and HTN as compared to those who did not had T2DM and HTN though this was statistically not significant. This was consisted with Tziomalos K et al [18] which revealed that at admission NIHSS score did not differ between patients with or without T2DM and mRS score also did not differ between the two groups. This was consisted with Kumar NSS et al [19] which revealed that Hypertension did not have positive correlation among patients with severity of stroke on basis of NIHSS and none of the risk factors studied were having independent impact on the stroke functional outcome at the follow up on basis of mRS.

Thus this study has shown that thyroid disorders are common in patients of ischemic stroke, it has also shown that cerebrovascular diseases is milder in presence of subclinical hypothyroidism.

SUMMARY AND CONCLUSION IN present study of 82 ischemic stroke patients 71.95 % were male and 28.04 % were female. & population ,23.17 % patients were under 49 years of age, 21.95 % patients were under age group of 50 – 59 years, 21.95 % patients were under age group of 60 – 69 years and 32.92 % patients were above 70 years of age.

1) In the present study of 82 ischemic stroke patients male predominance was seen in all age group except for age group above 70 years where females were more affected.
2) In patients of more than 70 years age group, males were 22.03% and females were 60.86%.
3) In present study majority 59 patients (71.95 %) were male and 23 patients (28.04 %) were female.
4) In the present study of 82 patients depending on serum free T3, serum free T4 and serum TSH levels; patients were divided into 5 categories namely – NTIS, Euthyroid, Subclinical hypothyroid, Hypothyroid and Hyperthyroid.
5) 54.87 % patients were NTIS, 18.29% patients were euthyroid, 12.19 % patients were subclinical hypothyroid, 8.53 % patients were hyperthyroid and 6.09 % patients were hypothyroid.
6) In present study of 82 patients, 32 patients (39.02 %) were having mild stroke, 30 patients (36.58 %) were having moderate stroke and 20 patients (24.39 %) were having severe stroke.
7) In present study, among all ischemic stroke patients49 (59.75 %) were having poor functional outcome and 33 (40.24 %) were having good functional outcome.
8) In present study, milder form of stroke severity on admission was seen in patients with subclinical hypothyroidism and the data was statistically significant.
9) In present study of 82 patients, patient's having subclinical hypothyroidism have

good functional outcome after 3 months of follow up on basis of modified Rankin Scale (mRS) and the data was statistically significant.

10) Out of 82 patients, there was reported death of 7 patients (8.53 %) who died at different time interval.
11) The 7 patients who died, all were having NTIS on admission.

This study conducted in SRIMSR hospital, concludes that there was a significant association of subclinical hypothyroidism and acute ischemic stroke with stroke severity and its functional outcome therefore, subclinical hypothyroidism may have a role in stroke prevention in the presence/absence of other risk factors. However, this is a single center trial study and further large cohort study will be needed to conclusively say so.

RECOMMENDATIONS:

This study is a unicentric small study, so for further assessment we need multi centric studies for confirmation of our result. Limitations in the present study include small sample size, single baseline measurement of thyroid function, lack of long-term follow-up and interactions from any drugs known to affect thyroid functions which should all be taken into account in the future study. Further studies with large number of stroke patients having hypothyroidism, euthyroidism or hyperthyroidism controlling for other known risk factors should be done to assess a wider range of thyroid values and outcome. In this study thyroid disorders were considered as an entity but individual thyroid hormone levels can also be assessed to further elucidate this relationship.

Abbreviations

NIHSS - National Institutes of Health Stroke Scale, mRS - modified Rankin Scale, OPD – Out Patient Department, FT3 – Free Triiodothyronine, FT4 – Free Tetraiodothyronine TSH – Thyroid Stimulating Harmone HPT - Hypothalamus-Pituitary-Thyroid TAAR - Receptor - Thyroglobulin IA – Transient Ischemic Attack NTIS – Non Thyroidal Illness Syndrome SCH – Subclinical Hypothyroid
ATP – Adenosine triphosphate, TRH – Thyrotropin Releasing Hormone, WHO – World health Organization, IA – Transient Ischemic Attack, VA – Cerebrovascular Accidents
ICU – Intensive Care Unit, AUC – Area Under Curve, NT- pro BNP – N-terminal pro b-type natriuretic peptide, RI – Net Reclassification Improvement, IDI – Integrated Discrimination Index, OR – Odds Ratio, WML – White Matter Lesion, CMB – Cerebral Micro bleed
CSVD – Cerebral small vessel disease, I - Confidence Interval, CRP - C - reactive protein
T2DM - Type 2 diabetes mellitus, TN – Hypertension

Declaration by Authors

Ethical Approval: Approved
Acknowledgement: Thankful to Dean SRIMSR Dr. Kundan Gedam Sir for unrestricted support and guidance.
Source of Funding: None
Conflict of Interest: The authors declare no conflict of interest.

REFERENCES

1. J. Rankin, “Cerebral vascular accidents in patients over the age of 60. II. Prognosis,” Scottish Medical Journal, vol. 2, no. 5, pp. 200–215, 1957.
2. R. Bonita and R. Beaglehole, “Modification of Rankin scale: recovery of motor function after stroke,” Stroke, vol. 19, no. 12, pp. 1497–1500, 1988.
3. O'Keefe LM, Conway SE, Czap A, Malchoff CD, Benashski S, Fortunato G, Staff I, McCullough LD. Thyroid hormones and functional outcomes after ischemic stroke. Thyroid Res. 2015 Jul 4; 8:9. Doi: 10.1186/s13044-015-0021-7. E Collection 2015. PubMed PMID: 26157487; PubMed Central PMCID: PMC4495802.
4. Pande A, Goel VK, Rastogi A, Gupta A. Department of medicine, Subharti Institute of Medical Sciences, Meerut, Uttar Pradesh, India. Thyroid dysfunction in patients of ischemic cerebrovascular accidents,

ORIGINAL ARTICLE Vol. 14, 2017. Pages 32-37, Issue: 1

5. Wade S. Smith, S. Claiborne Johnston, J. Claude Hemphill, III. Cerebrovascular Diseases. 19th edition. Part 17, Section 2, chapter 446.Harrison principles of internal medicine. Fauci, Longo, Kasper, Hauser, Jameson, Loscalzo ed New York. McGraw Hill medical publishing division 2008; p.2559.
6. Go AS, Mozaffarian D, Roger VL, et al. American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics--2014 update: a report from the American Heart Association. Circulation. 2014 Jan 21; 129(3): e28-e292.
7. www.nhlbi.nih.gov/. March 26, 2014. Archived from the original on 18 February 2015. Retrieved 26 February 2015.
8. Gao N, Zhang W, Zhang YZ, Yang Q, Chen SH. Carotid intima-media thickness in patients with subclinical hypothyroidism: a meta-analysis. Atherosclerosis.2013Mar; 227(1): 1825.doi: 10.1016/j.atherosclerosis.2012.10.070.Epub 2012 Nov 6. Review. -PubMed PMID: 23159101.
9. Iwen KA, Schröder E, Brabant G. Thyroid hormones and the metabolic syndrome. Eur Thyroid J. 2013 Jun; 2(2):83-92. Doi: 10.1159/000351249. Epub 2013 May 28. Review. PubMed PMID: 24783045; PubMed Central PMCID: PMC3821514.
10. Bai MF, Gao CY, Yang CK, Wang XP, Liu J, Qi DT, Zhang Y, Hao PY, Li MW. Effects of thyroid dysfunction on the severity of coronary artery lesions and its prognosis. J Cardiol. 2014 Dec; 64(6):496-500. doi: 10.1016/j.jjcc.2014.03.009. Epub 2014 Jun 17. PubMed PMID: 24951271.
11. Chen Q, Yan Y, Zhang L, Cheng K, Liu Y, Zhu W. Effect of hyperthyroidism on the hypercoagulable state and thromboembolic events in patients with atrial fibrillation. J Cardiol.2014; 127:17682. doi:10.1159/000356954
12. Smith JW, Evans AT, Costall B, Smythe JW. Thyroid hormones, brain function and cognition: A brief review. Neurosci Biobehav Rev 2002; 26:45-60
13. Alevizaki M, Synetou M, Xynos K, Alevizaki CC, Vemmos KN. Hypothyroidism as a protective factor in acute stroke patients. Clin Endocrinol (Oxf) 2006; 65:369-72.
14. Jenny Richardson, Diana Murray, C. Ken House, Ted Lowenkopf. "Successful Implementation of the National Institutes of Health Stroke Scale on a Stroke/Neurovascular Unit." Journal of Neuroscience Nursing, September 2006, page 310, Volume 38, Number 4 Supplement.
15. Rankin J. "Cerebral vascular accidents in patients over the age of 60." Scott Med J 1957; 2:200-15
16. Bonita R, Beaglehole R. "Modification of Rankin Scale: Recovery of motor function after stroke." Stroke 1988 Dec;19(12):1497-1500
17. Van Swieten JC, Koudstaal PJ, Visser MC, Schouten HJ, van Gijn J. "Interobserver agreement for the assessment of handicap in stroke patients." Stroke 1988;19(5):604-.
18. Konstantinos Tziomalos, Marianna Spanou, Stella D Bouziana, Maria Papadopoulou, Vasilios Giampatzis, Stavroula Kostaki, Vasiliki Dourliou, Maria Tsopozidi, Christos Savopoulos, Apostolos I Hatzitolios. Type 2 diabetes is associated with a worse functional outcome of ischemic stroke. World J Diabetes 2014 December 15; 5(6): 939-944. ISSN 1948-9358.
19. Sai Sampath Kumar Natuva, Sunanda Tirupati, Amaresh P. Reddy, Ganesh Vallampalli and Sangamithra Gandra. Independent Predictors of Severity and Functional Outcome of Acute Ischemic Stroke in Patients with Diabetes. Journal of neurology & experimental neuroscience July 12, 2016.

How to cite this article: A. K. Shadani, Anand Yadao, Akash Nema, Vigneswar T. Study of thyroid disorders in patients of stroke. *International Journal of Science & Healthcare Research.* 2024; 9(4): 383-396. DOI: *https://doi.org/10.52403/ijshr.20240444*

******