Thyroid Function Hormones Profile in Acute Stroke Patients

Thesis

Submitted for Partial Fulfillment
of Master Degree of ***Neurology***

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2020

سورة البقرة الآية: ٣٢

Acknowledgments

First and foremost, I feel always indebted to ***Allah*** *the Most Beneficent and Merciful.*

There are no words to show my appreciation for ***Prof. Dr. Hala Mahmoud El Khawas****, Professor of Neurology, Faculty of Medicine, Ain Shams University, for her enormous help, for the enduring wisdom that this work retains from his invaluable years of expertise and input. Her constructive criticism, meticulous revision, her guidance, and tremendous support that enabled me to accomplish this work.*

I am profoundly grateful to ***Dr. Shahinaz Mohamed Helmy,*** *Lecturer of Neurology, Faculty of Medicine, Ain Shams University, for being there when I needed her most, for giving me answers when I couldn't find them anywhere else, for being there every single step and for her inspiring passion for this work. Thank you for your encouragement, supervision, and continuous support.*

My most sincere appreciation goes to ***Dr. Mohamed Mohamed Tawfik*** *Lecturer of Neurology, Faculty of Medicine, Ain Shams University, for his generous help and his precious time, and for his relentless mentoring and determination to set this work straight from the beginning, his sincere effort and tolerance were inspiring.*

I would like to express my feelings of admiration, love and respect to my Family for their overwhelming support.

Nehad Elsaied Abdelmaksoud Elkhiat

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List of Abbreviations

Abb.	Full term
AF	*Atrial Fibrillation*
AIS	*Acute Ischemic Stroke*
BMI	*Body mass index*
CBC	*Complete blood count*
CHD	*Coronary heart Disease*
CT	*Computed tomography*
CV	*Cerebrovascular or cardiovascular*
D2	*Deiodinase 2*
DM	*Diabetes Mellitus*
ECG	*Electrocardiogram*
ECHO	*Echocardiography*
ER	*Emergency room*
ESS	*Euthyroid sick syndrome*
HPT axis	*Hypothalamic–pituitary–thyroid axis*
HTN	*Hypertension*
IHD	*Ischemic Heart Disease*
MRI	*Magnetic Resonance Imaging*
mRS	*Modified Rankin Scale*
NIHSS	*National Institutes of Health Stroke Scale*
NTIS	*Non thyroidal illness syndrome*
PG	*Pitutary gland*
SBSS	*Statistical package for social science*
SD	*Standard deviation*

List of Abbreviations cont...

Abb.	Full term
T3	*Triiodothyronine*
T4	*Tetraiodothyronine*
THRs	*Thyroid hormones receptors*
THs	*Thyroid hormones*
TOAST	*Trial of Org 10172 in Acute Stroke Treatment*
TRH	*Thyrotropin releasing hormone*
TSH	*Thyroid stimulating hormone*

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INTRODUCTION

Cerebrovascular stroke is defined by The World Health Organization as "rapidly developing clinical signs of focal (at times global) disturbance of cerebral function, lasting for more than 24 hours or leading to death, with no apparent cause other than of vascular origin" ***(Mozaffarian et al., 2015).*** Stroke is considered the third common cause of mortality worldwide and a major cause of long-term disability ***(Al-Mahdawi et al., 2013)***.

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 cerebro-vascular stroke ***(Pande et al., 2017).***

Disorders of thyroid gland may include: hyperthyroidism, hypothyroidism (whether overt or in subclinical form) and euthyroid sick syndrome. Euthyroid sick syndrome can be described as abnormal findings in thyroid function tests that occur in the setting of a non-thyroidal. Alterations in thyroid function test findings may reflect changes in production of thyroid hormones by effects on the thyroid itself, on the hypothalamic-pituitary-thyroid axis, or on peripheral tissue

metabolism of the hormones, or by a combination of these effects ***(Al-Mahdawi et al., 2013).***

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, also hyperthyroidism is associated with atrial fibrillation, which is a common cause of cardio embolic stroke ***(Gao et al., 2012).***

The relationship between thyroid hormones and functional outcomes post-stroke is complex. Current data has shown that low T3 levels immediately following acute ischemic stroke (AIS) are associated with greater stroke severity and mortality, and poorer functional outcomes. This is also true in critically ill hospitalized patients who have non-thyroidal illness syndrome (NTIS; or 'euthyroid sick syndrome'), where T3 levels are low, but TSH is normal, NTIS patients have poorer short-term prognosis and higher mortality rates at 12 months compared to non-NTIS patients However, data regarding the association between thyroid hormones level and functional outcomes after stroke are conflicting ***(Q'keefe et al., 2015).***

This study is going to examine the association between thyroid hormones level (T3, T4, and TSH) and cerebrovascular stroke severity and outcomes.

AIM OF THE WORK

The objective of this study is to examine the association between serum thyroid hormones levels (T3, T4, TSH) and neurological and functional outcomes in patients with acute cerebrovascular ischemic stroke.

Chapter 1

NEUROENDOCRINE PRINCIPLES OF THYROID FUNCTIONS

The thyroid, one of the largest endocrine glands, is comprised of two types of hormone-producing cells; the predominant follicular cell, which produces thyroxine (T4; tetraiodothyronine, containing four iodine atoms) and triiodothyronine (T3; containing three iodine atoms), and the neuroendocrine parafollicular or C cell, which secretes calcitonin. The secretion of T4 and T3 is controlled by the hypothalamic–pituitary system, whereas calcitonin, primarily involved in calcium regulation, is released in response to hypercalcemia ***(Larsen et al., 2008).***

The thyroid gland synthesizes both T4 and T3 in a relative ratio of approximately 17:1, with a daily production of T4 and T3 being around 100 and 6 mcg, respectively. T4 acts as a prohormone that is converted to the biologically active T3 by deiodinase enzymes in target cells. The half-life of T4 is approximately 5–7 days and that of T3 is 1 day; about 80% of the T3 comes from the extra-thyroid conversion of T4 to T3 ***(Larsen et al., 2008).***

The synthesis of T4 and T3 is dependent upon the availability of iodine, which is actively transported into the thyroid follicular cells, where it is oxidized and attached to the

tyrosine molecule. This process is called organification. Coupling of two diiodotyrosine residues produces T4, whereas T3 is formed by coupling of one dioiodotyrosine and one monoiodotyrosine. Most of the circulating T4 and T3 are bound to various proteins including thyroidbinding globulin (TBG), pre-albumin, albumin and transthyretin. The free hormones, in equilibrium with the bound hormones, constitute about 0.02% of the total T4 and 0.3% of the total T3 ***(Larsen et al., 2008).***

Thyroid hormones (THs) exert multiple effects on most cells throughout the body, influencing basal metabolic and respiration rates, cardiovascular function, oxygen consumption, carbohydrate and protein metabolism, thermogenesis and sodium pump activity, and provide negative feedback regulation of thyrotropin releasing hormone (TRH) and thyroid stimulating hormone (TSH; also called thyrotropin) secretion. THs also regulate critical aspects of growth and differentiation, stimulating maturation of the brain, skeleton, heart and lungs during prenatal and early postnatal development ***(Jabbar et al., 2017).***

Neuroendocrine pathways:

The proper function of the pituitary gland (PG) is regulated by the hypothalamus releasing trophic factors that modulate cell proliferation, hormone synthesis, and secretion. The hypothalamic–pituitary axis represents a complex organization of interactions between the hypothalamus and