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Thyroid Dysfunction Relation to Morbidity and Mortality in Critically ill Patients

An Essay
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Ahmed Mohamed

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List of Abbreviations

Abb.	Full term
ACS	Acute Coronary Syndrome
AF	Atrial Fibrillation
AIDS	Acquired Immune Deficiency Syndrome
anti-TPO	Anti-Thyroid Peroxidase
APACHE II	Acute Physiology And Chronic Health Evaluation II
ARDS	Acute Respiratory Distress Syndrome
ARF	Acute renal failure
CAD	Coronary Artery Disease
CKD	Chronic Kidney Disease
CRP	C- Reactive Protein
D1	Type 1 deiodinase
D2	Type 2 deiodinase
D3	Type 3 deiodinase
DIT	Di-Iodothyronine
ESS	Euthyroid sickness syndrome
FT3	Free Triiodothyronine
FT4	Free Thyroxine
FTI	Free Thyroxine Index
GCS	Glascow Coma Score
GFR	Glomerular Filtration Rate
GH	Growth hormone
GHPR-2	Growth hormone releasing peptide-2
HF	Heart Failure
ICU	Intensive care unit
IGF	Insulin Growth Factor
IL	Interlukin
KDa	Kilodalton
L-T4	L-thyroxine
MIT	Mono-Iodothyronine
MV	Mechanical ventilation
NTIS	Non-Thyroidal Illness Syndrome
NYHA	New York Heart Associan
rT3	Reverse Triiodothyronine
SREAT	Steroid responsive encephalopathy associated with autoimmune thyroiditis

Abb.	Full term
T3	Triiodothyronine
T2	Diiodothyronine
T4	Thyroxine
TBG	Thyroid Binding Globulin
TBPA	Thyroxine-Binding Prealbumin
Tg	Thyroglobulin
TH	Thyroid Hormone
THBR	Thyroid Hormone Binding Ratio
TNF	Tumor Necrosis Factor
TRH	Thyrotropin-Releasing Hormone
TSH	Thyroid Stimulating Hormone
TT3	Total Triiodothyronine
TT4	Total Thyroxine
TTR	Transthyretin
US	Ultrasonography

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Introduction

During critical illness, changes in circulating hormonal levels are a common phenomenon. These alterations are correlated with the severity and outcome of patients in intensive care unit (ICU). Thyroid hormone plays a key role in the maintenance of the body growth modulating metabolism and the immune system ***(Marx et al., 2003).***

Patients suffering from critical illnesses who require treatment in the intensive care unit (ICU) uniformly present with alterations in circulating thyroid hormone levels that are referred to with several names such as "nonthyroidal illness syndrome," "sick euthyroid syndrome," or "low T3 syndrome" The most typical alterations are low plasma concentrations of triiodothyronine (T3), low or normal plasma concentrations of thyroxine (T4), or elevated plasma rT3 in the presence of normal thyrotropin (TSH). Together, these changes differ from those in primary and secondary thyroid disorders, which explains the name "nonthyroidal illness" (NTI). The normal TSH level in the presence of the low plasma T3 and at times also T4 concentrations has been interpreted as indicating a

"euthyroid" status, hence the name "sick euthyroid syndrome" ***(Boelen et al., 2011).***

Subsequent studies confirmed the association between NTIS and adverse outcome in patients with sepsis, multiple trauma, acute respiratory distress syndrome, respiratory failure and mechanically ventilated patients, as well as in unselected ICU patients ***(Angelousi et al., 2011).***

Some studies demonstrated the free triiodothyronine levels in nonsurvivors was significantly lower as compared with survivors while other studies shown that there was no association between FT3 levels and outcome of ICU patients ***(Ray et al., 2002).***

Patients with low or undetectable TSH levels have increased morbidity and mortality. Some authors have reported a relationship between hypothyroxinemia and mortality in seriously ill patients with sepsis.More so, it has been suggested that primary hypothyroidism affects respiration by causing abnormalities in the respiratory system; however, the mechanism underlying the need for mechanical ventilation (MV) in patients with ESS is unclear ***(Chinga-Alayo et al., 2005).***

APACHE II score and C-reactive protein (CRP) have been shown as independent predictors of ICU mortality. Whether thyroid hormonal indicators can predict ICU mortality independently of the both predictors is unclear. The performances of these variables to predict ICU mortality have not yet been compared ***(Wang et al., 2012).***

Aim of the Work

The aim of the study was to highlight the relation between thyroid dysfunction and morbidity and mortality in critically ill patients.

Chapter (I)

Thyroid Gland Physiology

The thyroid gland weighs about 10 to 20 grams in normal adults. Thyroid volume measured by ultrasonography (US) is slightly greater in men than women, increases with age and body weight, and decreases with increasing iodine intake ***(Maciel, 2015).***

The normal thyroid gland is immediately caudal to the larynx and encircles the anterolateral portion of the trachea **(fig 1-1)**. The thyroid gland borders are the trachea and esophagus medially and the carotid sheath laterally. The sternocleidomastoid muscle and the three strap muscles (sternohyoid, sternothyroid, and the superior belly of the omohyoid) border the thyroid gland anteriorly and laterally. There are many anatomic variations in thyroid gland shape and extent ***(Mahadevan & Crinnon, 2015).***

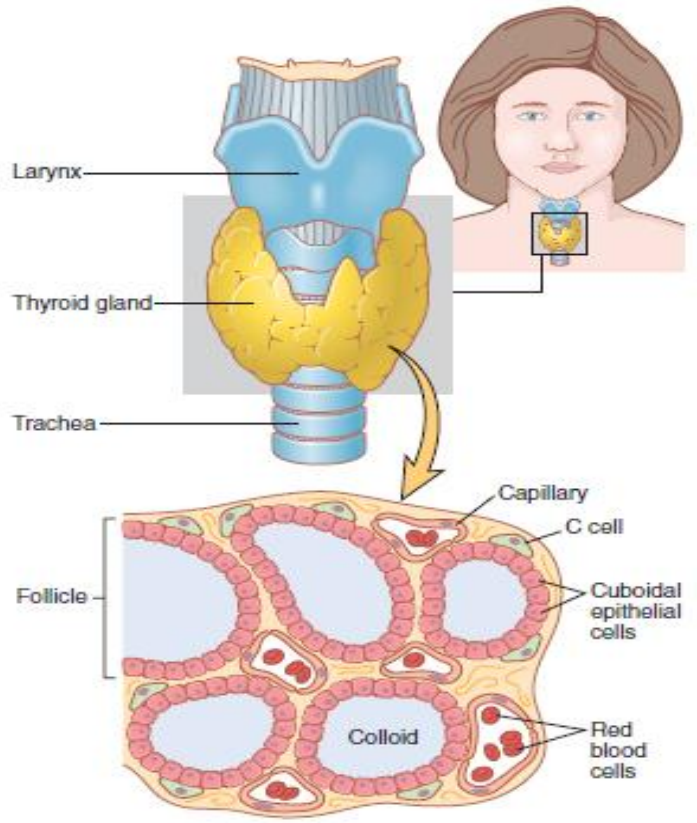

Figure (1-1): Showing anatomy and microscopic appearance of the thyroid gland ***(Bianco, 2016).***

Synthesis and Secretion of the Thyroid Metabolic Hormones:

About 93 % of the metabolically active hormones secreted by the thyroid gland are thyroxin, and 7 % triiodothyronine. However, almost all the thyroxine is eventually converted to triiodothyronine in the tissues, so that both are functionally important. The functions of these two hormones are qualitatively the same, but they differ in

rapidity and intensity of action. Triiodothyronine is about four times as potent as thyroxine, but it is present in the blood in much smaller quantities and persists for a much shorter time than does thyroxine ***(Bianco, 2016).***

Formation of thyroid hormones:

Biosynthesis of thyroid hormone is unique among endocrine glands because final assembly occurs extracellularly in the follicular lumen. The source of thyroid hormones (T4 and T3) is thyroglobulin (Tg), an iodo-protein produced by thyroid follicular cells. Thyroglobulin is the major portion of intraluminal colloid and is the most important protein of the thyroid gland ***(Dev et al., 2016).***

Iodide Pump (Iodide Trapping):

To form normal quantities of thyroxine, about 50 milligrams of ingested iodine in the form of iodides are required each year, or about 1 mg/week. The first stage in the formation of thyroid hormones is transport of iodides from the blood into the thyroid glandular cells and follicles **(fig 1-2)**. The basal membrane of the thyroid cell has the specific ability to pump the iodide actively to the interior of the cell. This is called iodide trapping ***(Miot et al., 2015).***

In a normal gland, the iodide pump concentrates the iodide to about 30 times its concentration in the blood. When the thyroid gland becomes maximally active, this concentration ratio can rise to as high as 250 times. The rate of iodide trapping by the thyroid is influenced by several factors, the most important being the concentration of Thyroid stimulating hormone (TSH***) (Huang et al., 2016).***

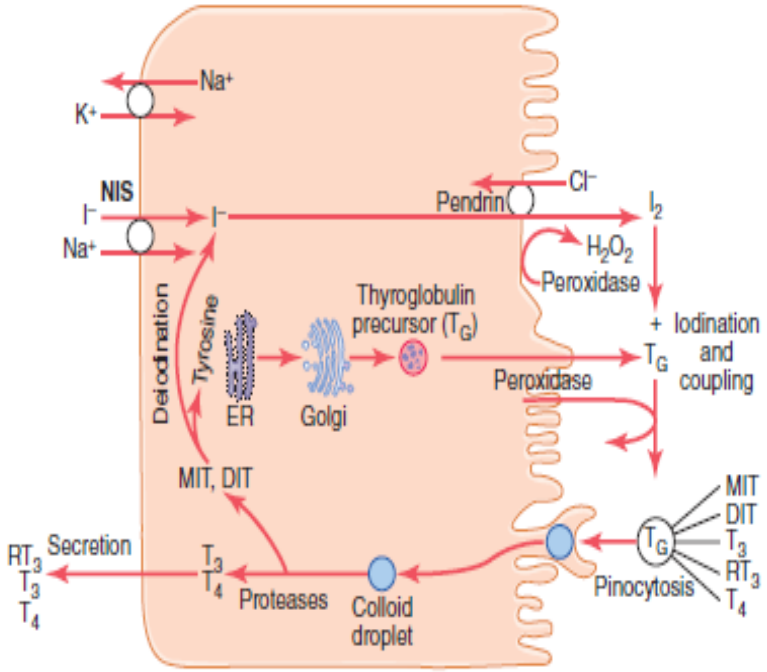

Figure (1-2): Showing Thyroid cellular mechanisms for iodine transport, thyroxine and triiodothyronine formation, and thyroxine and triiodothyronine release into the blood, **DIT** diiodotyrosine, **ER**, endoplasmic reticulum **I-**, iodide ion; **I2**, iodine **MIT**; monoiodotyrosine, **NIS**; sodium iodide-syrnporter; **RT3**, reverse triiodothyronine, **T3**; triiodothyronine. **T4**; thyroxine; **TG**, thyroglobulin ***(Bianco, 2016).***