

# Role of Tau Protein and Some Other Biochemical Parameters in Hypothyroidism Patients

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## Abstract

Hypothyroidism (HPT) is a disorder of the thyroid that is commonly prevalent in males and females worldwide. Women are more likely to develop HPT than men. In HPT, the thyroid gland cannot compete with the requirement of the body for thyroxine (T4) and triiodothyronine (T3), even when the gland is stimulated with a high amount of thyroid-stimulating hormone (TSH). HPT is linked widely with obesity in males and females. Tau protein is a peptide found mainly in the central nervous system (CNS) and linked to the pathophysiology of neurodegenerative diseases. In our research, tau protein was investigated in the pathophysiology of HPT on three levels that include age, body mass index (BMI), and gender comparisons to specify the influence of hypothyroidism and these variables on the expression of tau protein and identify the risks of hypothyroidism on the CNS. The results have shown a significant ( $P < 0.05$ ) increase in tau protein level in HPT patients compared to people with normal thyroid function. Nevertheless, obesity, age or gender did not show any significant influence on the level of tau protein in HPT patients and control. Tau protein has shown excellent sensitivity in the prognosis of HPT. In conclusion, tau protein was observed to be elevated in the HPT patients of this study. This suggests an important role of HPT in the pathophysiology of neurodegenerative diseases.

**Keywords:** hypothyroidism, TSH, tau protein, obesity.

## 1. Introduction

Hypothyroidism (HPT) is a disorder in the thyroid gland involved in reduced levels of the thyroid hormones thyroxine (T4) and triiodothyronine (T3) [1]. Generally, in HPT thyroid cannot compete with the requirements of the body for T4 and T3 hormones [2], and can be distinguished into two types; overt HPT [3] and subclinical HPT [4]. The subclinical type indicate a normal function of the thyroid gland but upon increased stimulation by thyroid stimulating hormone (TSH), while the overt type indicate that the thyroid cannot synthesize sufficient amounts of T3 and T4 even at high levels of TSH [5]. The prevalence of HPT is in quite rates with increasing statistics in both men and women [6]. Nevertheless, women are more likely to have HPT than men [7].

Obesity and HPT are two common clinical conditions that have been linked together closely [8]. The link has become more relevant in the context of an unprecedented rise in the prevalence of obesity worldwide. Obesity is generally regarded by patients as being secondary to thyroid dysfunction [9]. HPT is associated with decreased thermogenesis, decreased metabolic rate, and has also been shown to correlate with a higher body mass index (BMI) and a higher prevalence of obesity [10]. There is clinical evidence suggesting that even mild thyroid dysfunction in the form of subclinical hypothyroidism is linked to significant changes in body weight and represents a risk factor for overweight and obesity [11-13].

Tau protein is a biomolecule discovered in the seventies of the past century and related, mainly, to the health of the central nervous system (CNS) [14].

More than six isoforms of tau protein were identified to perform an important role in the CNS [15]. As it is predominant in the CNS parts, tau protein has been observed to be elevated in several neurological disorders, especially, in individuals with Alzheimer's disease [16, 17]. Nevertheless, tau protein research on topics that are far from the CNS was not investigated intensively. We have aimed to evaluate the level of tau protein in hypothyroidism patients on three levels that include age, BMI and gender comparisons to specify the influence of hypothyroidism and these variables on the expression of tau protein and identify the risks of hypothyroidism on the CNS. Aim of this work: To understand the role of Tau protein in hypothyroidism patients.

## 2. Materials and Methods

### 2.1. Subjects

A hundred and twenty blood samples were drawn and collected from the laboratories of Hospitals of Medicine City (educational laboratories), laboratories of Baghdad Teaching Hospital and laboratories of Al-Numan Teaching Hospital in the province of Baghdad for the period (October 2021 to February 2022). 60 individuals were diagnosed with HPT, while the other 60 people were healthy to control the study. Each of the two groups were subdivided into obese and slim participants equally.

### 2.2. Methods

Everyone was informed and accepted in written application to be involved in the study. The vein blood was collected and separated (1500 xg for 10 min) to obtain the serum. Once the subjects were completed to the limit count, the serum was used to

analyze the level of tau protein by using enzyme-linked immune sorbent assay (ELISA) kit from Sunlong (China) which was based on sandwich technology. Also, the levels of TSH, T3, and T4 were analyzed for each participant by using Biomerieux kits (France) in Vidas analyzer. The obtained data were analyzed statistically for mean comparison and receiver operating characteristics (ROC).

### 3. Results

The results are expressed in mean and standard deviation (SD). The age of the participants was ranged from 21 to 65 years old. In Table 1, the results

of the assessed biochemical parameters are demonstrated in obese and slim subjects. It was observed that the level of tau protein was increased significantly ( $P < 0.05$ ) in slim and obese patients compared to the corresponding category of healthy control. Also, the level of TSH was increased significantly in obese and slim HPT patients compared to the corresponding category of healthy control, but the levels of T3 and T4 were reduced significantly. Additionally, TSH level was increased significantly in obese HPT patients compared to slim HPT patients, while T3 level was reduced significantly in obese HPT patients compared to slim HPT patients.

**Table 1. The levels of tau protein and thyroid hormones in participants based on their BMI.**

Parameter	HPT		Control	
	Obese, N=30	Slim, N=30	Obese, N=30	Slim, N=30
Tau protein (pg/mL)	56.64±5.98	54.39±4.93	22.973±2.0 <sup>a</sup>	21.07±2.84 <sub>b</sub>
TSH (mIU/mL)	48.212±3.16	9.51±1.093 *	1.86 ±0.204 <sup>a</sup>	1.96±0.076 <sub>b</sub>
T3 (nmol/L)	0.982±0.074	1.304±0.179 *	1.688±0.120 <sup>a</sup>	1.735±0.042 <sub>b</sub>
T4 (nmol/L)	58.310±4.85	65.016±4.42	94.911±5.8 <sup>a</sup>	97.509±8.7 <sub>b</sub>

\* Significant between obese and slim HPT, # significant between obese and slim control, <sup>a</sup> significant between obese HPT and obese control, <sub>b</sub> significant between slim HPT and slim control.

In Table 2, the level of tau protein was observed to be significantly ( $P < 0.05$ ) increased in female and male HPT patients compared to the corresponding category of healthy control. Also, TSH level was increased significantly in female and male HPT patients compared to the corresponding category of

healthy control, while T4 level was reduced significantly. Nevertheless, T3 level did not changed significantly between female or male HPT patients compared to the corresponding category of healthy control. Additionally, TSH level was significantly higher in female HPT category compared to male HPT category.

**Table 2. The levels of tau protein and thyroid hormones in participants based on their gender.**

Parameter	HPT		Control	
	Female, N=32	Male, N=28	Female, N=30	Male, N=30
Tau protein (pg/mL)	55.8087±5.58	53.6602±5.30	22.7135±2.36 <sup>a</sup>	20.2736±2.32 <sup>a</sup>
TSH (mIU/mL)	46.26±4.04 *	33.39±3.01	1.898±0.05 <sup>a</sup>	2.022±0.11 <sup>b</sup>
T3 (nmol/L)	1.142±0.19	1.143±0.12	1.715±0.31	1.687±0.20
T4 (nmol/L)	61.880±6.2	61.112±4.1	96.42±9.7 <sup>a</sup>	94.83±5.1 <sup>b</sup>

\* Significant between male and female HPT, # significant between male and female control, <sup>a</sup> significant between female HPT and female control, <sup>b</sup> significant between male HPT and male control.

In Table 3, the patients and the control were divided into two categories based on their age, which were A (21-40 years old), and B (41-65 years old). The level of tau protein was increased significantly in A and B categories of HPT patients compared to the corresponding categories of healthy control. Also, TSH level was increased significantly in A and B categories of HPT patients compared to the

corresponding category of healthy control, while T4 level was reduced significantly. Nevertheless, T3 level did not changed significantly between A or B categories of HPT patients compared to the corresponding category of healthy control. Additionally, TSH level was significantly higher in B category of HPT patients compared to A category of HPT patients.

**Table 3. The levels of tau protein and thyroid hormones in participants based on their age.**

Parameter	HPT		Control	
	B, N=34	A, N=26	B, N=32	A, N=28
Tau protein (pg/mL)	56.0±5.65	54.88±5.47	21.76±2.77 <sup>a</sup>	22.31±2.53 <sup>b</sup>
TSH (mIU/mL)	52.429±3.225	33.744±2.91 *	1.758±0.40 <sup>a</sup>	2.0347±0.35 <sup>b</sup>
T3 (nmol/L)	1.156±0.2133	1.127±0.26	1.783±0.09	1.656±0.173
T4 (nmol/L)	60.943±5.76	62.29±4.62	93.72±8.9 <sup>a</sup>	98.10±9.24 <sup>b</sup>

\* Significant between B and A HPT, # significant between B and A control, <sup>a</sup> significant between B HPT and B control, <sup>b</sup> significant between A HPT and A control.

The ROC curves were used to compare the performance of the biochemical diagnostic methods of disease in our study and to determine the appropriate cut-off "or criterion" values for the different markers. Sensitivity, specificity and area under the curve (AUC) are commonly used as a summary measure of diagnostic accuracy.

Table 4 and Figures 1, 2, and 3 show the criteria of

diagnosis validity (sensitivity, specificity, criterion and Accuracy tests) of TAU level in patients groups compared with the control group. The optimal cut-off value for TAU in all groups is estimated from ROC curves, according to these results, the test is positive if the test > threshold value (criterion values). These results indicated that the TAU is closely related to hypothyroidism and obesity increases this association.

Table 4. Predictive values of serum tau level.

Groups	Sensitivity	Specificity	Criterion	AUC
Control/ Patients	100%	100%	>29.9	1.000
Slim/ Obese (Control)	74.1%	3.7%	>17	0.503
Slim/ Obese (patients)	73.3%	86.7%	>58.9	0.818

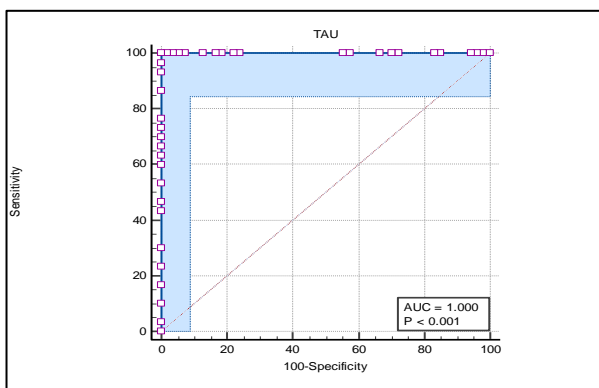


Figure 1. The ROC curve of tau protein in patients with respect to control.

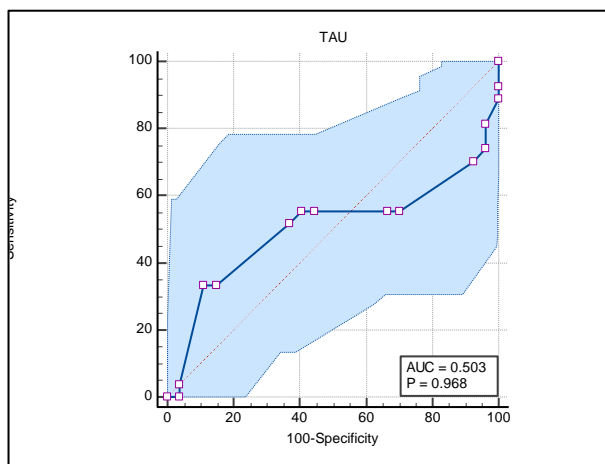


Figure 2. The ROC curve of tau protein in healthy obese with respect to slim control.

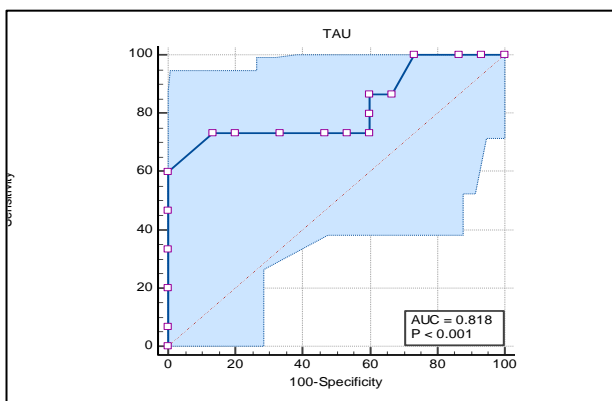


Figure 3. The ROC curve of Tau protein in hypothyroidism obese with respect to slim hypothyroidism patients.

## 4. Discussion

In HPT the thyroid gland cannot compete with the requirement of the body for its metabolism regulatory hormone T3 and its pre-hormone T4 [18]. In this study, overt HPT was observed in the patients from the results of TSH, and T4. Tau protein was significantly elevated in HPT patients compared to people with normal thyroid function. The increase was observed to give very excellent sensitivity in the prognosis of HPT with respect to control (Figure 1). On similar topic, Li et al. have indicated significant increase of tau protein level in patients with hyperthyroidism and it was significantly linked with the low level of serum TSH level of these patients [19]. This was exactly contradicting with our findings, in which hyperthyroidism in Li et al. study have shown major influence on the level of tau protein, which reveals that when the thyroid is extremely function, the risk of neurological disorders will be increased. Nevertheless, it may be attributed to the imbalance of the thyroid gland which can cause overexpression of tau protein at extreme high or low thyroid function. In Kim et al. study, the odd ratios of the prevalence of hypothyroidism and hyperthyroidism in patients with Alzheimer's disease was comparable and both were significantly prevalent [20]. Since tau protein is a key participant in the amyloid diseases [21], we suggest that the imbalance of thyroid function can cause significant influence on the expression of tau protein, especially, in HPT which was seen in the subjects of the present study. A previous review documented by Nomoto et al. have shown that impaired thyroid function is quite related to the presence of neurological disorders, including Alzheimer's disease [22]. Furthermore, the results have shown that obesity, gender, or age did not show any influence on the level of tau protein in HPT patients and in healthy people.

## 5. Conclusion

Tau protein was observed to be elevated in the HPT patients of this study. This suggests an important role of HPT in the pathophysiology of neurodegenerative diseases. Moreover, obesity and age did not show significant change of tau protein in HPT patients and

in people with normal thyroid function. Also, despite the greater prevalence of HPT in females, tau protein differences were not significant between males and females. Further investigations on the link between thyroid function and tau protein are required on larger population of study.

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