

Study on The Relationship between Thyroid Function and Frailty in Elderly

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ABSTRACT

Background: Frailty arises from the "physiologic triad" of sarcopenia, immune and neuroendocrine dysregulation. With aging, serum levels of thyroid hormones show marked changes.

Objectives: To study the circulating thyroid hormones (TSH, FT3, and FT4) and determine the relationship between circulating thyroid hormones and frailty in the Elderly.

Methods: This cross-sectional observational descriptive study included 50 subjects who were attending the outpatient geriatric clinic and geriatric unit at Alexandria Main University Hospital and were divided into; group A: 30 frail subjects aged ≥ 65 years (case group) and group B: 20 healthy subjects aged < 65 years (control group) during the period from March till October 2019. Frailty assessment was done using Frail Questionnaire as well as thyroid function tests (TSH, FT3, and FT4) and other routine laboratory investigations. Anthropometric measurements were taken, including weight, height, and BMI (body mass index).

Results: No statistically significant variation between the studied candidates as regards gender ($p=0.729$), BMI ($p=0.144$), or TSH levels ($p=0.401$) but T3 and T4 were significantly lower in group A. with noting of weak non-significance positive results parallel between age and TSH levels ($r=0.150$, $p=0.298$), high significant moderate negative correspondence in-between age and serum FT3 levels ($r=-0.530$, $p<0.001$) and non-significant weak negative correlation between age and FT4 ($r=-0.246$, $p=0.085$). TSH levels in group A were: (3.3%) low, (66.7%) normal, (30%) high. Level of FT3 was: (46.7%) low, and (53.3%) normal while FT4 level was: (26.7%) low, (66.7%) normal and (6.7%) high.

Conclusion: Aging and frailty are associated with changes in thyroid functions in the form of significantly decreased hormonal levels including FT3 and FT4, with a non-significant change in TSH levels.

Keywords: Elderly, Frailty, Thyroid function.

INTRODUCTION

Frailty is a common syndrome of the elderly with a high-risk decrease in general health and different body functions ^[1].

The concentration of triiodothyronine (T3) in the blood decreases as people become older. ^[2]

More than the two-fold increased risk for frailty in the elderly with high TSH levels suggests that the loss of thyroid function is associated with frailty. FT3, but not FT4, was significantly correlated with frailty ^[3].

Lower values of FT3 lead to greater severity of comorbidity and disability ^[4].

The purpose of the research was to look at the blood levels of thyroid gland hormones (TSH, FT3, FT4) and see whether there was a link between thyroid hormone levels and frailty in the elderly.

METHODS

This cross-sectional observational descriptive study included 50 subjects divided into two groups; group A included 30 elderly subjects aged ≥ 65 years living with frailty (cases group) attending the outpatient geriatric clinic and geriatric unit at Alexandria Main University Hospital throughout the dated time from March 2019 till October 2019 and group B included 20 healthy subjects < 65 years (control group).

The exclusion criteria included; thyroid dysfunction, patients on steroid therapy, presence of metabolic diseases, and muscle diseases. All individuals

included in this study were recruited after obtaining informed consent.

Thorough history taking, and complete general and local thyroid examination were performed for all subjects.

Laboratory investigations were done for all the subjects including:

- a. Routine laboratory examination (complete blood count, blood urea, serum creatinine, liver enzymes including ALT and AST).
- b. Thyroid function (TSH, FT3, and FT4).

Venous blood samples were taken using normal aseptic techniques and transferred to gel separator tubes. All samples were analyzed the same day they were collected. The study eliminated samples that were extensively haemolyzed.

Thyroid-stimulating hormone was measured by using The TSH EIA test. *Free tri-iodothyronine (fT3)* was measured using Competitive Enzyme Immunoassay Analog. *Free thyroxine (fT4)* was measured using the Standard strategy.

Anthropometric measures including the weight per Kg, the height per Cm, and body mass index (BMI) were considered for all candidates for the research and frailty assessment by using FRAIL Questionnaire. The FRAIL scale includes 5 components; Fatigue, Resistance, Ambulation, Illness, and Loss of weight. Frail scale scores range from 0–5 (i.e., 1 point for each component; 0=best to 5=worst) and represent frail (3–5), pre-frail (1–2), and robust (0) health status (14).

Statistical analysis

IBM SPSS statistics (Statistical Package for Social Sciences) software version 21.0, IBM Corp., Chicago, USA, 2013 and Microsoft Office Excel 2007. A computer program was designed for accounting the sample size, after checking for normality using the Kolmogorov-Smirnov and Shapiro-Wilk tests, baseline characteristics of the study population were provided as frequencies and percentages (percent) or mean values and standard deviations (SD) or median and interquartile range (range).

The Chi-Square test (also known as Fisher's exact test) was developed to compare two qualitative groups. The Independent-Samples t-test and the Mann-Whitney U test were used to compare two sets of parametric and nonparametric quantitative data. All tests are considered significant if the P-value is < 0.05.

Ethical considerations

The Ethics Board by Alexandria University authorized the study, and each participant signed an informed written permission form. This work was done in agreement with the Ethics of the World Medical Association's Program (Helsinki's Declaration).

RESULTS

According to the specified components for all candidates, the difference was non-significant between the two groups, whereas group A included 15 men (50%) and 15 females (50%) while group B had 9 males (45%) and 11 females (55%) (p= 0.729). There were no remarkable variations among the studied candidates related to BMI (p=0.144) (Table 1).

No noted variations among the studied candidates concerning hemoglobin level (p=0.627) or white blood cell count(WBCs)(p=0.418) but the platelets were significantly lesser in group A than in group B (p=0.004) (Table 2).

No statistically significant variations related to the studied groups as regard to serum creatinine level

(p=0.224), AST (P=0.593), or ALT (P=0.729), although the blood urea values in the group A was significantly higher than in the group B whereas (p<0.001) (Table 2).

The thyroid profiles of the participants in this study revealed that group A had lower mean FT3 and FT4 levels other than group B, with a statistical significance change in-between the two collections whereas (p=0.001) and (p=0.049), respectively. Although group A had elevated mean TSH levels than group B of non-significance difference statistically whereas (p=0.401) (Table3).

In the subjects of the frailty collection (group A), the TSH level was as (1 case with a low level, 20 cases with a normal level, and 9 cases with a high level). There were 14 cases with low FT3 hormone levels and 16 cases with normal FT3 hormone levels. Regarding the level of FT4 hormone, eight cases had low hormone levels, 20 cases with a normal level, and only two cases with a high level, however, in the control group only one case had a high TSH level (Table 3).

A slight non-significant positive association (r=0.150, p=0.298) was seen between age and TSH levels. There was a strong moderate negative association between age and FT3 levels (r=-0.530, p0.001). However, there is a modest negative association between age and FT4 levels. whereas (r=-0.246, p=0.085) (Table4).

Analysis of thyroid profile in the case group revealed that the TSH level was as follows (1 case with a low level, 20 cases with a normal level, and 9 cases with a high level). There were 14 cases with low FT3 hormone levels and 16 cases with normal FT3 hormone levels. Regarding the level of FT4 hormone, 8 cases had a low hormone level, 20 cases with a normal level, and only 2 cases with a high level as shown in (Table 5).

However, analysis of thyroid profile in the control group revealed that 19 subjects had normal levels of TSH and only one subject had higher levels of TSH, all subjects had normal levels of T3 and T4 (Table 6).

Table (1): Specified components of all candidates (Gender, Age, and BMI)

Gender	Cases		Control		Test of Sig.	P
	(≥ 65 years)	(n = 30)	(< 65 years)	(n = 20)		
Male	15	50 %	9	45%	$\chi^2 = 0.121$	0.729
Female	15	50 %	11	55%		
BMI (Kg/m ²)	22.83 ± 1.05		22.3 ± 1.49		t= 1.484	0.144

χ^2 : Chi square test

t: Student t-test

Table (2): Laboratory investigations among the studied groups

	Cases group (≥ 65 years) (n = 30)	Control group (< 65 years) (n = 20)	Test of Sig.	P
HGB (g/dl)	12.82 ± 0.75	13.09 ± 2.87	t= -0.489	0.627
WBCs (×10³/mm³)	7.31 ± 1.16	7.8 ± 1.82	t= -0.817	0.418
PLTs (×10³/mm³)	219.6 ± 6.11	298.75 ± 7.43	t= -3.023	0.004*
S.Creatinine (mg/dl)	1.11 ± 0.25	0.97 ± 0.27	z= 1.216	0.224
S.Urea (mg/dl)	35.86 ± 7.21	27.71 ± 7.45	t= 3.871	<0.001*
S.AST (U/l)	25.06 ± 6.69	24.1 ± 5.43	t= 0.538	0.593
S.ALT (U/l)	27.83 ± 1.38	25.41 ± 5.97	z= 0.347	0.729

*: Statistical significance at p ≤ 0.05

t: Student test

p: The p-value for comparing the two groups investigated

Table (3): Thyroid profile among the studied groups

	Cases (≥ 65 years) (n = 30)	Control (< 65 years) (n = 20)	Test of Sig.	P
TSH (μIU/ml)				
Mean± SD	3.56 ± 0.79	2.59 ± 0.06		
Median	2.95	1.9		
FREE T3 (pg/ml)				
Mean± SD	2.15 ± 0.32	2.93 ± 0.49		
Median	2	3		
FREE T 4 (ng/dl)				
Mean± SD	1.12 ± 0.27	1.35 ± 0.21		
Median	1.09	1.3		

t: Student test

p: The p-value for comparing the two groups investigated

*: statistical significance at p≤0.05

Table (4): Correlation between age and thyroid profile

	r	P
TSH	0.150	0.298
FT3	-0.530	< 0.001*
FT4	-0.246	0.085

r: spearman's correlation p: probability

*: statistical significance when p < 0.05

Table (5): Analysis of thyroid profile in the cases group

Items	Low	Normal	High
TSH	1(3.3%)	20 (66.7%)	9 (30%)
FT3	14 (46.7%)	16 (53.3%)	0 (0%)
FT4	8 (26.7%)	20 (66.7%)	2(6.7%)

Table (6): analysis of thyroid profile in the control group

Items	Low	Normal	High
TSH	0(0%)	19(95%)	1(5%)
FT3	0(0%)	20(100%)	0(0%)
FT4	0(0%)	20(100%)	0(0%)

DISCUSSION

The present study was performed on 50 subjects divided into two groups; group A included 30 elderly subjects aged ≥ 65 years living with frailty (cases group) and group B included 20 healthy subjects < 65 years (control group). The results of the current study declared non-significant variance in-between the groups of the research regarding gender.

The average age of the group of cases was 68.5 years, whereas the median age of the group of controls was 37 years, indicating a statistically significant difference.

These findings were in contrast to those of *Atzmon et al.*^[5] who performed a study on elderly Ashkenazi Jews with a median age of 98 years and Ashkenazi younger age as controls (median age of 72 years).

This study revealed no statistically significant difference between the two studied groups regarding BMI and this was compatible with *Carcaillon et al.*^[6] who clarified that BMI didn't reveal any significant difference between frail & non-frail groups.

The thyroid profiles of the participants in the two groups were analyzed, and TSH levels between the two groups were not statistically significant.

This result was convenient to a study performed by *Corsonello et al.*^[7] who declared no significant difference in the TSH result values in the frailty population in Southern Italy as compared to the control candidates. However, this came in contrast to *Gussekkloo et al.*^[8] who declared by a cohort study that old age persons had unusually elevation in the levels of the TSH as compared to the younger population. and also disagreed with *Surks and Boucai*^[9] study that reported an extra elevation in TSH hormone concentration with the age. Also, the results of the study performed by *Bremner*^[10] reported there was a rise in the TSH results with no changes in the FT4 levels. FT3 and FT4 levels in this study were significantly lower in group A.

These results were opposite to *Hoogendoorn et al.*^[11] whereas they found the serum TSH concentration levels diminished steadily with the age throughout the life, and the FT4 concentration levels amplified merely in the elderly candidates than 60 years.

Similar to the results of the present study *Waring*^[12] showed a decrease in T3 concentrations with aging. The results revealed a significant correlation between frailty and thyroid hormone levels in the studied groups in the form of a decrease in the level of FT3 and FT4 without a significant effect on TSH level in the case group. This is partially in agreement with *Yeap et al.*^[13] who described a significant effect of frailty and thyroid hormones.

Also, the research results implemented by *Yang et al.*^[14] whereas they indicated that patients with elevated TSH levels were at high risk of weakness.

Also, the study performed by *Beatrice et al.*^[15] discovered a relationship between the hormone levels of the thyroid gland and the frailty in the centenarians. However, these results were not compatible with the research results performed by *Maha et al.*^[16] as they found no correlation in-between frailty and TSH, FT4, and FT3 results. Although numerous studies demonstrate that the increased TSH level resulting from subclinical hypothyroidism further rises with aging^[17, 18], other findings suggest that aging is associated – in the absence of any thyroid disease – with lower TSH levels^[19, 20].

As it is well-known, in the older population there is a reduction in the secretion of TSH as a result of thyrotropin-releasing hormone (TRH) and even decreased the levels of free hormones of the thyroid gland in the elderly age persons, there is no concomitant increase in the TSH levels as compared with the young age indicating decreased sensitivity of thyrotrophic cells of the anterior pituitary, within the same contest, there is loss of nocturnal TSH surge in the elderly^[21]. In contrast, the presence of higher levels of TSH was thought to be associated with age-related alteration in the TSH set point or decreased TSH bioactivity^[22]. According to this study, there was a minor non-significant positive relationship between both age and TSH levels.

In agreement with this result, the study performed by *Naveen Agarawel*^[23] noted rising in the TSH serum levels throughout the age, especially beyond 70 years of age. Conversely to these results, cross-sectional research conducted in a region with borderline adequate iodine consumption revealed that blood TSH concentrations dropped steadily with progressed age throughout the life, but FT4 values elevated only in persons aged older than 60 years.^[24]

In the current research there was an increased significance of the moderate negative correlation between the age and FT3 values and also was a non-significant weak negative correlation between age and FT4, and this could be clarified by changes in thyroid function tests with the advancement of age as free T3 decline with age.

Also, the study by *Rozing et al.*^[25] in Leiden Longevity declared that children of nonagenarian siblings tended to have higher serum TSH levels, along with lower free T4 and lower free T3 levels, as compared to their spouses.

Also, these results came in agreement with the study performed by *Arshag Mooradian*^[26] who reported that the level of T4 and T3 decrease with advancing age.

CONCLUSION

Aging and frailty are associated with changes in thyroid functions in the form of a significant decrease in hormonal levels including FT3 and FT4, with a non-significant change in TSH levels.

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